

Mirdametinib (Ezmeckly)

SpringWorks Therapeutics Ireland Limited

*Behandlung von symptomatischen, inoperablen plexiformen
Neurofibromen (PN) bei pädiatrischen und erwachsenen Patienten
mit Neurofibromatose Typ 1 (NF1) ab einem Alter von 2 Jahren*

Anhang 4-H zu Modul 4A

Stand: 30.09.2025

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1 Baseline-Charakteristika

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Table 1: Demography and Baseline Characteristics: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Age at Time of Consent (Years)			
n (%)	56 (100%)	58 (100%)	114 (100%)
Mean (SD)	10.1 (4.50)	35.0 (13.17)	22.8 (15.94)
Median	10.0	34.5	18.0
Min, Max	2, 17	18, 69	2, 69
Q1, Q3	6, 14	22, 43	10, 35
Sex			
Male	26 (46.4%)	21 (36.2%)	47 (41.2%)
Female	30 (53.6%)	37 (63.8%)	67 (58.8%)
Childbearing Potential at Screening			
Yes	15 (50.0%)	29 (78.4%)	44 (65.7%)
No	15 (50.0%)	8 (21.6%)	23 (34.3%)
Race			
Black Or African American	11 (19.6%)	5 (8.6%)	16 (14.0%)
White	37 (66.1%)	49 (84.5%)	86 (75.4%)
Asian	2 (3.6%)	2 (3.4%)	4 (3.5%)
American Indian Or Alaska Native	1 (1.8%)	0	1 (0.9%)
Native Hawaiian Or Other Pacific Islander	0	0	0
Other	5 (8.9%)	2 (3.4%)	7 (6.1%)
Ethnicity			
Hispanic Or Latino	8 (14.3%)	1 (1.7%)	9 (7.9%)
Not Hispanic Or Latino	44 (78.6%)	52 (89.7%)	96 (84.2%)
Missing/ Not Reported/ Unknown	4 (7.1%)	5 (8.6%)	9 (7.9%)

SD: Standard Deviation; Min: Minimum; Max: Maximum.

N represents the number of participants in the corresponding cohort.

Childbearing potential percentages are calculated using the number of female participants in the corresponding cohort as the denominator.

The Karnofsky Performance Status scores range from 0 to 100. A higher score means the participant is better able to carry out daily activities.

Program Name: t_dm_fas.sas Output Generated: 2025-05-02T13:31 Source: ADSL Data Cutoff Date: 2023-09-20

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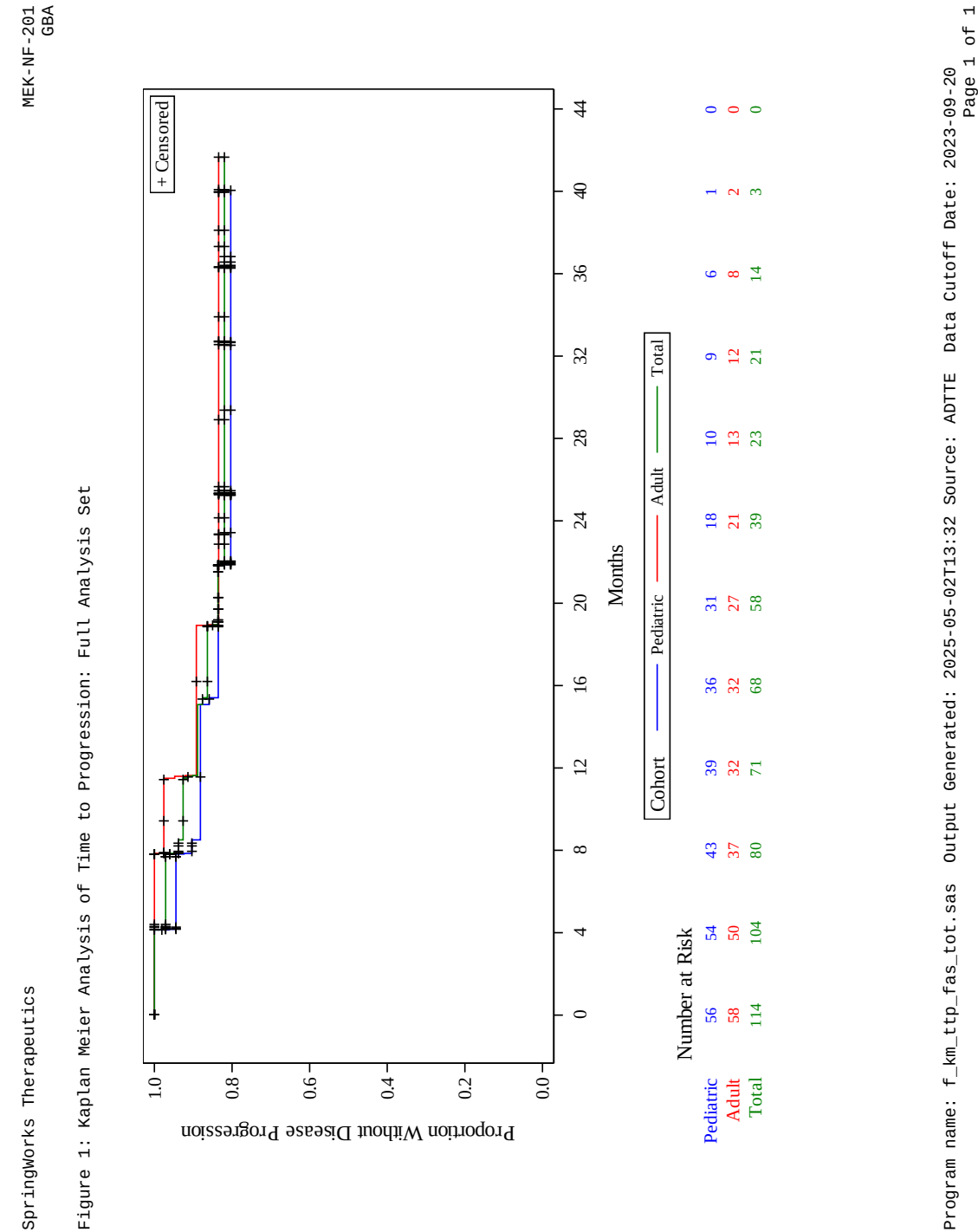
Table 1: Demography and Baseline Characteristics: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Karnofsky/Lansky Score			
n (%)	56 (100%)	58 (100%)	114 (100%)
Mean (SD)	94.5 (9.33)	87.1 (7.73)	90.7 (9.29)
Median	100.0	90.0	90.0
Min, Max	50, 100	70, 100	50, 100
Q1, Q3	90, 100	80, 90	90, 100
Time Since Target PN Diagnosis (Months)			
n (%)	42 (75.0%)	22 (37.9%)	64 (56.1%)
Mean (SD)	56.0 (50.71)	157.4 (169.24)	90.9 (116.54)
Median	43.0	82.8	59.4
Min, Max	2, 183	3, 599	2, 599
Q1, Q3	10, 84	40, 243	17, 121

SD: Standard Deviation; Min: Minimum; Max: Maximum.
N represents the number of participants in the corresponding cohort.
Childbearing potential percentages are calculated using the number of female participants in the corresponding cohort as the denominator.
The Karnofsky Performance Status scores range from 0 to 100. A higher score means the participant is better able to carry out daily activities.

Program Name: t_dm_fas.sas Output Generated: 2025-05-02T13:31 Source: ADSL Data Cutoff Date: 2023-09-20

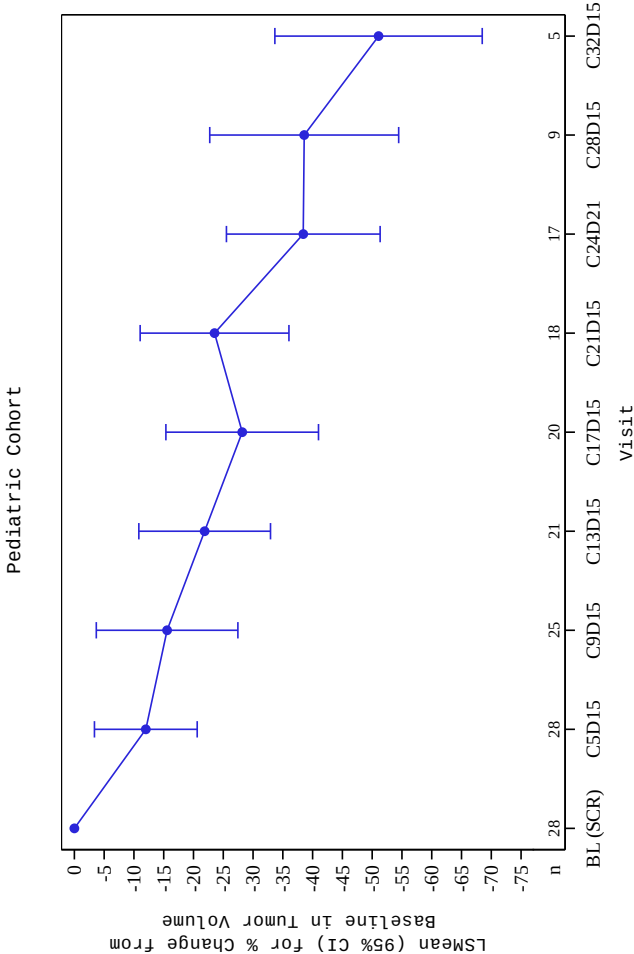
2 Tumoransprechen



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Figure 10.1: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Head and Neck Tumors: Full Analysis Set

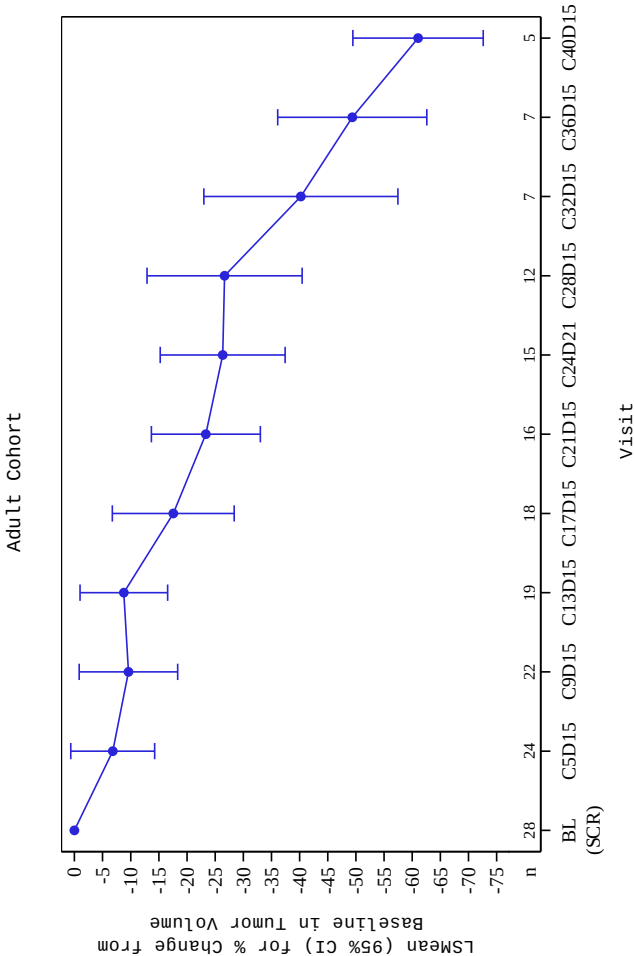


CI: Confidence interval; LSMean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

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Figure 10.1: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Head and Neck Tumors: Full Analysis Set

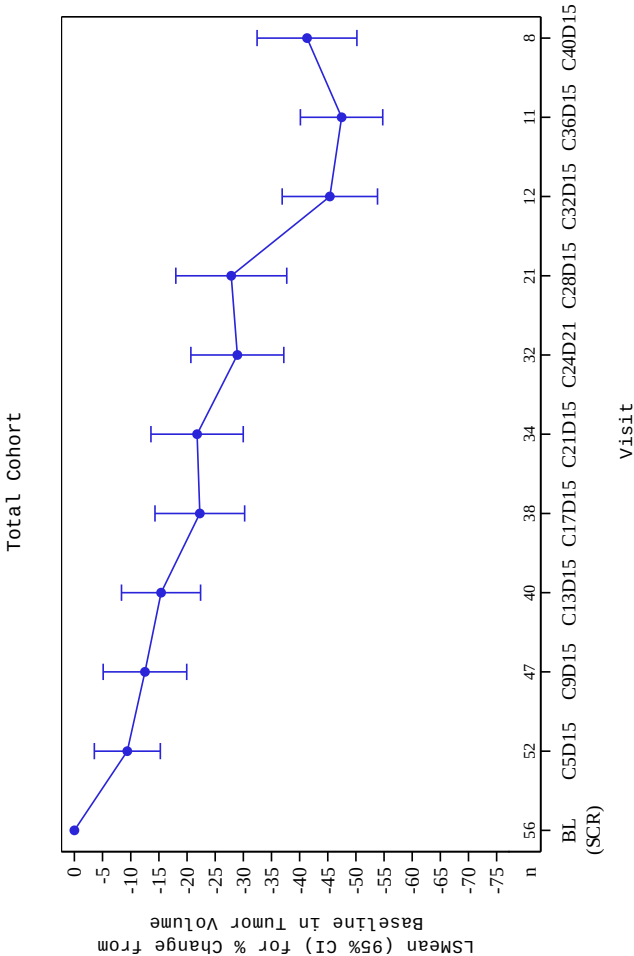


CI: Confidence interval; LSMean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

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Figure 10.1: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Head and Neck Tumors: Full Analysis Set

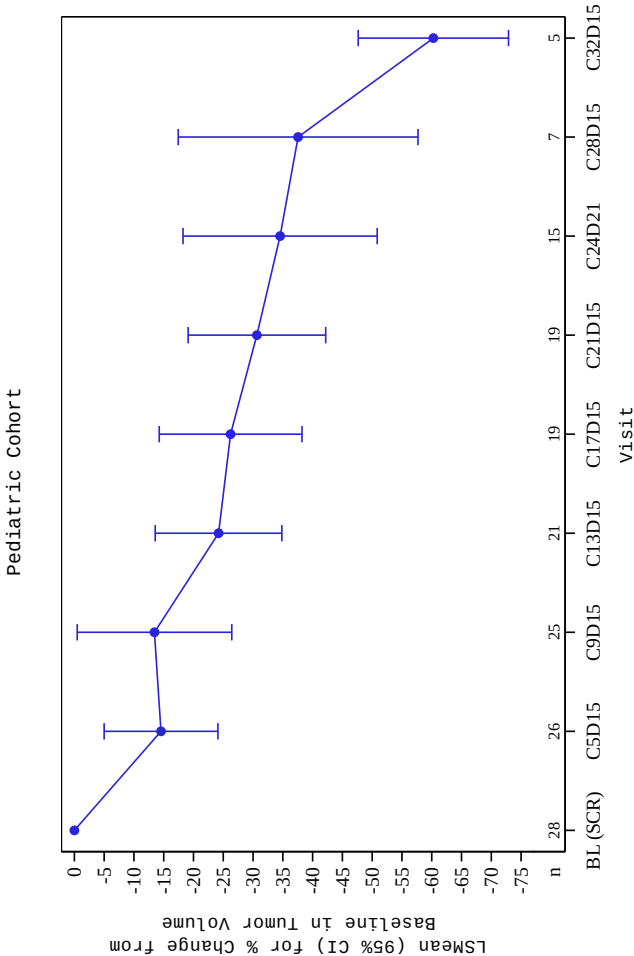


CI: Confidence interval; LSMean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

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Figure 10.2: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Disfigurement: Full Analysis Set

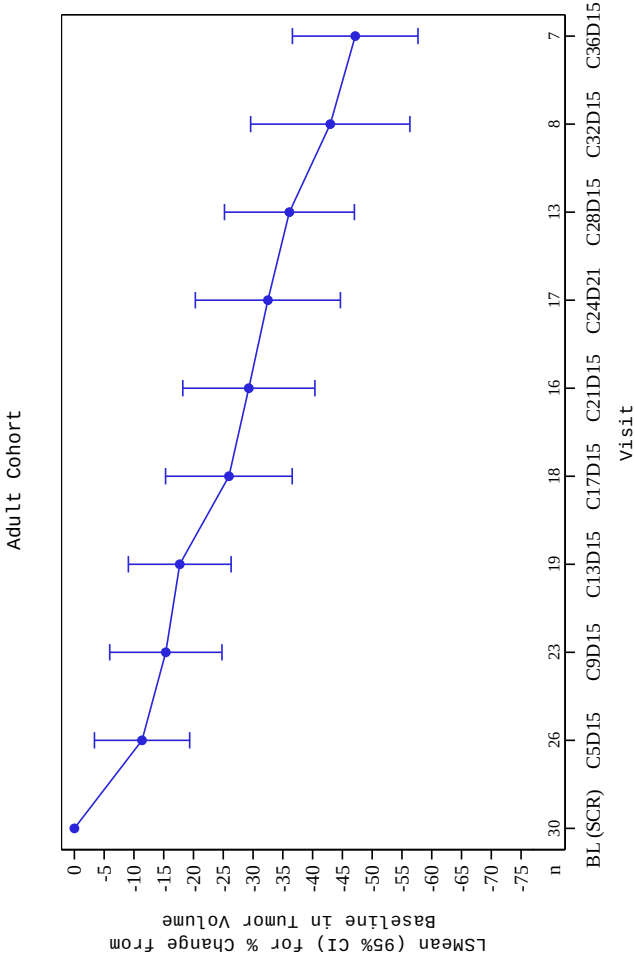


CI: Confidence interval; LS Mean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

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Figure 10.2: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Disfigurement: Full Analysis Set

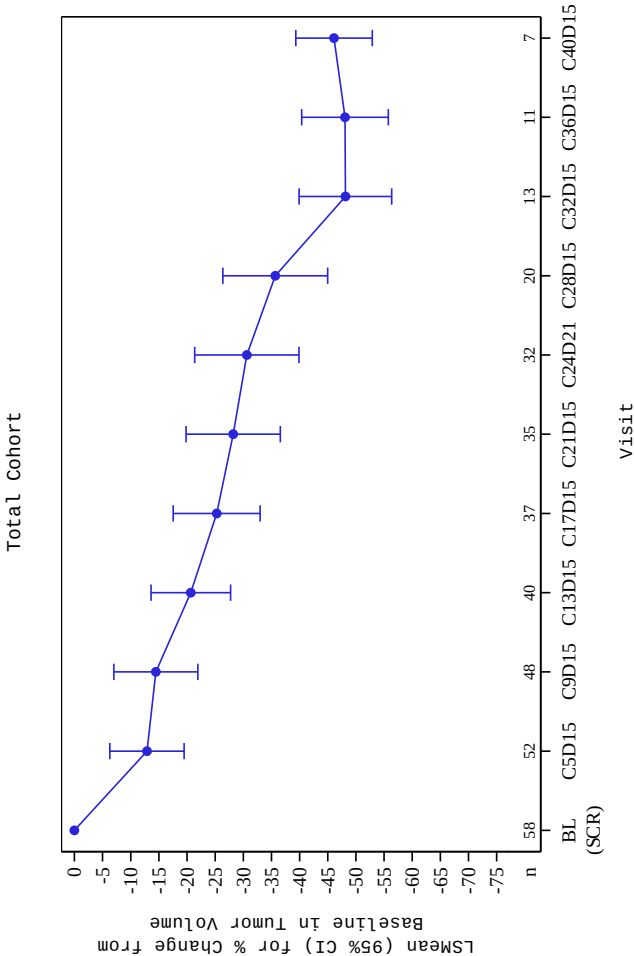


CI: Confidence interval; LS Mean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

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Figure 10.2: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume - Participants with Disfigurement: Full Analysis Set



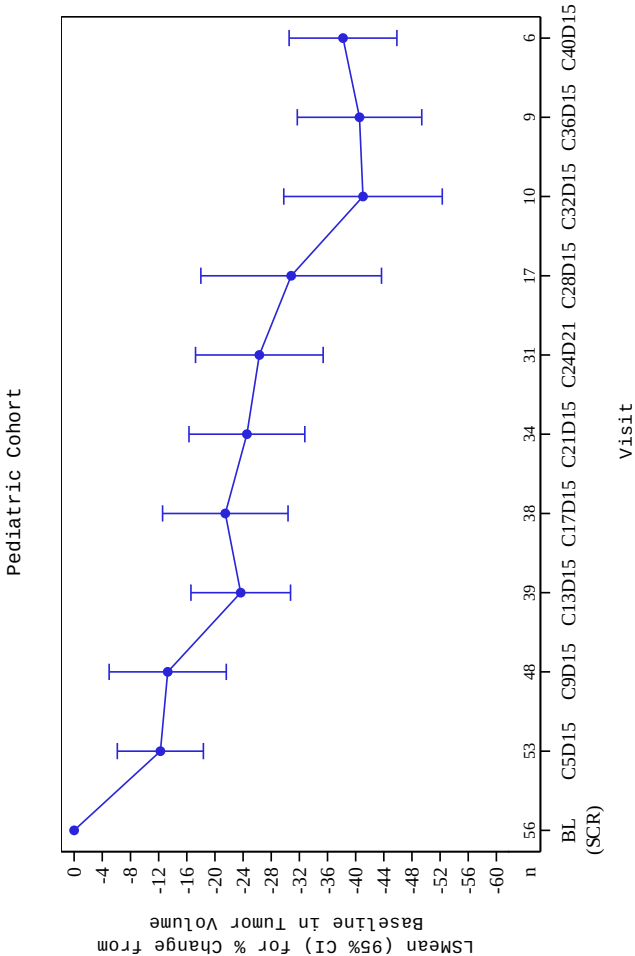
CI: Confidence interval; LSMean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

Program Name: f_tum_vol_df_mmrmm.sas Output Generated: 2025-06-06T15:16 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Figure 10: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume: Full Analysis Set



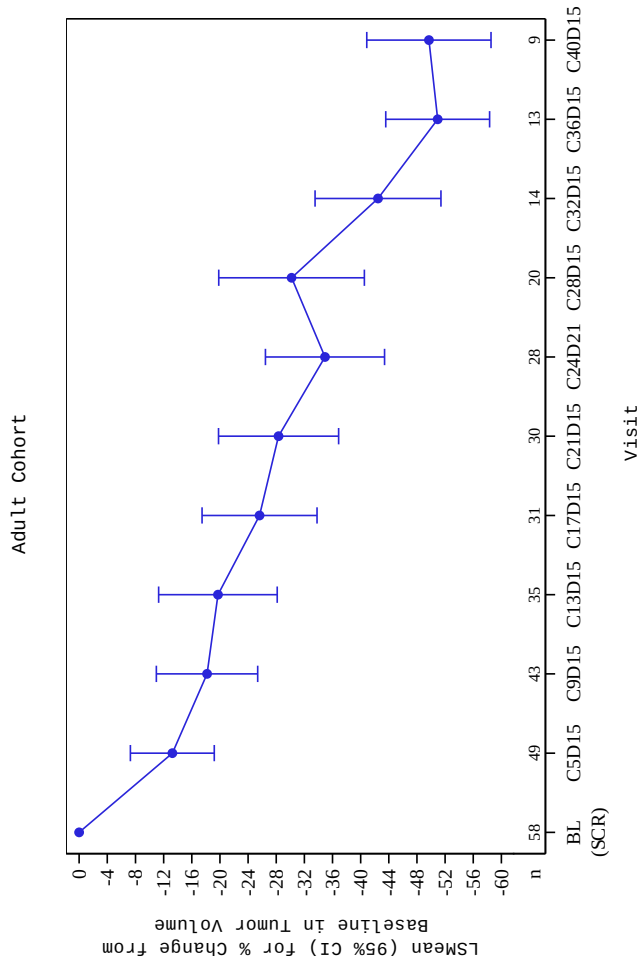
CI: Confidence interval; LS Mean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

Program Name: f_tum_vol_mmrmm.sas Output Generated: 2025-06-06T14:55 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Figure 10: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume: Full Analysis Set



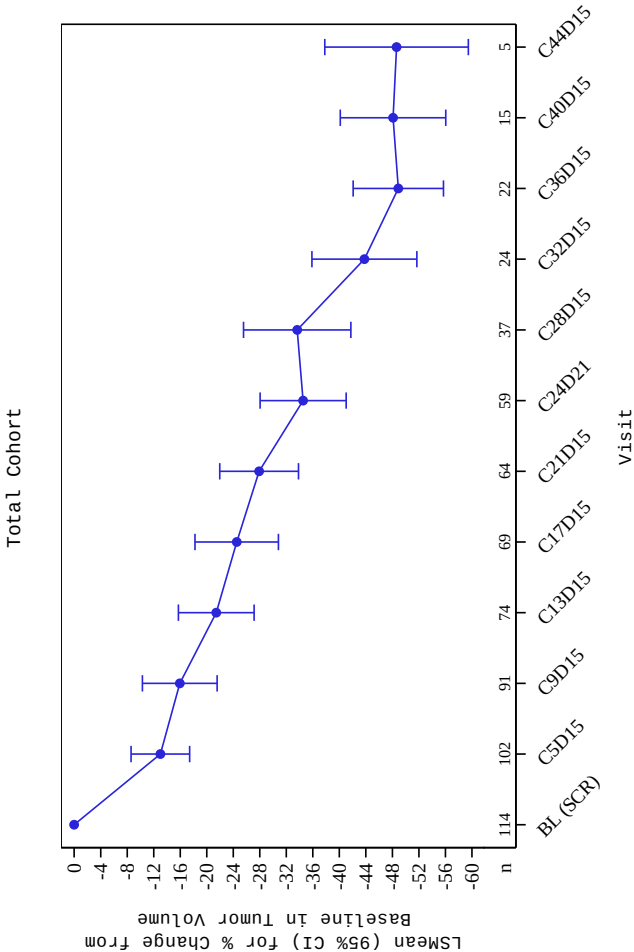
CI: Confidence interval; LS Mean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

Program Name: f_tum_vol_mmrmm.sas Output Generated: 2025-06-06T14:55 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Figure 10: Mixed Model Repeated Measures: Percent Change from Baseline in Tumor Volume: Full Analysis Set



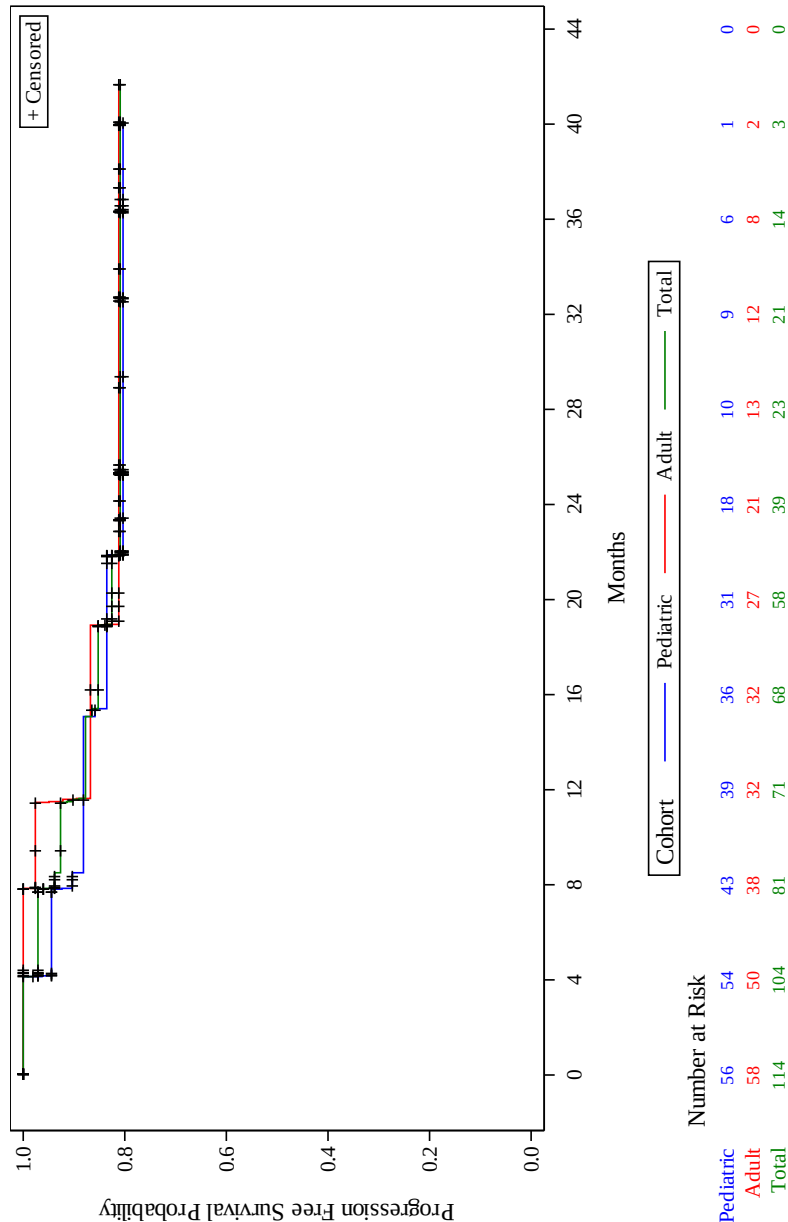
CI: Confidence interval; LSMean: Least Squares Mean; MMRM: Mixed model for repeated measures. Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used. Tumor volume recorded at Screening is considered as baseline.

Program Name: f_tum_vol_mmrmm.sas Output Generated: 2025-06-06T14:55 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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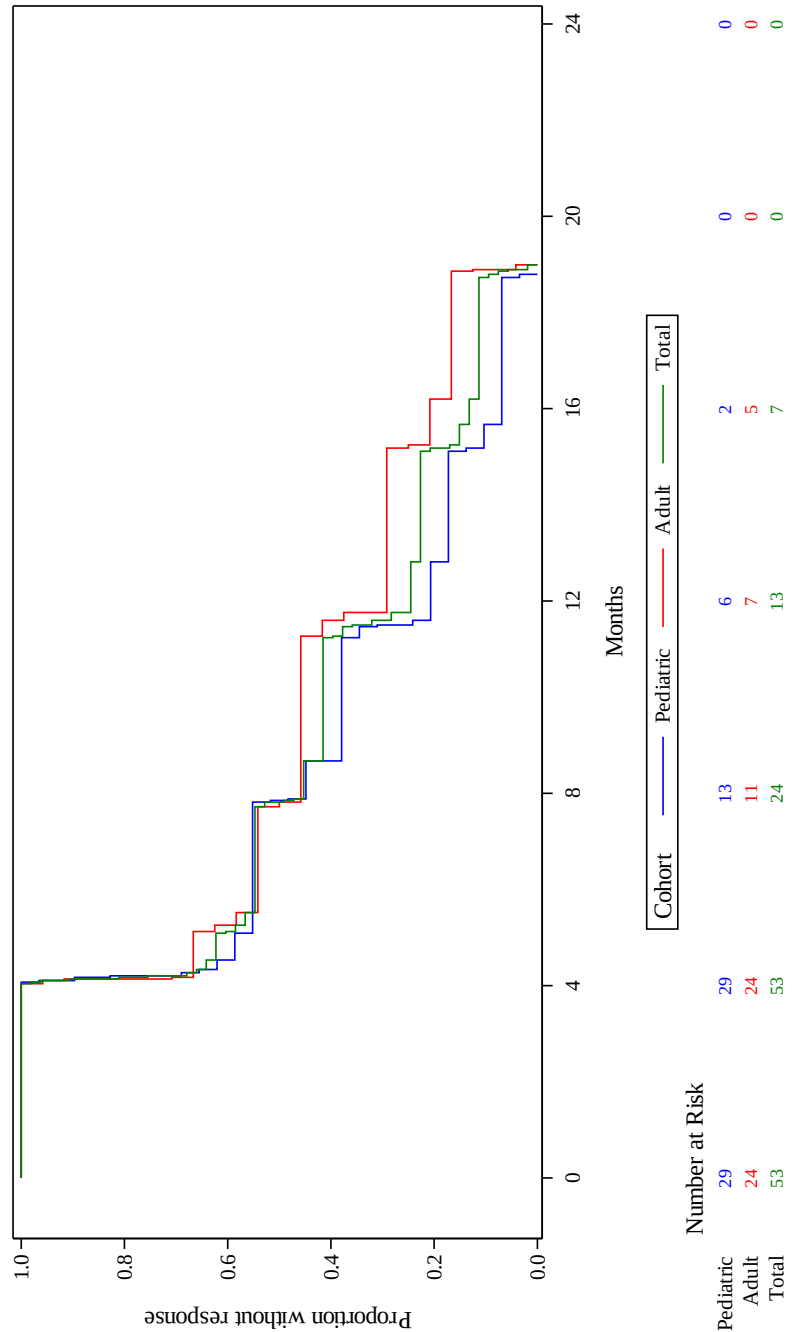
Figure 2: Kaplan Meier Analysis of Progression Free Survival: Full Analysis Set



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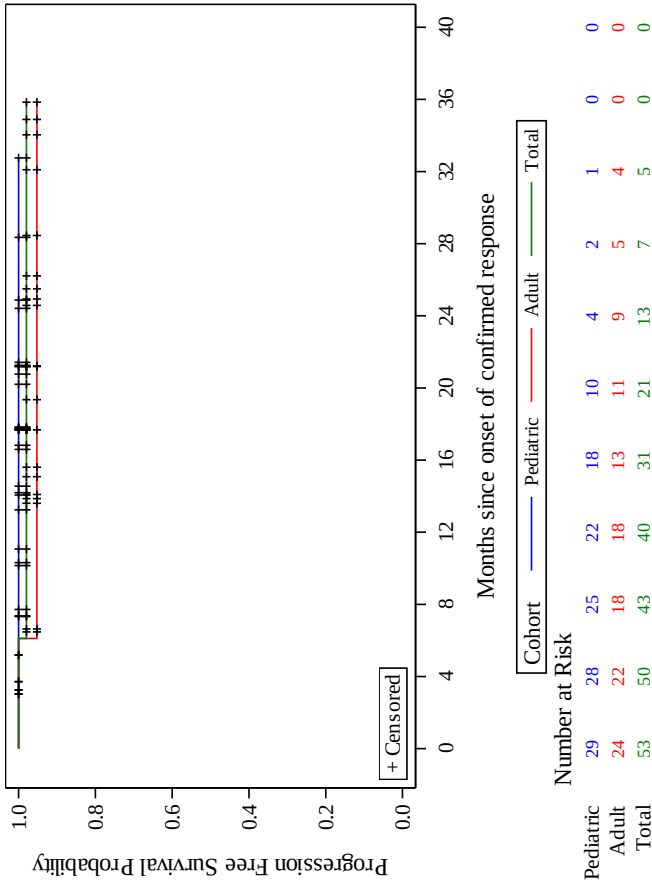
Figure 3: Kaplan Meir Analysis of Time to Response: Full Analysis Set



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Figure 4: Kaplan Meier Analysis of Duration of Response: Full Analysis Set



CR: Complete Response; PR: Partial Response.
Duration of response is defined as the time in months between the first instance of response that is subsequently confirmed, until the date of radiographic disease progression or death, whichever occurs first.
Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months as designated by BICR during the Treatment Phase.

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Table 10: Kaplan-Meier Analysis of Progression Free Survival: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Number of Participant events			
Event type	9 (16.1%)	7 (12.1%)	16 (14.0%)
Disease Progression	9 (100%)	6 (85.7%)	15 (93.8%)
Death	0	1 (14.3%)	1 (6.3%)
Number of Censored Participants	47 (83.9%)	51 (87.9%)	98 (86.0%)
Reason for Censoring			
No PD Post Baseline	43 (91.5%)	43 (84.3%)	86 (87.8%)
No Adequate Tumor Assessment Post Baseline	2 (4.3%)	8 (15.7%)	10 (10.2%)
Two or More Consecutive Missing/Non-Adequate Assessments	1 (2.1%)	0	1 (1.0%)
Death Before PD	0	0	0
Underwent PN Therapy/Surgery Prior to PD	1 (2.1%)	0	1 (1.0%)
Progression Free Survival (Months):			
1 st Quartile	NE (15.1, NE)	NE (11.6, NE)	NE (18.9, NE)
95% CI			
Median	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)
3 rd Quartile	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)
At 8 months:			
Number of events experienced by this point	5 (8.9%)	1 (1.7%)	6 (5.3%)
Number of participants still event free by this point (at risk)	43 (76.8%)	38 (65.5%)	81 (71.1%)
Kaplan Meier response rate estimate	0.90	0.98	0.94
95% CI	(0.78, 0.96)	(0.84, 1.00)	(0.87, 0.97)

CI: Confidence Interval; CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive Disease.

N represents the number of participants in the corresponding the cohort.

Progression free survival (PFS) is defined as the time from treatment start date to the first occurrence of radiographic disease

progression or death, whichever occurs first.

Percentages are calculated out of the number of participants in the corresponding cohort for the number with event/censored,

number of events experienced by this point and number of participants still event free by this point,

out of the total number of events for event type and out of the number censored for the reasons for censoring.

Program Name: t_km_pfs.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADTTE Data Cutoff Date: 2023-09-20

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Table 10: Kaplan-Meier Analysis of Progression Free Survival: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
At 12 months:			
Number of events experienced by this point	6 (10.7%)	5 (8.6%)	11 (9.6%)
Number of participants still event free by this point (at risk)	39 (69.6%)	32 (55.2%)	71 (62.3%)
Kaplan Meier response rate estimate	0.88	0.87	0.88
95% CI	(0.75, 0.95)	(0.71, 0.94)	(0.79, 0.93)
At 16 months:			
Number of events experienced by this point	8 (14.3%)	5 (8.6%)	13 (11.4%)
Number of participants still event free by this point (at risk)	36 (64.3%)	32 (55.2%)	68 (59.6%)
Kaplan Meier response rate estimate	0.84	0.87	0.85
95% CI	(0.70, 0.91)	(0.71, 0.94)	(0.76, 0.91)
At 20 months:			
Number of events experienced by this point	8 (14.3%)	7 (12.1%)	15 (13.2%)
Number of participants still event free by this point (at risk)	31 (55.4%)	27 (46.6%)	58 (50.9%)
Kaplan Meier response rate estimate	0.84	0.81	0.83
95% CI	(0.70, 0.91)	(0.64, 0.91)	(0.73, 0.89)
At 24 months:			
Number of events experienced by this point	9 (16.1%)	7 (12.1%)	16 (14.0%)
Number of participants still event free by this point (at risk)	18 (32.1%)	21 (36.2%)	39 (34.2%)
Kaplan Meier response rate estimate	0.80	0.81	0.81
95% CI	(0.65, 0.89)	(0.64, 0.91)	(0.71, 0.88)

CI: Confidence Interval; CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive Disease.

N represents the number of participants in the corresponding the cohort.

Progression free survival (PFS) is defined as the time from treatment start date to the first occurrence of radiographic disease progression or death, whichever occurs first.

Percentages are calculated out of the number of participants in the corresponding cohort for the number with event/censored, number of events experienced by this point and number of participants still event free by this point, out of the total number of events for event type and out of the number censored for the reasons for censoring.

Program Name: t_km_pfs.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADTTE Data Cutoff Date: 2023-09-29

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Table 11: Time to Response: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Time to Response (Months)			
n (%)	29 (51.8%)	24 (41.4%)	53 (46.5%)
Mean (SD)	8.63 (4.804)	9.71 (5.804)	9.12 (5.254)
Median	7.90	7.75	7.80
Min, Max	4.1, 18.8	4.0, 19.0	4.0, 19.0
Q1, Q3	4.2, 11.5	4.1, 15.2	4.2, 11.8
Cycle of 1st Response that was Subsequently Confirmed			
Cycle 5	13 (44.8%)	11 (45.8%)	24 (45.3%)
Cycle 9	5 (17.2%)	2 (8.3%)	7 (13.2%)
Cycle 13	6 (20.7%)	4 (16.7%)	10 (18.9%)
Cycle 17	3 (10.3%)	3 (12.5%)	6 (11.3%)
Cycle 21	2 (6.9%)	4 (16.7%)	6 (11.3%)

SD: Standard deviation; Min: Minimum; Max: Maximum; NE: Not Evaluable.
Time to response is defined as the time in months from the start of treatment to the date of first response that was subsequently confirmed.

Program Name: t_resp_fas.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADEFF Data Cutoff Date: 2023-09-20

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Table 12: Analysis of Disease Control Rate: Full Analysis Set

Disease Control Rate	Pediatric (N=56)		Adult (N=58)		Total (N=114)
	n	%	n	%	
	51	91.1	50	86.2	101
95% CI	(80.4, 97.0)		(74.6, 93.9)		(81.3, 93.8)

BOR: Best Overall Response; CI: Confidence interval; SD: Stable Disease.
Disease control rate is defined as having a confirmed BOR of SD or better post-baseline during the Treatment Phase.
95% CIs are derived using the Clopper-Pearson approach.
Participants who had no response data or discontinued early from the study without responding are considered to have not presented disease control.

Program Name: t_ds_fas.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADEFF Data Cutoff Date: 2023-09-20

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Table 6: Analysis of Confirmed Objective Response Rate – Treatment Phase: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Confirmed Objective Response Rate			
n	29	24	53
%	51.8	41.4	46.5
95% CI	(38.0, 65.3)	(28.6, 55.1)	(37.1, 56.1)
p-value	<0.001	<0.001	
Best Overall Confirmed Response Status			
Complete Response	0	0	0
Partial Response	29 (51.8%)	24 (41.4%)	53 (46.5%)
Stable Disease	22 (39.3%)	26 (44.8%)	48 (42.1%)
Progressive Disease	3 (5.4%)	0	3 (2.6%)
Not Evaluable	0	0	0
Missing	2 (3.6%)	8 (13.8%)	10 (8.8%)

CI: Confidence interval; CR: Complete Response; PR: Partial Response.

Target lesion baseline occurs at Screening.

N represents the number of participants in the corresponding cohort. n is the number of confirmed objective responders.

Confirmed objective response is defined as two consecutive assessments of PR or CR assessed by a BICR within 2-6 months during the Treatment Phase.

95% CIs are derived using the Clopper-Pearson approach.

P-values are calculated using a one-sample two-sided binomial test compared to the minimally clinically relevant response rates of 23% for the adult cohort and 20% for the pediatric cohort. P-value for the total group is not calculated due to differing null hypotheses for each age cohort.

Participants who had no post-baseline MRI assessment or no confirmed objective response are treated as non-responders.

Best overall confirmed response status is defined as the best confirmed response prior to disease progression during the Treatment Phase.

Missing contains participants who have no post-baseline MRI assessments.

Program Name: t_morb_orr1.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADEFF Data Cutoff Date: 2023-09-20

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Table 63: Tumor Reduction Summary Table: Full Analysis Set

	Pediatric (N=56)		Adult (N=58)		Total (N=114)	
	n	(%)	n	(%)	n	(%)
Any Tumor Reduction from Baseline	46	(82.1%)	46	(79.3%)	92	(80.7%)
Tumor Reduction >=20% from Baseline	37	(66.1%)	35	(60.3%)	72	(63.2%)
Tumor Reduction >=40% from Baseline	30	(53.6%)	26	(44.8%)	56	(49.1%)
Tumor Reduction >=60% from Baseline	12	(21.4%)	12	(20.7%)	24	(21.1%)
Tumor Reduction >=80% from Baseline	4	(7.1%)	3	(5.2%)	7	(6.1%)

Program Name: t_63_tum_red.sas Output Generated: 2025-05-09T11:27 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
Baseline (Screening)			
n (%)	28 (100%)	28 (100%)	56 (100%)
Mean (SD)	142.1 (193.14)	253.9 (468.38)	198.0 (359.43)
Median	84.6	153.5	106.5
Min, Max	5, 981	17, 2518	5, 2518
C5D15			
n (%)	28 (100%)	24 (85.7%)	52 (92.9%)
Mean (SD)	126.6 (172.26)	218.5 (392.28)	169.0 (295.39)
Median	78.4	88.9	82.2
Min, Max	3, 887	15, 1955	3, 1955
Change from Baseline at C5D15			
n (%)	28 (100%)	24 (85.7%)	52 (92.9%)
Mean (SD)	-15.6 (43.54)	-39.9 (120.02)	-26.8 (87.47)
Median	-4.2	-2.3	-3.7
Min, Max	-180, 61	-563, 67	-563, 67
LS Mean (SE)	-17.54 (6.8)	-54.51 (10.9)	-36.78 (6.2)
95% CI	(-31.03, -4.06)	(-76.14, -32.87)	(-48.90, -24.65)
p-value	0.0113	<0.0001	<0.0001
Percent Change from Baseline at C5D15			
n (%)	28 (100%)	24 (85.7%)	52 (92.9%)
Mean (SD)	-12.0 (22.31)	-6.4 (18.50)	-9.4 (20.64)
Median	-8.1	-5.7	-6.8
Min, Max	-66, 48	-41, 40	-66, 48
LS Mean (SE)	-11.99 (4.4)	-6.81 (3.8)	-9.40 (3.0)
95% CI	(-20.61, -3.36)	(-14.26, 0.64)	(-15.26, -3.53)
p-value	0.0069	0.0728	0.0018

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C9D15			
n (%)	25 (89.3%)	22 (78.6%)	47 (83.9%)
Mean (SD)	132.7 (218.75)	203.4 (385.95)	165.8 (306.98)
Median	72.9	78.5	75.0
Min, Max	2, 1041	19, 1877	2, 1877
Change from Baseline at C9D15			
n (%)	25 (89.3%)	22 (78.6%)	47 (83.9%)
Mean (SD)	-12.8 (57.16)	-48.7 (138.49)	-29.6 (103.86)
Median	-9.0	-3.3	-6.4
Min, Max	-148, 157	-641, 32	-641, 157
LS Mean (SE)	-6.66 (13.6)	-64.54 (9.1)	-37.16 (9.3)
95% CI	(-33.64, 20.33)	(-82.62, -46.47)	(-55.56, -18.76)
p-value	0.6259	<0.0001	<0.0001
Percent Change from Baseline at C9D15			
n (%)	25 (89.3%)	22 (78.6%)	47 (83.9%)
Mean (SD)	-19.5 (27.46)	-8.7 (22.67)	-14.5 (25.65)
Median	-18.1	-4.4	-12.9
Min, Max	-77, 49	-65, 28	-77, 49
LS Mean (SE)	-15.56 (6.0)	-9.59 (4.4)	-12.53 (3.8)
95% CI	(-27.44, -3.67)	(-18.34, -0.85)	(-19.96, -5.10)
p-value	0.0108	0.0318	0.0010

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C13D15			
n (%)	21 (75.0%)	19 (67.9%)	40 (71.4%)
Mean (SD)	122.1 (190.08)	253.5 (395.72)	184.5 (308.57)
Median	68.3	146.7	81.2
Min, Max	2, 873	32, 1771	2, 1771
Change from Baseline at C13D15			
n (%)	21 (75.0%)	19 (67.9%)	40 (71.4%)
Mean (SD)	-30.4 (38.74)	-57.0 (170.57)	-43.0 (119.90)
Median	-15.0	-6.8	-7.9
Min, Max	-118, 9	-747, 35	-747, 35
LS Mean (SE)	-24.63 (6.8)	-59.85 (11.2)	-42.10 (7.5)
95% CI	(-38.19, -11.07)	(-82.02, -37.69)	(-56.97, -27.24)
p-value	0.0005	<0.0001	<0.0001
Percent Change from Baseline at C13D15			
n (%)	21 (75.0%)	19 (67.9%)	40 (71.4%)
Mean (SD)	-27.6 (24.04)	-9.2 (18.57)	-18.9 (23.27)
Median	-30.7	-7.0	-15.4
Min, Max	-77, 21	-43, 35	-77, 35
LS Mean (SE)	-21.87 (5.6)	-8.78 (3.9)	-15.39 (3.6)
95% CI	(-32.92, -10.82)	(-16.55, -1.00)	(-22.41, -8.37)
p-value	0.0002	0.0273	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C17D15			
n (%)	20 (71.4%)	18 (64.3%)	38 (67.9%)
Mean (SD)	107.6 (168.20)	228.5 (327.94)	164.9 (260.15)
Median	58.0	141.0	81.8
Min, Max	2, 750	24, 1396	2, 1396
Change from Baseline at C17D15			
n (%)	20 (71.4%)	18 (64.3%)	38 (67.9%)
Mean (SD)	-34.2 (65.13)	-97.2 (261.15)	-64.0 (185.82)
Median	-17.2	-11.1	-14.5
Min, Max	-232, 43	-1123, 11	-1123, 43
LS Mean (SE)	-28.83 (10.9)	-96.60 (24.9)	-60.03 (15.0)
95% CI	(-50.45, -7.20)	(-145.94, -47.27)	(-89.54, -30.53)
p-value	0.0095	0.0002	<0.0001
Percent Change from Baseline at C17D15			
n (%)	20 (71.4%)	18 (64.3%)	38 (67.9%)
Mean (SD)	-32.7 (28.71)	-20.0 (23.84)	-26.7 (26.94)
Median	-34.9	-16.9	-23.9
Min, Max	-73, 27	-77, 9	-77, 27
LS Mean (SE)	-28.17 (6.5)	-17.56 (5.5)	-22.28 (4.0)
95% CI	(-40.98, -15.37)	(-28.39, -6.73)	(-30.24, -14.32)
p-value	<0.0001	0.0017	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C21D15			
n (%)	18 (64.3%)	16 (57.1%)	34 (60.7%)
Mean (SD)	107.2 (180.68)	241.3 (404.24)	170.3 (309.37)
Median	41.3	126.4	78.2
Min, Max	2, 752	29, 1694	2, 1694
Change from Baseline at C21D15			
n (%)	18 (64.3%)	16 (57.1%)	34 (60.7%)
Mean (SD)	-37.2 (64.97)	-108.3 (200.12)	-70.7 (147.23)
Median	-9.1	-44.3	-17.9
Min, Max	-229, 7	-825, 15	-825, 15
LS Mean (SE)	-27.91 (12.0)	-97.73 (9.4)	-65.36 (7.8)
95% CI	(-51.79, -4.02)	(-116.44, -79.01)	(-80.73, -49.99)
p-value	0.0224	<0.0001	<0.0001
Percent Change from Baseline at C21D15			
n (%)	18 (64.3%)	16 (57.1%)	34 (60.7%)
Mean (SD)	-29.8 (24.73)	-25.0 (23.05)	-27.6 (23.72)
Median	-31.5	-27.6	-29.2
Min, Max	-81, 5	-72, 21	-81, 21
LS Mean (SE)	-23.52 (6.3)	-23.35 (4.9)	-21.79 (4.2)
95% CI	(-36.02, -11.03)	(-33.03, -13.66)	(-29.99, -13.59)
p-value	0.0003	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C24D21			
n (%)	17 (60.7%)	15 (53.6%)	32 (57.1%)
Mean (SD)	86.7 (142.87)	233.3 (362.04)	155.4 (274.32)
Median	36.3	130.1	68.3
Min, Max	1, 597	20, 1463	1, 1463
Change from Baseline at C24D21			
n (%)	17 (60.7%)	15 (53.6%)	32 (57.1%)
Mean (SD)	-60.6 (102.41)	-123.0 (264.94)	-89.8 (195.22)
Median	-11.4	-26.5	-21.8
Min, Max	-384, -1	-1055, 5	-1055, 5
LS Mean (SE)	-51.93 (16.6)	-114.77 (21.7)	-85.04 (13.4)
95% CI	(-84.82, -19.04)	(-157.71, -71.83)	(-111.40, -58.67)
p-value	0.0022	<0.0001	<0.0001
Percent Change from Baseline at C24D21			
n (%)	17 (60.7%)	15 (53.6%)	32 (57.1%)
Mean (SD)	-41.8 (27.25)	-26.7 (22.74)	-34.7 (25.98)
Median	-39.3	-27.6	-36.7
Min, Max	-82, -8	-66, 13	-82, 13
LS Mean (SE)	-38.43 (6.5)	-26.34 (5.6)	-28.94 (4.2)
95% CI	(-51.34, -25.52)	(-37.43, -15.25)	(-37.20, -20.68)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C28D15			
n (%)	9 (32.1%)	12 (42.9%)	21 (37.5%)
Mean (SD)	125.0 (213.05)	290.4 (444.71)	219.5 (366.01)
Median	47.4	168.6	123.5
Min, Max	1, 676	43, 1669	1, 1669
Change from Baseline at C28D15			
n (%)	9 (32.1%)	12 (42.9%)	21 (37.5%)
Mean (SD)	-68.6 (110.41)	-149.0 (231.46)	-114.5 (189.74)
Median	-11.8	-74.3	-57.1
Min, Max	-306, -0	-849, 11	-849, 11
LS Mean (SE)	-54.05 (14.0)	-107.25 (13.5)	-81.44 (9.4)
95% CI	(-81.80, -26.30)	(-133.98, -80.51)	(-99.98, -62.89)
p-value	0.0002	<0.0001	<0.0001
Percent Change from Baseline at C28D15			
n (%)	9 (32.1%)	12 (42.9%)	21 (37.5%)
Mean (SD)	-37.6 (28.88)	-30.0 (19.89)	-33.2 (23.80)
Median	-30.6	-32.6	-31.1
Min, Max	-91, -0	-65, 15	-91, 15
LS Mean (SE)	-38.58 (8.0)	-26.68 (7.0)	-27.86 (5.0)
95% CI	(-54.44, -22.73)	(-40.45, -12.90)	(-37.71, -18.00)
p-value	<0.0001	0.0002	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C32D15			
n (%)	5 (17.9%)	7 (25.0%)	12 (21.4%)
Mean (SD)	142.0 (178.24)	174.8 (130.18)	161.1 (145.20)
Median	72.6	125.8	124.1
Min, Max	1, 435	26, 385	1, 435
Change from Baseline at C32D15			
n (%)	5 (17.9%)	7 (25.0%)	12 (21.4%)
Mean (SD)	-135.4 (230.29)	-140.7 (61.90)	-138.5 (146.23)
Median	-45.9	-154.7	-102.5
Min, Max	-546, -8	-246, -55	-546, -8
LS Mean (SE)	-97.11 (49.3)	-142.68 (20.8)	-113.14 (21.2)
95% CI	(-194.83, 0.60)	(-183.91, -101.45)	(-154.96, -71.31)
p-value	0.0514	<0.0001	<0.0001
Percent Change from Baseline at C32D15			
n (%)	5 (17.9%)	7 (25.0%)	12 (21.4%)
Mean (SD)	-51.3 (23.73)	-48.8 (19.74)	-49.8 (20.47)
Median	-51.2	-43.7	-47.5
Min, Max	-86, -20	-86, -27	-86, -20
LS Mean (SE)	-51.07 (8.8)	-40.23 (8.7)	-45.37 (4.3)
95% CI	(-68.47, -33.66)	(-57.46, -22.99)	(-53.83, -36.90)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C36D15			
n (%)	4 (14.3%)	7 (25.0%)	11 (19.6%)
Mean (SD)	190.8 (219.17)	161.0 (129.72)	171.8 (157.27)
Median	119.9	149.0	149.0
Min, Max	16, 508	52, 414	16, 508
Change from Baseline at C36D15			
n (%)	4 (14.3%)	7 (25.0%)	11 (19.6%)
Mean (SD)	-153.4 (214.21)	-154.5 (60.18)	-154.1 (126.25)
Median	-57.5	-128.5	-121.3
Min, Max	-474, -25	-221, -68	-474, -25
LS Mean (SE)	NA (NA)	-151.74 (18.9)	-109.26 (16.4)
95% CI	(NA, NA)	(-189.19, -114.30)	(-141.56, -76.95)
p-value	NA	<0.0001	<0.0001
Percent Change from Baseline at C36D15			
n (%)	4 (14.3%)	7 (25.0%)	11 (19.6%)
Mean (SD)	-44.1 (13.82)	-53.2 (16.19)	-49.9 (15.35)
Median	-42.5	-48.2	-48.2
Min, Max	-62, -30	-79, -34	-79, -30
LS Mean (SE)	NA (NA)	-49.36 (6.7)	-47.46 (3.7)
95% CI	(NA, NA)	(-62.61, -36.12)	(-54.78, -40.14)
p-value	NA	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

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Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C40D15			
n (%)	3 (10.7%)	5 (17.9%)	8 (14.3%)
Mean (SD)	308.5 (306.94)	82.9 (46.91)	167.5 (204.46)
Median	193.1	71.2	89.0
Min, Max	76, 656	36, 154	36, 656
Change from Baseline at C40D15			
n (%)	3 (10.7%)	5 (17.9%)	8 (14.3%)
Mean (SD)	-136.9 (163.13)	-146.4 (46.94)	-142.8 (94.27)
Median	-52.4	-144.5	-141.2
Min, Max	-325, -33	-197, -74	-325, -33
LS Mean (SE)	NA (NA)	-160.07 (12.3)	-107.87 (14.9)
95% CI	(NA, NA)	(-184.37, -135.77)	(-137.33, -78.42)
p-value	NA	<0.0001	<0.0001
Percent Change from Baseline at C40D15			
n (%)	3 (10.7%)	5 (17.9%)	8 (14.3%)
Mean (SD)	-29.6 (13.38)	-64.7 (12.74)	-51.5 (21.80)
Median	-33.1	-63.6	-53.2
Min, Max	-41, -15	-80, -47	-80, -15
LS Mean (SE)	NA (NA)	-61.05 (5.8)	-41.32 (4.5)
95% CI	(NA, NA)	(-72.62, -49.47)	(-50.18, -32.45)
p-value	NA	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 7.1: Tumor Volume (mL) by Visit - Participants with Head and Neck Tumors: Full Analysis Set

	Pediatric (N=28)	Adult (N=28)	Total (N=56)
C44D15			
n (%)	0	2 (7.1%)	2 (3.6%)
Mean (SD)	NA (NA)	100.9 (0.93)	100.9 (0.93)
Median	NA	100.9	100.9
Min, Max	(NA, NA)	100, 102	100, 102
Change from Baseline at C44D15			
n (%)	0	2 (7.1%)	2 (3.6%)
Mean (SD)	NA (NA)	-173.3 (8.09)	-173.3 (8.09)
Median	NA	-173.3	-173.3
Min, Max	(NA, NA)	-179, -168	-179, -168
Percent Change from Baseline at C44D15			
n (%)	0	2 (7.1%)	2 (3.6%)
Mean (SD)	NA (NA)	-63.2 (0.87)	-63.2 (0.87)
Median	NA	-63.2	-63.2
Min, Max	(NA, NA)	-64, -63	-64, -63

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_hn.sas Output Generated: 2025-06-05T11:04 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
Baseline (Screening)			
n (%)	28 (100%)	30 (100%)	58 (100%)
Mean (SD)	164.8 (204.73)	614.1 (865.10)	397.2 (672.24)
Median	120.6	257.7	163.9
Min, Max	5, 981	17, 3457	5, 3457
C5D15			
n (%)	26 (92.9%)	26 (86.7%)	52 (89.7%)
Mean (SD)	145.5 (185.29)	504.9 (777.74)	325.2 (588.44)
Median	101.5	200.7	147.7
Min, Max	3, 887	15, 3118	3, 3118
Change from Baseline at C5D15			
n (%)	26 (92.9%)	26 (86.7%)	52 (89.7%)
Mean (SD)	-24.3 (49.89)	-93.4 (157.78)	-58.9 (120.99)
Median	-5.6	-42.2	-13.5
Min, Max	-180, 61	-563, 67	-563, 67
LS Mean (SE)	-25.76 (7.3)	-54.73 (39.5)	-48.01 (13.4)
95% CI	(-40.25, -11.26)	(-133.04, 23.59)	(-74.46, -21.56)
p-value	0.0006	0.1689	0.0004
Percent Change from Baseline at C5D15			
n (%)	26 (92.9%)	26 (86.7%)	52 (89.7%)
Mean (SD)	-15.1 (24.60)	-11.7 (18.92)	-13.4 (21.80)
Median	-13.3	-13.0	-13.0
Min, Max	-66, 48	-43, 40	-66, 48
LS Mean (SE)	-14.54 (4.8)	-11.36 (4.0)	-12.89 (3.3)
95% CI	(-24.09, -5.00)	(-19.36, -3.36)	(-19.49, -6.29)
p-value	0.0032	0.0058	0.0002

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_df.sas Output Generated: 2025-06-05T11:05 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C9D15			
n (%)	25 (89.3%)	23 (76.7%)	48 (82.8%)
Mean (SD)	149.1 (223.62)	357.6 (563.92)	249.0 (430.67)
Median	81.2	187.4	91.0
Min, Max	2, 1041	19, 2202	2, 2202
Change from Baseline at C9D15			
n (%)	25 (89.3%)	23 (76.7%)	48 (82.8%)
Mean (SD)	-19.7 (63.65)	-117.8 (281.64)	-66.7 (204.08)
Median	-7.8	-38.1	-11.9
Min, Max	-159, 157	-1255, 20	-1255, 157
LS Mean (SE)	-14.63 (14.1)	-108.78 (19.3)	-62.77 (18.3)
95% CI	(-42.56, 13.29)	(-147.08, -70.48)	(-98.76, -26.78)
p-value	0.3011	<0.0001	0.0007
Percent Change from Baseline at C9D15			
n (%)	25 (89.3%)	23 (76.7%)	48 (82.8%)
Mean (SD)	-17.2 (30.01)	-15.8 (24.31)	-16.5 (27.14)
Median	-12.9	-13.0	-13.0
Min, Max	-79, 49	-65, 28	-79, 49
LS Mean (SE)	-13.44 (6.5)	-15.34 (4.8)	-14.47 (3.8)
95% CI	(-26.42, -0.47)	(-24.77, -5.92)	(-21.93, -7.00)
p-value	0.0424	0.0016	0.0002

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C13D15			
n (%)	21 (75.0%)	19 (63.3%)	40 (69.0%)
Mean (SD)	138.0 (196.33)	361.5 (443.85)	244.2 (351.38)
Median	68.3	209.8	111.5
Min, Max	2, 873	13, 1771	2, 1771
Change from Baseline at C13D15			
n (%)	21 (75.0%)	19 (63.3%)	40 (69.0%)
Mean (SD)	-42.2 (45.29)	-83.2 (169.28)	-61.6 (121.27)
Median	-22.1	-40.7	-26.4
Min, Max	-127, 9	-747, 26	-747, 26
LS Mean (SE)	-36.07 (7.2)	-97.87 (20.3)	-63.88 (11.4)
95% CI	(-50.34, -21.80)	(-138.10, -57.63)	(-86.42, -41.33)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C13D15			
n (%)	21 (75.0%)	19 (63.3%)	40 (69.0%)
Mean (SD)	-29.1 (23.79)	-18.8 (21.24)	-24.2 (22.93)
Median	-30.7	-11.2	-27.3
Min, Max	-77, 21	-65, 8	-77, 21
LS Mean (SE)	-24.20 (5.4)	-17.69 (4.4)	-20.67 (3.6)
95% CI	(-34.84, -13.56)	(-26.31, -9.07)	(-27.74, -13.61)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C17D15			
n (%)	19 (67.9%)	18 (60.0%)	37 (63.8%)
Mean (SD)	117.3 (176.86)	339.0 (407.59)	225.2 (326.67)
Median	59.1	194.1	108.0
Min, Max	2, 750	9, 1396	2, 1396
Change from Baseline at C17D15			
n (%)	19 (67.9%)	18 (60.0%)	37 (63.8%)
Mean (SD)	-42.0 (68.18)	-118.7 (273.54)	-79.4 (197.91)
Median	-16.5	-20.8	-16.5
Min, Max	-232, 43	-1123, 172	-1123, 172
LS Mean (SE)	-39.88 (10.3)	-135.66 (33.3)	-87.42 (18.7)
95% CI	(-60.25, -19.52)	(-201.53, -69.79)	(-124.27, -50.56)
p-value	0.0002	<0.0001	<0.0001
Percent Change from Baseline at C17D15			
n (%)	19 (67.9%)	18 (60.0%)	37 (63.8%)
Mean (SD)	-30.6 (28.08)	-24.7 (27.49)	-27.7 (27.56)
Median	-33.5	-29.1	-32.2
Min, Max	-83, 27	-77, 15	-83, 27
LS Mean (SE)	-26.23 (6.0)	-25.94 (5.4)	-25.27 (3.9)
95% CI	(-38.22, -14.24)	(-36.58, -15.30)	(-32.99, -17.55)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C21D15			
n (%)	19 (67.9%)	16 (53.3%)	35 (60.3%)
Mean (SD)	122.7 (187.72)	355.2 (491.45)	229.0 (372.86)
Median	48.3	165.7	75.8
Min, Max	2, 752	9, 1694	2, 1694
Change from Baseline at C21D15			
n (%)	19 (67.9%)	16 (53.3%)	35 (60.3%)
Mean (SD)	-48.9 (64.00)	-121.1 (221.20)	-81.9 (158.39)
Median	-15.6	-94.0	-42.6
Min, Max	-229, 7	-825, 251	-825, 251
LS Mean (SE)	-41.95 (11.2)	-123.39 (29.4)	-89.59 (14.5)
95% CI	(-64.06, -19.83)	(-181.67, -65.11)	(-118.12, -61.06)
p-value	0.0003	<0.0001	<0.0001
Percent Change from Baseline at C21D15			
n (%)	19 (67.9%)	16 (53.3%)	35 (60.3%)
Mean (SD)	-35.0 (23.83)	-30.5 (27.35)	-33.0 (25.22)
Median	-32.4	-30.3	-32.4
Min, Max	-81, 2	-76, 22	-81, 22
LS Mean (SE)	-30.64 (5.8)	-29.28 (5.6)	-28.20 (4.2)
95% CI	(-42.20, -19.09)	(-40.37, -18.20)	(-36.58, -19.83)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C24D21			
n (%)	15 (53.6%)	17 (56.7%)	32 (55.2%)
Mean (SD)	111.3 (163.96)	323.1 (414.21)	223.8 (335.00)
Median	72.6	147.1	111.5
Min, Max	1, 597	8, 1463	1, 1463
Change from Baseline at C24D21			
n (%)	15 (53.6%)	17 (56.7%)	32 (55.2%)
Mean (SD)	-71.4 (107.49)	-159.1 (253.07)	-118.0 (200.62)
Median	-21.5	-118.9	-54.4
Min, Max	-384, 22	-1055, 55	-1055, 55
LS Mean (SE)	-60.57 (18.0)	-157.74 (27.6)	-107.21 (16.0)
95% CI	(-96.24, -24.89)	(-212.49, -103.00)	(-138.79, -75.63)
p-value	0.0011	<0.0001	<0.0001
Percent Change from Baseline at C24D21			
n (%)	15 (53.6%)	17 (56.7%)	32 (55.2%)
Mean (SD)	-38.8 (32.35)	-35.3 (28.32)	-36.9 (29.83)
Median	-45.3	-41.1	-41.5
Min, Max	-82, 40	-79, 13	-82, 40
LS Mean (SE)	-34.53 (8.2)	-32.49 (6.1)	-30.62 (4.7)
95% CI	(-50.83, -18.24)	(-44.67, -20.31)	(-39.88, -21.36)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C28D15			
n (%)	7 (25.0%)	13 (43.3%)	20 (34.5%)
Mean (SD)	131.6 (242.44)	288.1 (428.94)	233.3 (375.01)
Median	47.4	173.4	141.1
Min, Max	1, 676	10, 1669	1, 1669
Change from Baseline at C28D15			
n (%)	7 (25.0%)	13 (43.3%)	20 (34.5%)
Mean (SD)	-88.1 (121.01)	-183.3 (215.87)	-150.0 (190.34)
Median	-13.0	-121.8	-96.5
Min, Max	-306, -0	-849, -19	-849, -0
LS Mean (SE)	-64.97 (16.4)	-176.08 (13.0)	-120.34 (14.0)
95% CI	(-97.48, -32.46)	(-201.90, -150.26)	(-147.89, -92.79)
p-value	0.0001	<0.0001	<0.0001
Percent Change from Baseline at C28D15			
n (%)	7 (25.0%)	13 (43.3%)	20 (34.5%)
Mean (SD)	-48.3 (29.84)	-43.9 (18.52)	-45.5 (22.41)
Median	-54.0	-39.7	-41.6
Min, Max	-91, -0	-75, -11	-91, -0
LS Mean (SE)	-37.56 (10.2)	-36.10 (5.5)	-35.68 (4.7)
95% CI	(-57.69, -17.42)	(-47.01, -25.19)	(-44.99, -26.36)
p-value	0.0003	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C32D15			
n (%)	5 (17.9%)	8 (26.7%)	13 (22.4%)
Mean (SD)	113.2 (182.84)	177.4 (154.71)	152.7 (161.75)
Median	54.5	124.1	72.6
Min, Max	1, 435	7, 385	1, 435
Change from Baseline at C32D15			
n (%)	5 (17.9%)	8 (26.7%)	13 (22.4%)
Mean (SD)	-140.8 (228.90)	-139.8 (70.26)	-140.2 (142.64)
Median	-55.7	-154.7	-117.7
Min, Max	-546, -8	-246, -31	-546, -8
LS Mean (SE)	-109.63 (53.2)	-186.77 (18.0)	-136.61 (24.7)
95% CI	(-215.07, -4.18)	(-222.37, -151.17)	(-185.34, -87.89)
p-value	0.0417	<0.0001	<0.0001
Percent Change from Baseline at C32D15			
n (%)	5 (17.9%)	8 (26.7%)	13 (22.4%)
Mean (SD)	-64.8 (17.08)	-53.1 (21.51)	-57.6 (20.05)
Median	-61.3	-49.5	-55.6
Min, Max	-86, -43	-86, -27	-86, -27
LS Mean (SE)	-60.27 (6.4)	-42.96 (6.7)	-48.14 (4.2)
95% CI	(-72.89, -47.66)	(-56.32, -29.60)	(-56.37, -39.91)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol_df.sas Output Generated: 2025-06-05T11:05 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C36D15			
n (%)	4 (14.3%)	7 (23.3%)	11 (19.0%)
Mean (SD)	167.3 (229.96)	141.0 (142.03)	150.6 (167.76)
Median	80.4	59.6	79.5
Min, Max	1, 508	9, 414	1, 508
Change from Baseline at C36D15			
n (%)	4 (14.3%)	7 (23.3%)	11 (19.0%)
Mean (SD)	-147.7 (218.41)	-141.7 (76.46)	-143.9 (133.52)
Median	-54.1	-128.5	-121.3
Min, Max	-474, -9	-221, -29	-474, -9
LS Mean (SE)	NA (NA)	-198.51 (17.5)	-135.91 (15.8)
95% CI	(NA, NA)	(-233.27, -163.75)	(-167.09, -104.72)
p-value	NA	<0.0001	<0.0001
Percent Change from Baseline at C36D15			
n (%)	4 (14.3%)	7 (23.3%)	11 (19.0%)
Mean (SD)	-54.8 (24.58)	-57.6 (17.60)	-56.6 (19.21)
Median	-45.9	-53.8	-48.3
Min, Max	-91, -37	-79, -34	-91, -34
LS Mean (SE)	NA (NA)	-47.15 (5.3)	-48.07 (3.9)
95% CI	(NA, NA)	(-57.70, -36.60)	(-55.77, -40.37)
p-value	NA	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C40D15			
n (%)	3 (10.7%)	4 (13.3%)	7 (12.1%)
Mean (SD)	269.3 (335.25)	85.8 (53.63)	164.4 (220.26)
Median	75.9	76.6	75.9
Min, Max	75, 656	36, 154	36, 656
Change from Baseline at C40D15			
n (%)	3 (10.7%)	4 (13.3%)	7 (12.1%)
Mean (SD)	-147.5 (153.83)	-133.8 (43.43)	-139.7 (94.26)
Median	-65.1	-141.2	-137.9
Min, Max	-325, -52	-178, -74	-325, -52
LS Mean (SE)	NA (NA)	NA (NA)	-135.48 (9.5)
95% CI	(NA, NA)	(NA, NA)	(-154.21, -116.74)
p-value	NA	NA	<0.0001
Percent Change from Baseline at C40D15			
n (%)	3 (10.7%)	4 (13.3%)	7 (12.1%)
Mean (SD)	-40.1 (6.63)	-62.5 (13.60)	-52.9 (15.85)
Median	-40.8	-61.4	-47.2
Min, Max	-46, -33	-80, -47	-80, -33
LS Mean (SE)	NA (NA)	NA (NA)	-46.11 (3.4)
95% CI	(NA, NA)	(NA, NA)	(-52.90, -39.32)
p-value	NA	NA	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7.2: Tumor Volume (mL) by Visit - Participants with Disfigurement: Full Analysis Set

	Pediatric (N=28)	Adult (N=30)	Total (N=58)
C44D15			
n (%)	0	1 (3.3%)	1 (1.7%)
Mean (SD)	NA (NA)	101.5 (NA)	101.5 (NA)
Median	NA	101.5	101.5
Min, Max	(NA, NA)	102, 102	102, 102
Change from Baseline at C44D15			
n (%)	0	1 (3.3%)	1 (1.7%)
Mean (SD)	NA (NA)	-179.0 (NA)	-179.0 (NA)
Median	NA	-179.0	-179.0
Min, Max	(NA, NA)	-179, -179	-179, -179
Percent Change from Baseline at C44D15			
n (%)	0	1 (3.3%)	1 (1.7%)
Mean (SD)	NA (NA)	-63.8 (NA)	-63.8 (NA)
Median	NA	-63.8	-63.8
Min, Max	(NA, NA)	-64, -64	-64, -64

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Baseline (Screening)			
n (%)	56 (100%)	58 (100%)	114 (100%)
Mean (SD)	255.0 (559.13)	450.0 (744.02)	354.2 (664.07)
Median	98.9	196.3	128.2
Min, Max	5, 3630	1, 3457	1, 3630
C5D15			
n (%)	53 (94.6%)	49 (84.5%)	102 (89.5%)
Mean (SD)	167.0 (256.31)	345.2 (600.21)	252.6 (461.56)
Median	83.2	165.5	96.5
Min, Max	3, 1533	1, 3118	1, 3118
Change from Baseline at C5D15			
n (%)	53 (94.6%)	49 (84.5%)	102 (89.5%)
Mean (SD)	-30.2 (86.53)	-61.5 (129.23)	-45.2 (109.72)
Median	-4.3	-16.3	-6.4
Min, Max	-553, 61	-563, 67	-563, 67
LS Mean (SE)	-43.18 (9.2)	-44.67 (13.9)	-43.93 (8.5)
95% CI	(-61.24, -25.13)	(-72.14, -17.20)	(-60.60, -27.25)
p-value	<0.0001	0.0016	<0.0001
Percent Change from Baseline at C5D15			
n (%)	53 (94.6%)	49 (84.5%)	102 (89.5%)
Mean (SD)	-12.9 (21.98)	-12.8 (20.29)	-12.9 (21.08)
Median	-9.6	-10.1	-10.0
Min, Max	-66, 48	-67, 40	-67, 48
LS Mean (SE)	-12.25 (3.1)	-13.24 (3.0)	-13.00 (2.3)
95% CI	(-18.37, -6.14)	(-19.21, -7.28)	(-17.43, -8.58)
p-value	0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol.sas Output Generated: 2025-06-03T14:28 Source: ADSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C9D15			
n (%)	48 (85.7%)	43 (74.1%)	91 (79.8%)
Mean (SD)	180.7 (310.98)	266.8 (447.30)	221.4 (381.76)
Median	73.9	92.2	81.2
Min, Max	2, 1800	1, 2202	1, 2202
Change from Baseline at C9D15			
n (%)	48 (85.7%)	43 (74.1%)	91 (79.8%)
Mean (SD)	-26.7 (76.28)	-72.4 (211.49)	-48.3 (156.33)
Median	-11.7	-8.1	-11.6
Min, Max	-285, 195	-1255, 38	-1255, 195
LS Mean (SE)	-36.44 (9.6)	-66.73 (14.7)	-51.35 (9.6)
95% CI	(-55.39, -17.49)	(-95.78, -37.69)	(-70.19, -32.51)
p-value	0.0002	<0.0001	<0.0001
Percent Change from Baseline at C9D15			
n (%)	48 (85.7%)	43 (74.1%)	91 (79.8%)
Mean (SD)	-17.1 (27.43)	-17.4 (24.65)	-17.3 (26.01)
Median	-14.9	-11.9	-13.7
Min, Max	-79, 49	-73, 28	-79, 49
LS Mean (SE)	-13.30 (4.2)	-18.17 (3.7)	-15.93 (2.9)
95% CI	(-21.62, -4.97)	(-25.37, -10.97)	(-21.57, -10.29)
p-value	0.0019	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

Program Name: t_tum_vol.sas Output Generated: 2025-06-03T14:28 Source: ABSL, ADTR Data Cutoff Date: 2023-09-20

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C13D15			
n (%)	39 (69.6%)	35 (60.3%)	74 (64.9%)
Mean (SD)	171.8 (323.47)	250.0 (360.85)	208.8 (341.55)
Median	68.3	108.6	80.3
Min, Max	2, 1857	1, 1771	1, 1857
Change from Baseline at C13D15			
n (%)	39 (69.6%)	35 (60.3%)	74 (64.9%)
Mean (SD)	-53.2 (71.12)	-65.3 (151.01)	-58.9 (115.29)
Median	-22.1	-24.7	-22.6
Min, Max	-268, 9	-747, 88	-747, 88
LS Mean (SE)	-56.92 (10.6)	-68.84 (16.1)	-63.84 (8.9)
95% CI	(-77.90, -35.94)	(-100.66, -37.03)	(-81.25, -46.42)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C13D15			
n (%)	39 (69.6%)	35 (60.3%)	74 (64.9%)
Mean (SD)	-29.4 (22.48)	-19.7 (26.32)	-24.8 (24.69)
Median	-31.5	-16.9	-28.3
Min, Max	-77, 21	-67, 48	-77, 48
LS Mean (SE)	-23.67 (3.6)	-19.72 (4.3)	-21.43 (2.9)
95% CI	(-30.74, -16.59)	(-28.14, -11.30)	(-27.14, -15.72)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C17D15			
n (%)	38 (67.9%)	31 (53.4%)	69 (60.5%)
Mean (SD)	153.7 (263.29)	248.9 (361.49)	196.5 (312.49)
Median	66.8	123.2	83.1
Min, Max	2, 1459	0, 1396	0, 1459
Change from Baseline at C17D15			
n (%)	38 (67.9%)	31 (53.4%)	69 (60.5%)
Mean (SD)	-60.3 (127.79)	-84.7 (212.60)	-71.3 (170.22)
Median	-17.2	-12.6	-17.0
Min, Max	-627, 60	-1123, 172	-1123, 172
LS Mean (SE)	-67.45 (10.8)	-84.23 (17.0)	-76.47 (10.9)
95% CI	(-88.70, -46.20)	(-117.72, -50.73)	(-97.81, -55.12)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C17D15			
n (%)	38 (67.9%)	31 (53.4%)	69 (60.5%)
Mean (SD)	-28.2 (28.52)	-27.9 (24.95)	-28.1 (26.78)
Median	-29.6	-31.3	-30.5
Min, Max	-83, 27	-77, 15	-83, 27
LS Mean (SE)	-21.47 (4.5)	-25.63 (4.1)	-24.52 (3.2)
95% CI	(-30.39, -12.56)	(-33.81, -17.46)	(-30.81, -18.23)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C21D15			
n (%)	34 (60.7%)	30 (51.7%)	64 (56.1%)
Mean (SD)	154.2 (281.94)	248.6 (401.58)	198.5 (343.69)
Median	46.1	118.9	57.7
Min, Max	2, 1450	0, 1694	0, 1694
Change from Baseline at C21D15			
n (%)	34 (60.7%)	30 (51.7%)	64 (56.1%)
Mean (SD)	-66.3 (122.84)	-82.7 (170.11)	-74.0 (145.92)
Median	-15.9	-28.0	-25.9
Min, Max	-635, 7	-825, 251	-825, 251
LS Mean (SE)	-71.27 (11.4)	-80.97 (17.2)	-77.33 (8.7)
95% CI	(-93.71, -48.83)	(-114.92, -47.03)	(-94.49, -60.17)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C21D15			
n (%)	34 (60.7%)	30 (51.7%)	64 (56.1%)
Mean (SD)	-32.3 (23.85)	-32.0 (26.88)	-32.2 (25.11)
Median	-30.9	-32.5	-32.2
Min, Max	-81, 15	-90, 22	-90, 22
LS Mean (SE)	-24.55 (4.2)	-28.34 (4.3)	-27.90 (3.0)
95% CI	(-32.78, -16.32)	(-36.88, -19.80)	(-33.83, -21.96)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C24D21			
n (%)	31 (55.4%)	28 (48.3%)	59 (51.8%)
Mean (SD)	159.3 (290.16)	236.2 (355.88)	195.8 (322.50)
Median	58.6	98.2	70.1
Min, Max	1, 1428	1, 1463	1, 1463
Change from Baseline at C24D21			
n (%)	31 (55.4%)	28 (48.3%)	59 (51.8%)
Mean (SD)	-79.1 (139.23)	-122.0 (215.67)	-99.4 (179.30)
Median	-22.0	-37.0	-27.5
Min, Max	-658, 22	-1055, 55	-1055, 55
LS Mean (SE)	-78.99 (11.9)	-113.15 (17.7)	-96.96 (10.4)
95% CI	(-102.46, -55.52)	(-148.11, -78.19)	(-117.44, -76.49)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C24D21			
n (%)	31 (55.4%)	28 (48.3%)	59 (51.8%)
Mean (SD)	-35.3 (28.98)	-37.6 (24.93)	-36.4 (26.92)
Median	-39.2	-43.0	-41.4
Min, Max	-82, 40	-79, 13	-82, 40
LS Mean (SE)	-26.31 (4.6)	-34.93 (4.3)	-34.53 (3.3)
95% CI	(-35.38, -17.25)	(-43.39, -26.46)	(-41.03, -28.04)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C28D15			
n (%)	17 (30.4%)	20 (34.5%)	37 (32.5%)
Mean (SD)	159.9 (293.98)	212.0 (359.12)	188.0 (327.36)
Median	47.4	141.1	79.0
Min, Max	1, 1115	1, 1669	1, 1669
Change from Baseline at C28D15			
n (%)	17 (30.4%)	20 (34.5%)	37 (32.5%)
Mean (SD)	-123.2 (236.85)	-125.7 (190.46)	-124.5 (209.95)
Median	-47.1	-65.7	-58.4
Min, Max	-971, 2	-849, 11	-971, 11
LS Mean (SE)	-112.42 (16.0)	-114.01 (20.5)	-109.07 (12.0)
95% CI	(-143.94, -80.89)	(-154.34, -73.68)	(-132.56, -85.59)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C28D15			
n (%)	17 (30.4%)	20 (34.5%)	37 (32.5%)
Mean (SD)	-40.8 (28.19)	-36.3 (23.16)	-38.3 (25.32)
Median	-46.6	-38.8	-39.7
Min, Max	-91, 23	-75, 15	-91, 23
LS Mean (SE)	-30.84 (6.5)	-30.18 (5.3)	-33.64 (4.1)
95% CI	(-43.68, -18.01)	(-40.53, -19.83)	(-41.75, -25.54)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C32D15			
n (%)	10 (17.9%)	14 (24.1%)	24 (21.1%)
Mean (SD)	239.2 (383.41)	169.4 (207.88)	198.5 (288.42)
Median	78.9	96.6	78.9
Min, Max	1, 1255	1, 713	1, 1255
Change from Baseline at C32D15			
n (%)	10 (17.9%)	14 (24.1%)	24 (21.1%)
Mean (SD)	-177.4 (283.07)	-116.1 (109.38)	-141.6 (197.66)
Median	-50.8	-102.5	-70.9
Min, Max	-830, 14	-381, -1	-830, 14
LS Mean (SE)	-133.53 (20.8)	-122.11 (24.0)	-122.49 (13.3)
95% CI	(-174.58, -92.47)	(-169.38, -74.84)	(-148.60, -96.38)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C32D15			
n (%)	10 (17.9%)	14 (24.1%)	24 (21.1%)
Mean (SD)	-45.5 (29.84)	-50.0 (19.12)	-48.1 (23.67)
Median	-47.3	-46.6	-46.6
Min, Max	-86, 20	-86, -27	-86, 20
LS Mean (SE)	-41.05 (5.7)	-42.47 (4.5)	-43.78 (4.0)
95% CI	(-52.32, -29.78)	(-51.41, -33.52)	(-51.69, -35.87)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C36D15			
n (%)	9 (16.1%)	13 (22.4%)	22 (19.3%)
Mean (SD)	281.7 (426.85)	132.1 (169.13)	193.3 (302.36)
Median	101.2	57.9	80.4
Min, Max	1, 1343	0, 535	0, 1343
Change from Baseline at C36D15			
n (%)	9 (16.1%)	13 (22.4%)	22 (19.3%)
Mean (SD)	-186.0 (256.50)	-132.3 (151.69)	-154.2 (197.34)
Median	-61.1	-118.8	-67.8
Min, Max	-742, -9	-559, -1	-742, -1
LS Mean (SE)	-127.36 (22.0)	-143.90 (24.8)	-134.66 (13.8)
95% CI	(-170.64, -84.08)	(-192.76, -95.03)	(-161.87, -107.44)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C36D15			
n (%)	9 (16.1%)	13 (22.4%)	22 (19.3%)
Mean (SD)	-45.9 (20.84)	-56.0 (15.36)	-51.9 (18.07)
Median	-43.5	-51.1	-47.8
Min, Max	-91, -19	-79, -34	-91, -19
LS Mean (SE)	-40.55 (4.5)	-50.95 (3.7)	-48.89 (3.5)
95% CI	(-49.40, -31.70)	(-58.33, -43.57)	(-55.70, -42.08)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C40D15			
n (%)	6 (10.7%)	9 (15.5%)	15 (13.2%)
Mean (SD)	447.3 (525.04)	103.6 (143.70)	241.1 (375.00)
Median	225.0	51.1	75.9
Min, Max	75, 1426	1, 465	1, 1426
Change from Baseline at C40D15			
n (%)	6 (10.7%)	9 (15.5%)	15 (13.2%)
Mean (SD)	-225.2 (241.34)	-154.3 (192.97)	-182.7 (208.25)
Median	-140.2	-137.9	-137.9
Min, Max	-660, -33	-629, -1	-660, -1
LS Mean (SE)	-108.90 (26.9)	-160.14 (29.3)	-135.40 (19.2)
95% CI	(-161.98, -55.81)	(-217.85, -102.42)	(-173.18, -97.63)
p-value	<0.0001	<0.0001	<0.0001
Percent Change from Baseline at C40D15			
n (%)	6 (10.7%)	9 (15.5%)	15 (13.2%)
Mean (SD)	-35.4 (11.82)	-56.6 (14.84)	-48.1 (17.06)
Median	-37.0	-57.5	-46.3
Min, Max	-46, -15	-80, -34	-80, -15
LS Mean (SE)	-38.20 (3.9)	-49.70 (4.5)	-48.10 (4.0)
95% CI	(-45.86, -30.54)	(-58.53, -40.88)	(-56.05, -40.14)
p-value	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 7: Tumor Volume (mL) by Visit: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
C44D15			
n (%)	1 (1.8%)	4 (6.9%)	5 (4.4%)
Mean (SD)	1697.2 (NA)	61.3 (48.26)	388.5 (732.79)
Median	1697.2	70.6	100.2
Min, Max	1697, 1697	3, 102	3, 1697
Change from Baseline at C44D15			
n (%)	1 (1.8%)	4 (6.9%)	5 (4.4%)
Mean (SD)	-388.4 (NA)	-95.7 (90.50)	-154.3 (152.58)
Median	-388.4	-100.3	-167.6
Min, Max	-388, -388	-179, -3	-388, -3
LS Mean (SE)	NA (NA)	NA (NA)	-79.93 (49.8)
95% CI	(NA, NA)	(NA, NA)	(-177.79, 17.93)
p-value	NA	NA	0.1091
Percent Change from Baseline at C44D15			
n (%)	1 (1.8%)	4 (6.9%)	5 (4.4%)
Mean (SD)	-18.6 (NA)	-56.8 (8.81)	-49.2 (18.71)
Median	-18.6	-59.4	-56.3
Min, Max	-19, -19	-64, -45	-64, -19
LS Mean (SE)	NA (NA)	NA (NA)	-48.63 (5.5)
95% CI	(NA, NA)	(NA, NA)	(-59.46, -37.80)
p-value	NA	NA	<0.0001

SD: Standard deviation; MRI: Magnetic Resonance Imaging; Min: Minimum; Max: Maximum.
Tumor volume was assessed by MRI scan, volume measurements were independently calculated by two blinded central reviewers. The two calculated volumes were averaged to give the visit volume assessment, unless they represent different tumor response statuses, in which case, the volume of the reader assessment chosen by adjudication was used.
Tumor volume recorded at Screening is considered as baseline.

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Table 8: Kaplan-Meier Analysis of Duration of Response: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Number of Participants with Confirmed Response	29 (51.8%)	24 (41.4%)	53 (46.5%)
Number of Participant Events			
PD	0	1 (4.2%)	1 (1.9%)
Death	0	1 (100%)	1 (100%)
Number of Censored Participants	29 (100%)	23 (95.8%)	52 (98.1%)
Reason for Censoring			
No Adequate Tumor Assessment Post Confirmed Response	1 (3.4%)	3 (13.0%)	4 (7.7%)
No PD/Death Post Response confirmation	27 (93.1%)	20 (87.0%)	47 (90.4%)
Underwent PN Therapy/Surgery Prior to PD/Death	1 (3.4%)	0	1 (1.9%)
Two or More Consecutive Missing/Non-Adequate Assessments	0	0	0
Duration of Response (Months):			
1 st Quartile	NE	NE	NE
95% CI	(NE, NE)	(6.1, NE)	(NE, NE)
Median	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)
3 rd Quartile	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)

CI: Confidence Interval; CR: Complete Response; PR: Partial Response; PD: Progressive Disease; NE: Not estimable.
Duration of response is defined as the time in months between the first instance of response that is subsequently confirmed, until the date of radiographic disease progression or death, whichever occurs first.
Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months as designated by BICR during the Treatment Phase.
Percentages are calculated out of the number of participants with a confirmed objective response for the number with event/censored, number of events experienced by this point and number of participants still event free by this point.
Percentages for event type are based on the total number of events, and out of the number censored for the reasons for censoring.

Program Name: t_morb_dor.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADTTE Data Cutoff Date: 2023-09-20

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Table 8: Kaplan-Meier Analysis of Duration of Response: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
At 8 months:			
Number of events experienced by this point	0	1 (4.2%)	1 (1.9%)
Number of participants still event free by this point (at risk)	25 (86.2%)	18 (75.0%)	43 (81.1%)
Kaplan Meier response rate estimate	1.00	0.95	0.98
95% CI	(1.00, 1.00)	(0.71, 0.99)	(0.86, 1.00)
At 12 months:			
Number of events experienced by this point	0	1 (4.2%)	1 (1.9%)
Number of participants still event free by this point (at risk)	22 (75.9%)	18 (75.0%)	40 (75.5%)
Kaplan Meier response rate estimate	1.00	0.95	0.98
95% CI	(1.00, 1.00)	(0.71, 0.99)	(0.86, 1.00)
At 16 months:			
Number of events experienced by this point	0	1 (4.2%)	1 (1.9%)
Number of participants still event free by this point (at risk)	18 (62.1%)	13 (54.2%)	31 (58.5%)
Kaplan Meier response rate estimate	1.00	0.95	0.98
95% CI	(1.00, 1.00)	(0.71, 0.99)	(0.86, 1.00)

CI: Confidence Interval; CR: Complete Response; PR: Partial Response; PD: Progressive Disease; NE: Not estimable.
Duration of response is defined as the time in months between the first instance of response that is subsequently confirmed, until the date of radiographic disease progression or death, whichever occurs first.
Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months as designated by BICR during the Treatment Phase.
Percentages are calculated out of the number of participants with a confirmed objective response for the number with event/censored, number of events experienced by this point and number of participants still event free by this point.
Percentages for event type are based on the total number of events, and out of the number censored for the reasons for censoring.

Program Name: t_morb_dor.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADTTE Data Cutoff Date: 2023-09-20

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Table 8: Kaplan-Meier Analysis of Duration of Response: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
At 20 months:			
Number of events experienced by this point		1 (4.2%)	1 (1.9%)
Number of participants still event free by this point (at risk)	0 10 (34.5%)	11 (45.8%)	21 (39.6%)
Kaplan Meier response rate estimate	1.00	0.95	0.98
95% CI	(1.00, 1.00)	(0.71, 0.99)	(0.86, 1.00)
At 24 months:			
Number of events experienced by this point		1 (4.2%)	1 (1.9%)
Number of participants still event free by this point (at risk)	0 4 (13.8%)	9 (37.5%)	13 (24.5%)
Kaplan Meier response rate estimate	1.00	0.95	0.98
95% CI	(1.00, 1.00)	(0.71, 0.99)	(0.86, 1.00)

CI: Confidence Interval; CR: Complete Response; PR: Partial Response; PD: Progressive Disease; NE: Not estimable.
Duration of response is defined as the time in months between the first instance of response that is subsequently confirmed, until the date of radiographic disease progression or death, whichever occurs first.
Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months as designated by BICR during the Treatment Phase.
Percentages are calculated out of the number of participants with a confirmed objective response for the number with event/censored, number of events experienced by this point and number of participants still event free by this point.
Percentages for event type are based on the total number of events, and out of the number censored for the reasons for censoring.

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Table 9: Kaplan-Meier Analysis of Time to Progression: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
Number of Participants with PD	9 (16.1%)	6 (10.3%)	15 (13.2%)
Number of Censored Participants	47 (83.9%)	52 (89.7%)	99 (86.8%)
Reason for Censoring			
No PD Post Baseline	43 (91.5%)	43 (82.7%)	86 (86.9%)
No Adequate Tumor Assessment Post Baseline	2 (4.3%)	8 (15.4%)	10 (10.1%)
Two or More Consecutive Missing/Non-Adequate Assessments	1 (2.1%)	0	1 (1.0%)
Death Before PD	0	1 (1.9%)	1 (1.0%)
Underwent PN Therapy/Surgery Prior to PD	1 (2.1%)	0	1 (1.0%)
Time to PD (Months):			
1 st Quartile	NE	NE	NE
95% CI	(15.1, NE)	(11.6, NE)	(19.0, NE)
Median	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)
3 rd Quartile	NE	NE	NE
95% CI	(NE, NE)	(NE, NE)	(NE, NE)

CI: Confidence Interval; PD: Progressive Disease.

N represents the number of participants in the corresponding the cohort.

Time to progression (TTP) is defined as the time in months between the start of treatment to the first date of radiographic disease

progression as measured by MRI.

Percentages are calculated out of the number of participants in the corresponding cohort for the number with event/censored, number

of events experienced by this point and number of participants still event free by this point,

out of the total number of events for event type and out of the number censored for the reasons for censoring.

Program Name: t_km_ttp.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADTTE Data Cutoff Date: 2023-09-20

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Table 9: Kaplan-Meier Analysis of Time to Progression: Full Analysis Set

	Pediatric (N=56)	Adult (N=58)	Total (N=114)
At 8 months:			
Number of events experienced by this point	5 (8.9%)	1 (1.7%)	6 (5.3%)
Number of participants still event free by this point (at risk)	43 (76.8%)	37 (63.8%)	80 (70.2%)
Kaplan Meier response rate estimate	0.90	0.98	0.94
95% CI	(0.78, 0.96)	(0.84, 1.00)	(0.87, 0.97)
At 12 months:			
Number of events experienced by this point	6 (10.7%)	4 (6.9%)	10 (8.8%)
Number of participants still event free by this point (at risk)	39 (69.6%)	32 (55.2%)	71 (62.3%)
Kaplan Meier response rate estimate	0.88	0.89	0.89
95% CI	(0.75, 0.95)	(0.74, 0.96)	(0.80, 0.94)
At 16 months:			
Number of events experienced by this point	8 (14.3%)	4 (6.9%)	12 (10.5%)
Number of participants still event free by this point (at risk)	36 (64.3%)	32 (55.2%)	68 (59.6%)
Kaplan Meier response rate estimate	0.84	0.89	0.86
95% CI	(0.70, 0.91)	(0.74, 0.96)	(0.77, 0.92)
At 20 months:			
Number of events experienced by this point	8 (14.3%)	6 (10.3%)	14 (12.3%)
Number of participants still event free by this point (at risk)	31 (55.4%)	27 (46.6%)	58 (50.9%)
Kaplan Meier response rate estimate	0.84	0.83	0.84
95% CI	(0.70, 0.91)	(0.67, 0.92)	(0.74, 0.90)
At 24 months:			
Number of events experienced by this point	9 (16.1%)	6 (10.3%)	15 (13.2%)
Number of participants still event free by this point (at risk)	18 (32.1%)	21 (36.2%)	39 (34.2%)
Kaplan Meier response rate estimate	0.80	0.83	0.82
95% CI	(0.65, 0.89)	(0.67, 0.92)	(0.72, 0.89)

CI: Confidence Interval; PD: Progressive Disease.

N represents the number of participants in the corresponding the cohort.

Time to progression (TTP) is defined as the time in months between the start of treatment to the first date of radiographic disease progression as measured by MRI.

Percentages are calculated out of the number of participants in the corresponding cohort for the number with event/censored, number of events experienced by this point and number of participants still event free by this point, out of the total number of events for event type and out of the number censored for the reasons for censoring.

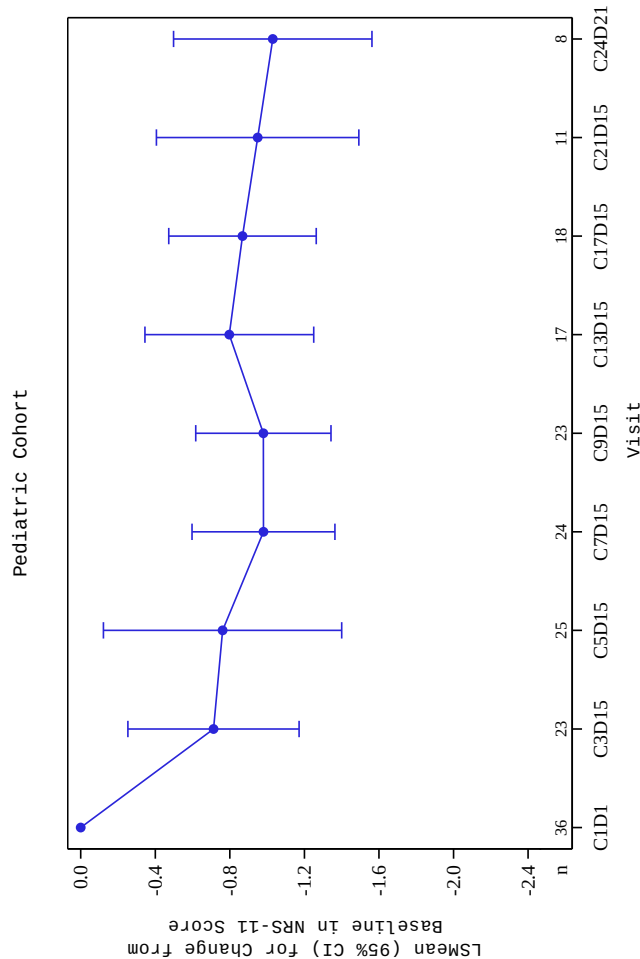
Program Name: t_km_ttp.sas Output Generated: 2025-05-02T13:32 Source: ADL, ADITE Data Cutoff Date: 2023-09-29

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Primary Analysis

Figure 14.2.5.3.2 Mixed Model Repeated Measures: Change from Baseline in NRS-11 Score Through Cycle 24: Full Analysis Set



CI: Confidence interval; LSmean: Least Squares Mean; NRS-11: Numeric Rating Scale-11. MMRM: Mixed model for repeated measures.
A MMRM was fitted separately by age cohort with visit as a fixed effect, baseline NRS-11 score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Pediatric and heterogeneous toeplitz covariance matrix for Adult.
The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

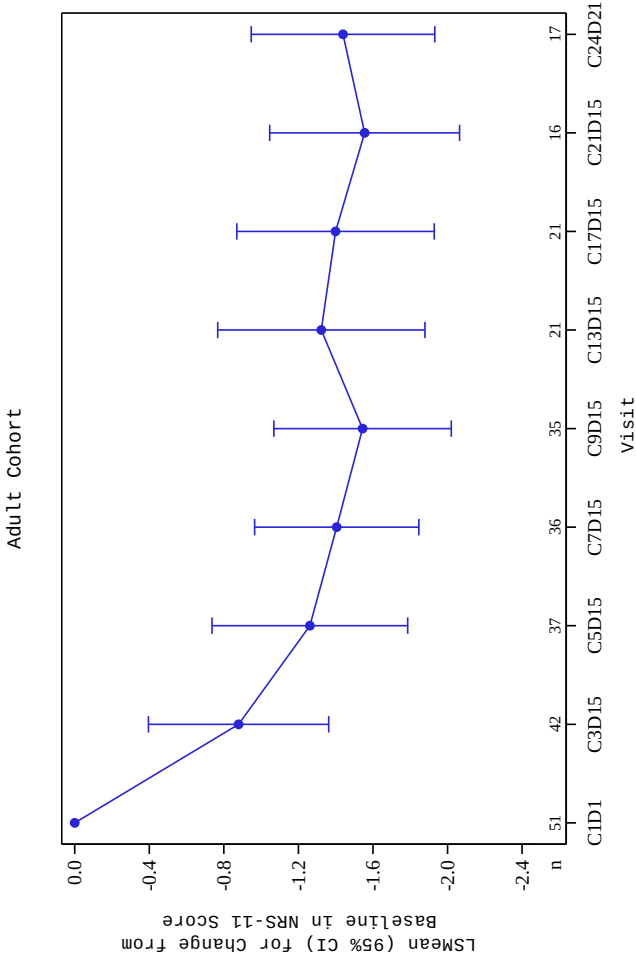
Program Name: f_mmrm_cfb_nrs11_c24.sas Output Generated: 2024-04-10T14:06 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.5.3.2 Mixed Model Repeated Measures: Change from Baseline in NRS-11 Score Through Cycle 24: Full Analysis Set

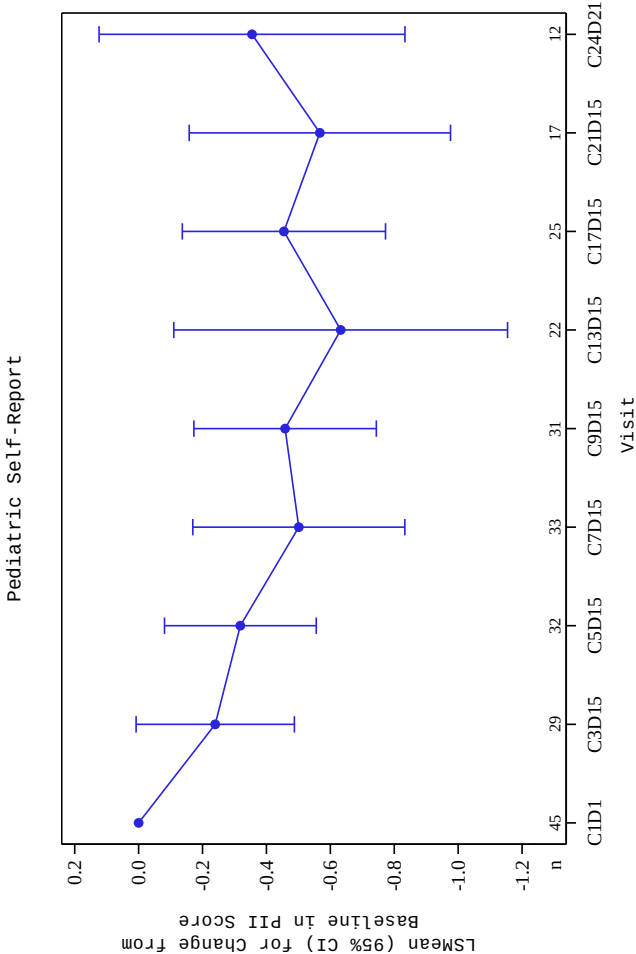


CI: Confidence interval; LSMean: Least Squares Mean; NRS-11: Numeric Rating Scale-11. MMRM: Mixed model for repeated measures.
A MMRM was fitted separately by age cohort with visit as a fixed effect, baseline NRS-11 score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Pediatric and heterogeneous toeplitz covariance matrix for Adult.
The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

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Primary Analysis

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Figure 14.2.6.3.1.2 Mixed Model Repeated Measures: Change from Baseline in PII Score Through Cycle 24 - Pediatric Cohort: Full Analysis Set



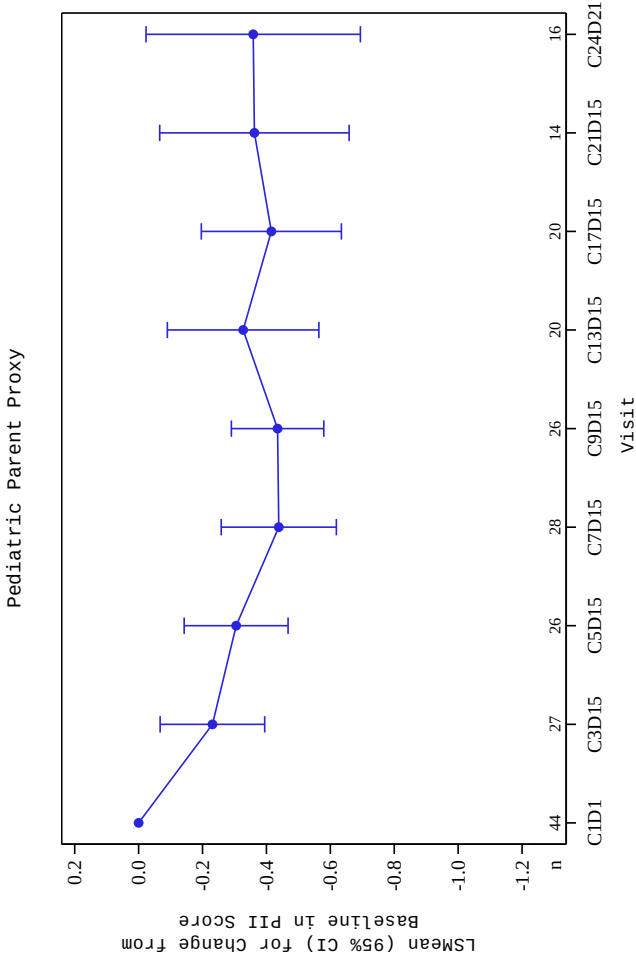
CI: Confidence interval; LSMean: Least Squares Mean; PII: Pain Interference Index; MMRM: Mixed model for repeated measures.
A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PII score as a covariate and a Heterogenous Toeplitz covariance matrix.
The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent PII score taken on or before treatment start date.

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Primary Analysis

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Figure 14.2.6.3.1.2 Mixed Model Repeated Measures: Change from Baseline in PII Score Through Cycle 24 – Pediatric Cohort: Full Analysis Set



CI: Confidence interval; LS Mean: Least Squares Mean; PII: Pain Interference Index; MMRM: Mixed model for repeated measures.

A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PII score as a covariate and a Heterogenous Toeplitz covariance matrix.

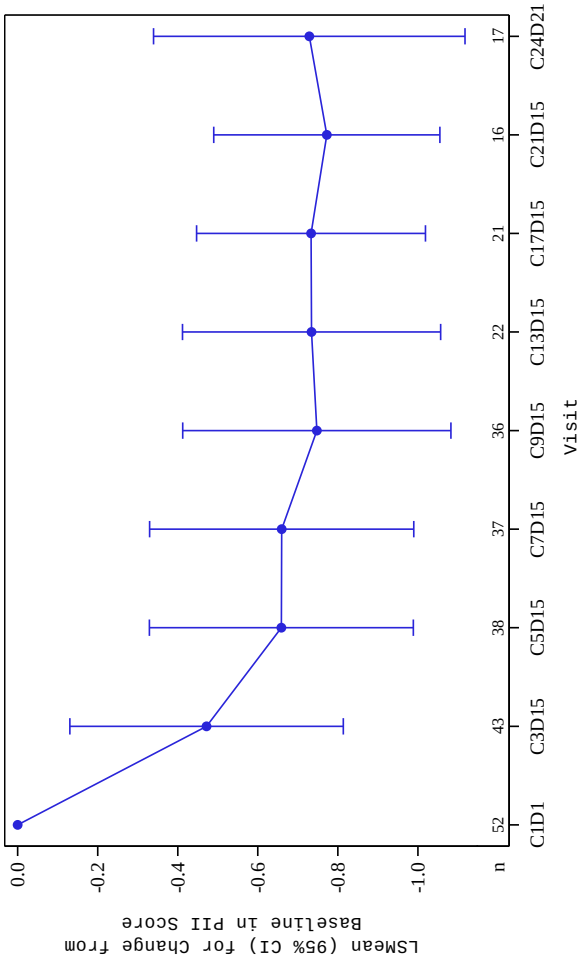
The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 – “Not at all” to 6 – “Completely”. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Baseline is defined as the most recent PII score taken on or before treatment start date.

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Primary Analysis

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Figure 14.2.6.3.2.2 Mixed Model Repeated Measures: Change from Baseline in PII Score Through Cycle 24 – Adult Cohort: Full Analysis Set

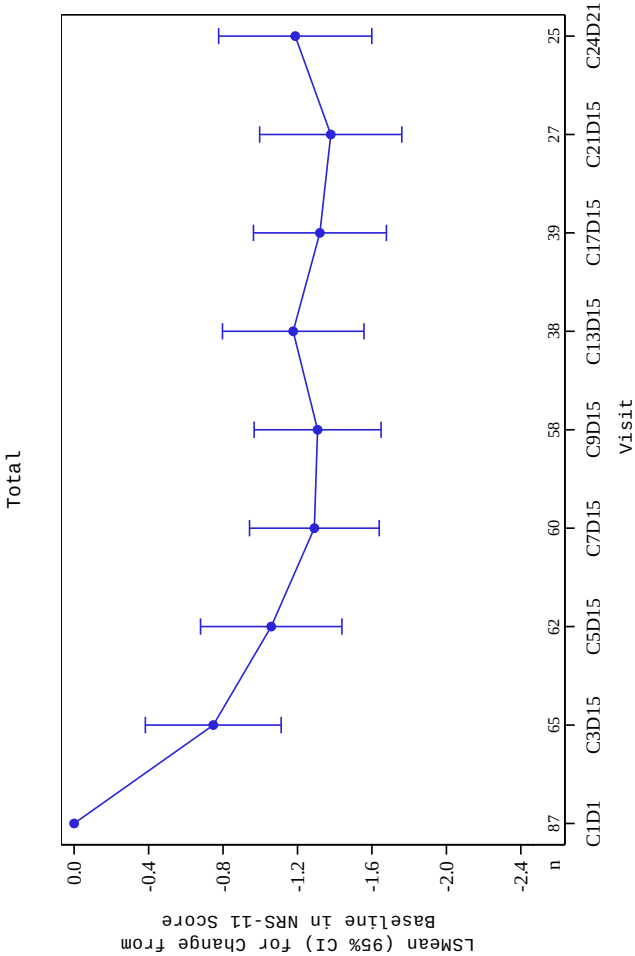


CI: Confidence interval; LSMean: Least Squares Mean; PII: Pain Interference Index; MMRM: Mixed model for repeated measures.
A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PII score as a covariate and a Heterogenous Toeplitz covariance matrix.
The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 – “Not at all” to 6 – “Completely”. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent PII score taken on or before treatment start date.

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Figure 8: Mixed Model Repeated Measures: Change from Baseline in NRS-11 Score Through Cycle 24: Full Analysis Set



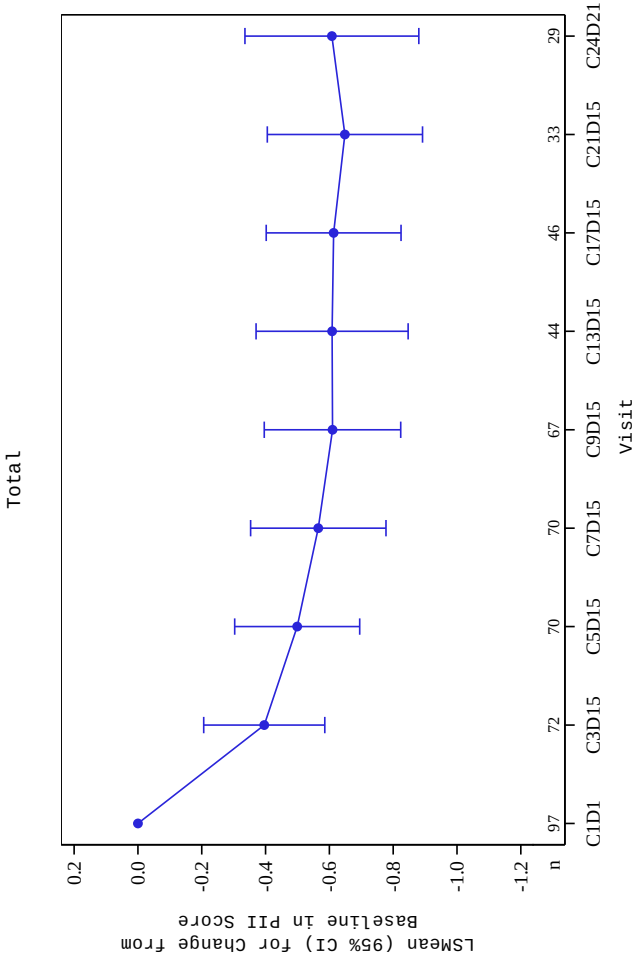
CI: Confidence interval; LSMean: Least Squares Mean; NRS-11: Numeric Rating Scale-11. MMRM: Mixed model for repeated measures. A MMRM was fitted with visit as a fixed effect, baseline NRS-11 score and age cohort as covariates and an unstructured covariance matrix. The NRS-11 assesses target tumor pain on a scale from 0 - 'no pain' to 10 - 'worst pain you can imagine'. NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score. Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: f_8_nrs11_mmrn_t.sas Output Generated: 2025-05-12T15:02 Source: ADQS Data Cutoff Date: 2023-09-20
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Figure 9: Mixed Model Repeated Measures: Change from Baseline in PII Score Through Cycle 24: Full Analysis Set



CI: Confidence interval; LSMean: Least Squares Mean; PII: Pain Interference Index; MMRM: Mixed model for repeated measures.
A MMRM was fitted with visit as a fixed effect, the respective baseline PII score and age cohort as covariates and an unstructured covariance matrix.
The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - 'Not at all' to 6 - 'Completely'. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent PII score taken on or before treatment start date.

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Table 13: Compliance Rate for NRS-11 by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Baseline			
PRO Expected	37 (100%)	58 (100%)	95 (100%)
PRO Completed	36 (97.3%)	51 (87.9%)	87 (91.6%)
PRO Not Completed	1 (2.7%)	7 (12.1%)	8 (8.4%)
C3D15			
PRO Expected	35 (94.6%)	51 (87.9%)	86 (90.5%)
PRO Completed	24 (68.6%)	45 (88.2%)	69 (80.2%)
PRO Not Completed	11 (31.4%)	6 (11.8%)	17 (19.8%)
C5D15			
PRO Expected	35 (94.6%)	50 (86.2%)	85 (89.5%)
PRO Completed	25 (71.4%)	41 (82.0%)	66 (77.6%)
PRO Not Completed	10 (28.6%)	9 (18.0%)	19 (22.4%)
C7D15			
PRO Expected	32 (86.5%)	46 (79.3%)	78 (82.1%)
PRO Completed	25 (78.1%)	38 (82.6%)	63 (80.8%)
PRO Not Completed	7 (21.9%)	8 (17.4%)	15 (19.2%)
C9D15			
PRO Expected	30 (81.1%)	46 (79.3%)	76 (80.0%)
PRO Completed	23 (76.7%)	38 (82.6%)	61 (80.3%)
PRO Not Completed	7 (23.3%)	8 (17.4%)	15 (19.7%)

NRS-11: Numeric Rating Scale-11; ET: Early Termination; SFU: Safety Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as completing the NRS-11 for a given visit if < 4 of the 7 NRS-11 readings were missing.
 Percentages completed/Not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_nrs11ce.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 13: Compliance Rate for NRS-11 by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C13D15			
PRO Expected	25 (67.6%)	36 (62.1%)	61 (64.2%)
PRO Completed	15 (60.0%)	24 (66.7%)	39 (63.9%)
PRO Not Completed	10 (40.0%)	12 (33.3%)	22 (36.1%)
C17D15			
PRO Expected	23 (62.2%)	34 (58.6%)	57 (60.0%)
PRO Completed	18 (78.3%)	22 (64.7%)	40 (70.2%)
PRO Not Completed	5 (21.7%)	12 (35.3%)	17 (29.8%)
C21D15			
PRO Expected	21 (56.8%)	32 (55.2%)	53 (55.8%)
PRO Completed	11 (52.4%)	17 (53.1%)	28 (52.8%)
PRO Not Completed	10 (47.6%)	15 (46.9%)	25 (47.2%)
C24D21			
PRO Expected	19 (51.4%)	31 (53.4%)	50 (52.6%)
PRO Completed	8 (42.1%)	18 (58.1%)	26 (52.0%)
PRO Not Completed	11 (57.9%)	13 (41.9%)	24 (48.0%)
ET			
PRO Expected	19 (51.4%)	28 (48.3%)	47 (49.5%)
PRO Completed	6 (31.6%)	8 (28.6%)	14 (29.8%)
PRO Not Completed	13 (68.4%)	20 (71.4%)	33 (70.2%)

NRS-11: Numeric Rating Scale-11; ET: Early Termination; SFU: Safety Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as completing the NRS-11 for a given visit if < 4 of the 7 NRS-11 readings were missing.
 Percentages completed/Not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_nrs11ce.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 13: Compliance Rate for NRS-11 by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
SFU			
PRO Expected	24 (64.9%)	39 (67.2%)	63 (66.3%)
PRO Completed	4 (16.7%)	7 (17.9%)	11 (17.5%)
PRO Not Completed	20 (83.3%)	32 (82.1%)	52 (82.5%)

NRS-11: Numeric Rating Scale-11; ET: Early Termination; SFU: Safety Follow-Up.
N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
Participants are considered as completing the NRS-11 for a given visit if < 4 of the 7 NRS-11 readings were missing.
Percentages completed/Not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_nrs11ce.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 15: Compliance Rate for PII by Visit: Full Analysis Set

	Pediatric Self-Report (N=47)	Adult (N=58)	Total (N=105)
Baseline			
PRO Expected	47 (100%)	58 (100%)	105 (100%)
PRO Completed	45 (95.7%)	52 (89.7%)	97 (92.4%)
PRO Not Completed	2 (4.3%)	6 (10.3%)	8 (7.6%)
C3D15			
PRO Expected	45 (95.7%)	51 (87.9%)	96 (91.4%)
PRO Completed	30 (66.7%)	45 (88.2%)	75 (78.1%)
PRO Not Completed	15 (33.3%)	6 (11.8%)	21 (21.9%)
C5D15			
PRO Expected	45 (95.7%)	50 (86.2%)	95 (90.5%)
PRO Completed	32 (71.1%)	41 (82.0%)	73 (76.8%)
PRO Not Completed	13 (28.9%)	9 (18.0%)	22 (23.2%)
C7D15			
PRO Expected	42 (89.4%)	46 (79.3%)	88 (83.8%)
PRO Completed	34 (81.0%)	38 (82.6%)	72 (81.8%)
PRO Not Completed	8 (19.0%)	8 (17.4%)	16 (18.2%)

PII: Pain Interference Index; ET: Early Termination; SFU: Safety Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

A participant is considered as completing the PII assessment at a visit if < 4 of the 7 PII daily assessments were missing. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_piior.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 15: Compliance Rate for PII by Visit: Full Analysis Set

	Pediatric Self-Report (N=47)		Adult (N=58)	Total (N=105)
C9D15	PRO Expected	40 (85.1%)	46 (79.3%)	86 (81.9%)
	PRO Completed	31 (77.5%)	38 (82.6%)	69 (80.2%)
	PRO Not Completed	9 (22.5%)	8 (17.4%)	17 (19.8%)
C13D15	PRO Expected	35 (74.5%)	36 (62.1%)	71 (67.6%)
	PRO Completed	20 (57.1%)	24 (66.7%)	44 (62.0%)
	PRO Not Completed	15 (42.9%)	12 (33.3%)	27 (38.0%)
C17D15	PRO Expected	33 (70.2%)	34 (58.6%)	67 (63.8%)
	PRO Completed	25 (75.8%)	22 (64.7%)	47 (70.1%)
	PRO Not Completed	8 (24.2%)	12 (35.3%)	20 (29.9%)
C21D15	PRO Expected	30 (63.8%)	32 (55.2%)	62 (59.0%)
	PRO Completed	17 (56.7%)	17 (53.1%)	34 (54.8%)
	PRO Not Completed	13 (43.3%)	15 (46.9%)	28 (45.2%)

PII: Pain Interference Index; ET: Early Termination; SFU: Safety Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

A participant is considered as completing the PII assessment at a visit if < 4 of the 7 PII daily assessments were missing. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_piior.sas Output Generated: 2025-05-02T13:32 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 15: Compliance Rate for PII by Visit: Full Analysis Set

	Pediatric Self-Report (N=47)	Adult (N=58)	Total (N=105)
C24D21			
PRO Expected	27 (57.4%)	31 (53.4%)	58 (55.2%)
PRO Completed	12 (44.4%)	18 (58.1%)	30 (51.7%)
PRO Not Completed	15 (55.6%)	13 (41.9%)	28 (48.3%)
ET			
PRO Expected	20 (42.6%)	28 (48.3%)	48 (45.7%)
PRO Completed	7 (35.0%)	9 (32.1%)	16 (33.3%)
PRO Not Completed	13 (65.0%)	19 (67.9%)	32 (66.7%)
SFU			
PRO Expected	26 (55.3%)	39 (67.2%)	65 (61.9%)
PRO Completed	4 (15.4%)	7 (17.9%)	11 (16.9%)
PRO Not Completed	22 (84.6%)	32 (82.1%)	54 (83.1%)

PII: Pain Interference Index; ET: Early Termination; SFU: Safety Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

A participant is considered as completing the PII assessment at a visit if < 4 of the 7 PII daily assessments were missing. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_piicr.sas Output Generated: 2025-05-02T13:32 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Baseline			
n (%)	36 (97.3%)	51 (87.9%)	87 (91.6%)
Mean (SD)	1.89 (2.343)	4.15 (2.769)	3.22 (2.818)
Median	1.00	4.67	3.00
Min, Max	0.0, 9.2	0.0, 8.7	0.0, 9.2

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C3D15			
n (%)	24 (64.9%)	46 (79.3%)	70 (73.7%)
Mean (SD)	0.89 (1.496)	3.29 (2.992)	2.47 (2.809)
Median	0.07	2.92	1.28
Min, Max	0.0, 6.2	0.0, 9.6	0.0, 9.6
Change from Baseline at C3D15			
n (%)	23 (62.2%)	42 (72.4%)	65 (68.4%)
Mean (SD)	-0.85 (1.907)	-1.02 (1.576)	-0.96 (1.688)
Median	-0.14	-0.59	-0.43
Min, Max	-7.5, 1.6	-5.0, 1.3	-7.5, 1.6
LS Mean (SE)	-0.71 (0.232)	-0.88 (0.245)	-0.75 (0.183)
95% CI	(-1.17, -0.25)	(-1.36, -0.40)	(-1.11, -0.38)
p-value	0.003	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
The NRS-11 assesses target tumor pain on a scale from 0 = "no pain" to 10 = "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
CSD15			
n (%)	25 (67.6%)	41 (70.7%)	66 (69.5%)
Mean (SD)	0.99 (2.147)	2.61 (2.881)	2.00 (2.728)
Median	0.00	1.83	0.72
Min, Max	0.0, 9.3	0.0, 9.3	0.0, 9.3
Change from Baseline at CSD15			
n (%)	25 (67.6%)	37 (63.8%)	62 (65.3%)
Mean (SD)	-0.78 (1.713)	-1.38 (1.737)	-1.14 (1.738)
Median	-0.17	-0.62	-0.58
Min, Max	-7.5, 1.3	-6.0, 1.3	-7.5, 1.3
LS Mean (SE)	-0.76 (0.322)	-1.26 (0.266)	-1.06 (0.191)
95% CI	(-1.40, -0.12)	(-1.79, -0.74)	(-1.44, -0.68)
p-value	0.020	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
 The NRS-11 assesses target tumor pain on a scale from 0 = "no pain" to 10 = "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C7D15			
n (%)	25 (67.6%)	40 (69.0%)	65 (68.4%)
Mean (SD)	0.92 (1.429)	2.59 (2.746)	1.95 (2.455)
Median	0.29	1.55	0.75
Min, Max	0.0, 5.0	0.0, 9.0	0.0, 9.0
Change from Baseline at C7D15			
n (%)	24 (64.9%)	36 (62.1%)	60 (63.2%)
Mean (SD)	-1.04 (1.643)	-1.21 (1.346)	-1.14 (1.461)
Median	-0.34	-1.23	-0.93
Min, Max	-5.9, 0.8	-5.4, 1.8	-5.9, 1.8
LS Mean (SE)	-0.98 (0.193)	-1.41 (0.223)	-1.29 (0.175)
95% CI	(-1.36, -0.60)	(-1.85, -0.96)	(-1.64, -0.94)
p-value	<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
 The NRS-11 assesses target tumor pain on a scale from 0 = "no pain" to 10 = "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

		Pediatric (N=37)	Adult (N=58)	Total (N=95)
C9D15	n (%)	24 (64.9%)	39 (67.2%)	63 (66.3%)
	Mean (SD)	0.68 (1.107)	2.27 (2.774)	1.66 (2.403)
	Median	0.07	1.00	0.20
	Min, Max	0.0, 4.2	0.0, 10.0	0.0, 10.0
Change from Baseline at C9D15				
SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11. The NRS-11 assesses target tumor pain on a scale from 0 = "no pain" to 10 = "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score. Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.	n (%)	23 (62.2%)	35 (60.3%)	58 (61.1%)
	Mean (SD)	-0.67 (1.188)	-1.59 (1.502)	-1.23 (1.448)
	Median	-0.33	-1.14	-1.00
	Min, Max	-4.2, 2.0	-5.7, 0.2	-5.7, 2.0
	LS Mean (SE)	-0.98 (0.183)	-1.54 (0.241)	-1.31 (0.171)
	95% CI	(-1.34, -0.62)	(-2.02, -1.07)	(-1.65, -0.97)
p-value		<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
The NRS-11 assesses target tumor pain on a scale from 0 = "no pain" to 10 = "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C13D15			
n (%)	17 (45.9%)	24 (41.4%)	41 (43.2%)
Mean (SD)	0.92 (1.119)	1.74 (2.174)	1.40 (1.840)
Median	0.75	0.86	0.75
Min, Max	0.0, 3.8	0.0, 6.7	0.0, 6.7
Change from Baseline at			
C13D15			
n (%)	17 (45.9%)	21 (36.2%)	38 (40.0%)
Mean (SD)	-1.24 (2.354)	-1.27 (1.550)	-1.25 (1.922)
Median	-0.60	-1.14	-0.91
Min, Max	-8.5, 1.7	-4.5, 1.1	-8.5, 1.7
LS Mean (SE)	-0.80 (0.228)	-1.32 (0.282)	-1.18 (0.191)
95% CI	(-1.25, -0.34)	(-1.88, -0.77)	(-1.56, -0.80)
p-value	<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C17D15			
n (%)	18 (48.6%)	22 (37.9%)	40 (42.1%)
Mean (SD)	0.88 (1.140)	1.72 (2.235)	1.34 (1.853)
Median	0.50	0.44	0.50
Min, Max	0.0, 3.3	0.0, 7.1	0.0, 7.1
Change from Baseline at			
C17D15			
n (%)	18 (48.6%)	21 (36.2%)	39 (41.1%)
Mean (SD)	-0.92 (1.325)	-1.73 (1.785)	-1.36 (1.622)
Median	-0.24	-1.10	-0.82
Min, Max	-3.7, 0.5	-5.7, 0.7	-5.7, 0.7
LS Mean (SE)	-0.87 (0.200)	-1.40 (0.268)	-1.32 (0.179)
95% CI	(-1.26, -0.47)	(-1.93, -0.87)	(-1.68, -0.96)
p-value	<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
 The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C21D15			
n (%)	11 (29.7%)	17 (29.3%)	28 (29.5%)
Mean (SD)	0.52 (0.617)	1.94 (2.434)	1.38 (2.038)
Median	0.00	0.50	0.25
Min, Max	0.0, 1.4	0.0, 6.7	0.0, 6.7
Change from Baseline at			
C21D15			
n (%)	11 (29.7%)	16 (27.6%)	27 (28.4%)
Mean (SD)	-0.79 (1.761)	-1.23 (1.493)	-1.05 (1.590)
Median	0.00	-0.46	-0.17
Min, Max	-4.2, 0.9	-4.1, 0.7	-4.2, 0.9
LS Mean (SE)	-0.95 (0.274)	-1.56 (0.258)	-1.38 (0.192)
95% CI	(-1.49, -0.41)	(-2.06, -1.05)	(-1.76, -1.00)
p-value	<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.

The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 3: NRS-11 Score by Visit: Full Analysis Set

	Pediatric (N=37)	Adult (N=58)	Total (N=95)
C24D21			
n (%)	8 (21.6%)	18 (31.0%)	26 (27.4%)
Mean (SD)	0.56 (0.907)	2.13 (2.457)	1.65 (2.210)
Median	0.00	1.18	0.90
Min, Max	0.0, 2.5	0.0, 7.3	0.0, 7.3
Change from Baseline at			
C24D21			
n (%)	8 (21.6%)	17 (29.3%)	25 (26.3%)
Mean (SD)	-0.78 (1.744)	-1.26 (1.306)	-1.11 (1.440)
Median	-0.07	-1.07	-0.43
Min, Max	-4.2, 1.2	-4.1, 1.0	-4.2, 1.2
LS Mean (SE)	-1.03 (0.268)	-1.44 (0.249)	-1.19 (0.207)
95% CI	(-1.56, -0.50)	(-1.93, -0.95)	(-1.60, -0.78)
p-value	<0.001	<0.001	<0.001

SD: Standard deviation; Min: Minimum; Max: Maximum; NRS-11: Numeric Rating Scale-11.
 The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". NRS-11 assessments were performed for six days prior to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Baseline is defined as the most recent NRS-11 score taken on or before treatment start date.

Program Name: t_nrs11.sas Output Generated: 2025-05-02T14:25 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
Baseline			
n (%)	45 (95.7%)	52 (89.7%)	97 (92.4%)
Mean (SD)	0.93 (1.282)	2.29 (1.683)	1.66 (1.649)
Median	0.47	2.62	1.08
Min, Max	0, 5.4	0, 5.3	0, 5.4

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.
The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".
PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Program Name: t_pii.sas Output Generated: 2025-05-02T14:26 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15			
n (%)	30 (63.8%)	46 (79.3%)	76 (72.4%)
Mean (SD)	0.42 (0.812)	1.64 (1.599)	1.16 (1.466)
Median	0.03	0.95	0.50
Min, Max	0, 3.6	0, 5.9	0, 5.9
Change from Baseline at C3D15			
n (%)	29 (61.7%)	43 (74.1%)	72 (68.6%)
Mean (SD)	-0.35 (0.786)	-0.67 (1.116)	-0.54 (1.002)
Median	-0.12	-0.46	-0.24
Min, Max	-3.8, 0.5	-3.3, 1.4	-3.8, 1.4
LS Mean (SE)	-0.24 (0.125)	-0.47 (0.173)	-0.40 (0.095)
95% CI	(-0.49, 0.01)	(-0.81, -0.13)	(-0.59, -0.21)
p-value	0.058	0.007	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Program Name: t_pii.sas Output Generated: 2025-05-02T14:26 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C5D15			
n (%)	32 (68.1%)	41 (70.7%)	73 (69.5%)
Mean (SD)	0.62 (1.210)	1.37 (1.649)	1.04 (1.511)
Median	0.02	0.60	0.21
Min, Max	0, 5.2	0, 5.9	0, 5.9
Change from Baseline at C5D15			
n (%)	32 (68.1%)	38 (65.5%)	70 (66.7%)
Mean (SD)	-0.30 (0.784)	-0.83 (1.133)	-0.59 (1.017)
Median	-0.11	-0.51	-0.28
Min, Max	-3.8, 1.0	-3.7, 1.0	-3.8, 1.0
LS Mean (SE)	-0.32 (0.120)	-0.66 (0.167)	-0.50 (0.099)
95% CI	(-0.56, -0.08)	(-0.99, -0.33)	(-0.69, -0.30)
p-value	0.009	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C7D15			
n (%)	34 (72.3%)	40 (69.0%)	74 (70.5%)
Mean (SD)	0.59 (1.208)	1.45 (1.662)	1.05 (1.524)
Median	0.10	0.65	0.18
Min, Max	0, 5.6	0, 5.5	0, 5.6
Change from Baseline at C7D15			
n (%)	33 (70.2%)	37 (63.8%)	70 (66.7%)
Mean (SD)	-0.36 (0.755)	-0.65 (0.918)	-0.51 (0.851)
Median	-0.14	-0.40	-0.33
Min, Max	-3.0, 1.4	-3.5, 0.6	-3.5, 1.4
LS Mean (SE)	-0.50 (0.168)	-0.66 (0.167)	-0.57 (0.107)
95% CI	(-0.83, -0.17)	(-0.99, -0.33)	(-0.78, -0.35)
p-value	0.003	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C9D15			
n (%)	32 (68.1%)	39 (67.2%)	71 (67.6%)
Mean (SD)	0.50 (1.116)	1.26 (1.583)	0.92 (1.434)
Median	0.13	0.33	0.17
Min, Max	0, 4.8	0, 4.6	0, 4.8
Change from Baseline at C9D15			
n (%)	31 (66.0%)	36 (62.1%)	67 (63.8%)
Mean (SD)	-0.22 (0.474)	-0.88 (1.043)	-0.57 (0.887)
Median	-0.14	-0.53	-0.29
Min, Max	-1.8, 0.6	-3.5, 1.0	-3.5, 1.0
LS Mean (SE)	-0.46 (0.144)	-0.75 (0.170)	-0.61 (0.108)
95% CI	(-0.74, -0.17)	(-1.08, -0.41)	(-0.82, -0.40)
p-value	0.002	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C13D15			
n (%)	22 (46.8%)	24 (41.4%)	46 (43.8%)
Mean (SD)	0.66 (0.982)	0.97 (1.228)	0.82 (1.116)
Median	0.10	0.24	0.13
Min, Max	0, 3.3	0, 3.3	0, 3.3
Change from Baseline at C13D15			
n (%)	22 (46.8%)	22 (37.9%)	44 (41.9%)
Mean (SD)	-0.41 (1.246)	-0.73 (1.032)	-0.57 (1.142)
Median	-0.24	-0.45	-0.31
Min, Max	-4.9, 1.1	-3.3, 0.6	-4.9, 1.1
LS Mean (SE)	-0.63 (0.264)	-0.73 (0.163)	-0.61 (0.120)
95% CI	(-1.15, -0.11)	(-1.06, -0.41)	(-0.85, -0.37)
p-value	0.018	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15			
n (%)	25 (53.2%)	22 (37.9%)	47 (44.8%)
Mean (SD)	0.57 (1.058)	0.88 (1.116)	0.72 (1.084)
Median	0	0.58	0.17
Min, Max	0, 4.0	0, 3.7	0, 4.0
Change from Baseline at C17D15			
n (%)	25 (53.2%)	21 (36.2%)	46 (43.8%)
Mean (SD)	-0.39 (0.723)	-0.84 (1.036)	-0.59 (0.899)
Median	-0.11	-0.63	-0.27
Min, Max	-2.1, 1.1	-2.8, 0.7	-2.8, 1.1
LS Mean (SE)	-0.45 (0.161)	-0.73 (0.145)	-0.61 (0.106)
95% CI	(-0.77, -0.14)	(-1.02, -0.45)	(-0.82, -0.40)
p-value	0.005	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C21D15			
n (%)	17 (36.2%)	17 (29.3%)	34 (32.4%)
Mean (SD)	0.52 (0.943)	1.07 (1.461)	0.79 (1.243)
Median	0.04	0.44	0.07
Min, Max	0, 3.7	0, 4.3	0, 4.3
Change from Baseline at C21D15			
n (%)	17 (36.2%)	16 (27.6%)	33 (31.4%)
Mean (SD)	-0.27 (0.798)	-0.61 (0.867)	-0.43 (0.837)
Median	-0.07	-0.38	-0.24
Min, Max	-2.7, 1.4	-2.7, 0.9	-2.7, 1.4
LS Mean (SE)	-0.57 (0.207)	-0.77 (0.143)	-0.65 (0.122)
95% CI	(-0.98, -0.16)	(-1.06, -0.49)	(-0.89, -0.41)
p-value	0.007	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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Table 5: PII Scores by Visit - Self Report: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C24D21			
n (%)	12 (25.5%)	18 (31.0%)	30 (28.6%)
Mean (SD)	0.35 (0.521)	0.98 (1.319)	0.73 (1.105)
Median	0.04	0.38	0.12
Min, Max	0, 1.5	0, 3.8	0, 3.8
Change from Baseline at C24D21			
n (%)	12 (25.5%)	17 (29.3%)	29 (27.6%)
Mean (SD)	-0.27 (0.994)	-0.72 (0.998)	-0.53 (1.004)
Median	0	-0.31	-0.09
Min, Max	-3.0, 0.9	-3.1, 0.6	-3.1, 0.9
LS Mean (SE)	-0.35 (0.242)	-0.73 (0.197)	-0.61 (0.137)
95% CI	(-0.83, 0.12)	(-1.12, -0.34)	(-0.88, -0.34)
p-value	0.145	<0.001	<0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; PII: Pain Interference Index.

The PII assesses the degree to which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely".

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Program Name: t_pii.sas Output Generated: 2025-05-02T14:26 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 53.11: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	42 (72.4%)	65 (68.4%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	16 (27.6%)	30 (31.6%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.7%)	0	1 (1.1%)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	25 (67.6%)	37 (63.8%)	62 (65.3%)
Number of Participants Missing the Assessment, n (%)	12 (32.4%)	21 (36.2%)	33 (34.7%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0

NRS-11: Numeric Rating Scale-11.

N represents the number of participants in the corresponding cohort.

The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_wrnsn_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 53.11: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	24 (64.9%)	36 (62.1%)	60 (63.2%)
Number of Participants Missing the Assessment, n (%)	13 (35.1%)	22 (37.9%)	35 (36.8%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.7%)	1 (1.1%)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	35 (60.3%)	58 (61.1%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	23 (39.7%)	37 (38.9%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.7%)	0	1 (1.1%)

NRS-11: Numeric Rating Scale-11.

N represents the number of participants in the corresponding cohort.

The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_wrsn_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 53.11: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	17 (45.9%)	21 (36.2%)	38 (40.0%)
Number of Participants Missing the Assessment, n (%)	20 (54.1%)	37 (63.8%)	57 (60.0%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.7%)	0	1 (1.1%)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	18 (48.6%)	21 (36.2%)	39 (41.1%)
Number of Participants Missing the Assessment, n (%)	19 (51.4%)	37 (63.8%)	56 (58.9%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0

NRS-11: Numeric Rating Scale-11.

N represents the number of participants in the corresponding cohort.

The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_wrnsn_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

Table 53.11: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Worsening by >=15% (1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	11 (29.7%)	16 (27.6%)	27 (28.4%)
Number of Participants Missing the Assessment, n (%)	26 (70.3%)	42 (72.4%)	68 (71.6%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	8 (21.6%)	17 (29.3%)	25 (26.3%)
Number of Participants Missing the Assessment, n (%)	29 (78.4%)	41 (70.7%)	70 (73.7%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0

NRS-11: Numeric Rating Scale-11.
N represents the number of participants in the corresponding cohort.
The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_wrnsn_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

Table 53.11: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Worsening by >=15% (1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Total			
Number of Participants Completed the Assessment, n (%)	33 (89.2%)	46 (79.3%)	79 (83.2%)
Number of Participants Missing the Assessment, n (%)	4 (10.8%)	12 (20.7%)	16 (16.8%)
Threshold for Meaningful Score Difference	1.5	1.5	1.5
Participants with Clinically Meaningful Score Worsening, n (%)	3 (8.1%)	1 (1.7%)	4 (4.2%)

NRS-11: Numeric Rating Scale-11.
N represents the number of participants in the corresponding cohort.
The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_wrnsn_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 53.3: Anchor-Based Analysis of Meaningful NRS-11 Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)
Visit C3D15		
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	42 (72.4%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	16 (27.6%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	12 (20.7%)
95% CI	(7.5, 43.7)	(15.7, 44.6)
Visit C5D15		
Number of Participants Completed the Assessment, n (%)	25 (67.6%)	37 (63.8%)
Number of Participants Missing the Assessment, n (%)	12 (32.4%)	21 (36.2%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	4 (10.8%)	14 (24.1%)
95% CI	(4.5, 36.1)	(22.5, 55.2)

NRS-11: Numeric Rating Scale-11; CI: Confidence Interval.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. 95% CIs are derived using the Clopper-Pearson approach.

The NRS-11 assesses target tumor pain on a scale from 0 – "no pain" to 10 – "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 53.3: Anchor-Based Analysis of Meaningful NRS-11 Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)
Visit C7D15		
Number of Participants Completed the Assessment, n (%)	24 (64.9%)	36 (62.1%)
Number of Participants Missing the Assessment, n (%)	13 (35.1%)	22 (37.9%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	15 (25.9%)
95% CI	(7.1, 42.2)	(25.5, 59.2)
Visit C9D15		
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	35 (60.3%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	23 (39.7%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	3 (8.1%)	15 (25.9%)
95% CI	(2.8, 33.6)	(26.3, 60.6)

NRS-11: Numeric Rating Scale-11; CI: Confidence Interval.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. 95% CIs are derived using the Clopper-Pearson approach.

The NRS-11 assesses target tumor pain on a scale from 0 – "no pain" to 10 – "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 53.3: Anchor-Based Analysis of Meaningful NRS-11 Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)
Visit C13D15		
Number of Participants Completed the Assessment, n (%)	17 (45.9%)	21 (36.2%)
Number of Participants Missing the Assessment, n (%)	20 (54.1%)	37 (63.8%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	9 (15.5%)
95% CI	(10.3, 56.0)	(21.8, 66.0)
Visit C17D15		
Number of Participants Completed the Assessment, n (%)	18 (48.6%)	21 (36.2%)
Number of Participants Missing the Assessment, n (%)	19 (51.4%)	37 (63.8%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	10 (17.2%)
95% CI	(9.7, 53.5)	(25.7, 70.2)

NRS-11: Numeric Rating Scale-11; CI: Confidence Interval.

N represents the number of participants in the corresponding cohort.
The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan.A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. 95% CIs are derived using the Clopper-Pearson approach.
The NRS-11 assesses target tumor pain on a scale from 0 – "no pain" to 10 – "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 53.3: Anchor-Based Analysis of Meaningful NRS-11 Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)
Visit C21D15		
Number of Participants Completed the Assessment, n (%)	11 (29.7%)	16 (27.6%)
Number of Participants Missing the Assessment, n (%)	26 (70.3%)	42 (72.4%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	3 (8.1%)	7 (12.1%)
95% CI	(6.0, 61.0)	(19.8, 70.1)
Visit C24D21		
Number of Participants Completed the Assessment, n (%)	8 (21.6%)	17 (29.3%)
Number of Participants Missing the Assessment, n (%)	29 (78.4%)	41 (70.7%)
Threshold for Meaningful Score Difference	-1.7	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	2 (5.4%)	7 (12.1%)
95% CI	(3.2, 65.1)	(18.4, 67.1)

NRS-11: Numeric Rating Scale-11; CI: Confidence Interval.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. 95% CIs are derived using the Clopper-Pearson approach.

The NRS-11 assesses target tumor pain on a scale from 0 – "no pain" to 10 – "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

Table 53.3: Anchor-Based Analysis of Meaningful NRS-11 Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric (N=37)		Adult (N=58)	
Total				
Number of Participants Completed the Assessment, n (%)	33 (89.2%)		46 (79.3%)	
Number of Participants Missing the Assessment, n (%)	4 (10.8%)		12 (20.7%)	
Threshold for Meaningful Score Difference	-1.7		-1.5	
Participants with Clinically Meaningful Score Improvement, n (%)	10 (27.0%)		26 (44.8%)	
95% CI	(15.6, 48.7)		(41.1, 71.1)	

NRS-11: Numeric Rating Scale-11; CI: Confidence Interval.
N represents the number of participants in the corresponding cohort.
The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. 95% CIs are derived using the Clopper-Pearson approach.
The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

Table 53.7: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Improvement by >=15% (-1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	42 (72.4%)	65 (68.4%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	16 (27.6%)	30 (31.6%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	12 (20.7%)	17 (17.9%)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	25 (67.6%)	37 (63.8%)	62 (65.3%)
Number of Participants Missing the Assessment, n (%)	12 (32.4%)	21 (36.2%)	33 (34.7%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	6 (16.2%)	14 (24.1%)	20 (21.1%)

NRS-11: Numeric Rating Scale-11.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.
The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

SpringWorks Therapeutics

MEK-NF-201
GBATable 53.7: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	24 (64.9%)	36 (62.1%)	60 (63.2%)
Number of Participants Missing the Assessment, n (%)	13 (35.1%)	22 (37.9%)	35 (36.8%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	15 (25.9%)	20 (21.1%)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	23 (62.2%)	35 (60.3%)	58 (61.1%)
Number of Participants Missing the Assessment, n (%)	14 (37.8%)	23 (39.7%)	37 (38.9%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	15 (25.9%)	20 (21.1%)

NRS-11: Numeric Rating Scale-11.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.

The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_impr_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 53.7: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	17 (45.9%)	21 (36.2%)	38 (40.0%)
Number of Participants Missing the Assessment, n (%)	20 (54.1%)	37 (63.8%)	57 (60.0%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	9 (15.5%)	14 (14.7%)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	18 (48.6%)	21 (36.2%)	39 (41.1%)
Number of Participants Missing the Assessment, n (%)	19 (51.4%)	37 (63.8%)	56 (58.9%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	5 (13.5%)	10 (17.2%)	15 (15.8%)

NRS-11: Numeric Rating Scale-11.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.

The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". Lower scores indicate decreased pain.

NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.

The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_impr_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

Table 53.7: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Improvement by >=15% (-1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	11 (29.7%)	16 (27.6%)	27 (28.4%)
Number of Participants Missing the Assessment, n (%)	26 (70.3%)	42 (72.4%)	68 (71.6%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	3 (8.1%)	7 (12.1%)	10 (10.5%)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	8 (21.6%)	17 (29.3%)	25 (26.3%)
Number of Participants Missing the Assessment, n (%)	29 (78.4%)	41 (70.7%)	70 (73.7%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	2 (5.4%)	7 (12.1%)	9 (9.5%)

NRS-11: Numeric Rating Scale-11.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.
The NRS-11 assesses target tumor pain on a scale from 0 - "no pain" to 10 - "worst pain you can imagine". Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

Table 53.7: Meaningful NRS-11 Score Difference - Non-Responder Imputation - Improvement by >=15% (-1.5): Full Analysis Set

Visits	Pediatric (N=37)	Adult (N=58)	Total (N=95)
Total			
Number of Participants Completed the Assessment, n (%)	33 (89.2%)	46 (79.3%)	79 (83.2%)
Number of Participants Missing the Assessment, n (%)	4 (10.8%)	12 (20.7%)	16 (16.8%)
Threshold for Meaningful Score Difference	-1.5	-1.5	-1.5
Participants with Clinically Meaningful Score Improvement, n (%)	12 (32.4%)	26 (44.8%)	38 (40.0%)

NRS-11: Numeric Rating Scale-11.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.
The NRS-11 assesses target tumor pain on a scale from 0 – “no pain” to 10 – “worst pain you can imagine”. Lower scores indicate decreased pain.
NRS-11 assessments were performed for six days prior to a visit as well as on the visit day.
The mean of these seven assessments is taken as the visit score.

Program Name: t_nrs_impr_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.11: Meaningful PII Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	29 (61.7%)	27 (57.4%)	43 (74.1%)	72 (68.6%)
Number of Participants Missing the Assessment, n (%)	18 (38.3%)	20 (42.6%)	15 (25.9%)	33 (31.4%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	0	0	2 (3.4%)	2 (1.9%)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	32 (68.1%)	26 (55.3%)	38 (65.5%)	70 (66.7%)
Number of Participants Missing the Assessment, n (%)	15 (31.9%)	21 (44.7%)	20 (34.5%)	35 (33.3%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	1 (2.1%)	0	1 (1.7%)	2 (1.9%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score. Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_wrsn_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.11: Meaningful PII Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	33 (70.2%)	28 (59.6%)	37 (63.8%)	70 (66.7%)
Number of Participants Missing the Assessment, n (%)	14 (29.8%)	19 (40.4%)	21 (36.2%)	35 (33.3%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	0	0	1 (1.0%)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	31 (66.0%)	26 (55.3%)	36 (62.1%)	67 (63.8%)
Number of Participants Missing the Assessment, n (%)	16 (34.0%)	21 (44.7%)	22 (37.9%)	38 (36.2%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	1 (1.7%)	1 (1.0%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET

visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_wrsn_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.11: Meaningful PII Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	22 (46.8%)	20 (42.6%)	22 (37.9%)	44 (41.9%)
Number of Participants Missing the Assessment, n (%)	25 (53.2%)	27 (57.4%)	36 (62.1%)	61 (58.1%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	2 (4.3%)	1 (2.1%)	0	2 (1.9%)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	25 (53.2%)	20 (42.6%)	21 (36.2%)	46 (43.8%)
Number of Participants Missing the Assessment, n (%)	22 (46.8%)	27 (57.4%)	37 (63.8%)	59 (56.2%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	1 (2.1%)	1 (2.1%)	0	1 (1.0%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET

visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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SpringWorks Therapeutics

MEK-NF-201
GBATable 54.11: Meaningful PII Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	17 (36.2%)	14 (29.8%)	16 (27.6%)	33 (31.4%)
Number of Participants Missing the Assessment, n (%)	30 (63.8%)	33 (70.2%)	42 (72.4%)	72 (68.6%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	1 (2.1%)	1 (2.1%)	1 (1.7%)	2 (1.9%)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	12 (25.5%)	16 (34.0%)	17 (29.3%)	29 (27.6%)
Number of Participants Missing the Assessment, n (%)	35 (74.5%)	31 (66.0%)	41 (70.7%)	76 (72.4%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)				
	0	1 (2.1%)	0	0

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET

visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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SpringWorks Therapeutics

MEK-NF-201
GBATable 54.11: Meaningful PII Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Total				
Number of Participants Completed the Assessment, n (%)	42 (89.4%)	37 (78.7%)	47 (81.0%)	89 (84.8%)
Number of Participants Missing the Assessment, n (%)	5 (10.6%)	10 (21.3%)	11 (19.0%)	16 (15.2%)
Threshold for Meaningful Score Difference	0.9	0.9	0.9	0.9
Participants with Clinically Meaningful Score Worsening, n (%)	4 (8.5%)	3 (6.4%)	4 (6.9%)	8 (7.6%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score. Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBA

Table 54.3: Anchor-Based Analysis of Meaningful PII Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	29 (61.7%)		43 (74.1%)
Number of Participants Missing the Assessment, n (%)	18 (38.3%)		15 (25.9%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)		11 (19.0%)
95% CI	(3.9, 31.7)		(13.5, 41.2)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	32 (68.1%)		38 (65.5%)
Number of Participants Missing the Assessment, n (%)	15 (31.9%)		20 (34.5%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)		10 (17.2%)
95% CI	(3.5, 29.0)		(13.4, 43.1)

PII: Pain Interference Index; CI: Confidence Interval. N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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SpringWorks Therapeutics

MEK-NF-201
GBA

Table 54.3: Anchor-Based Analysis of Meaningful PII Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	33 (70.2%)		37 (63.8%)
Number of Participants Missing the Assessment, n (%)	14 (29.8%)		21 (36.2%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.8%)		9 (15.5%)
95% CI	(7.0, 35.5)		(11.8, 41.2)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	31 (66.0%)		36 (62.1%)
Number of Participants Missing the Assessment, n (%)	16 (34.0%)		22 (37.9%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.4%)		11 (19.0%)
95% CI	(2.0, 25.8)		(16.3, 48.1)

PII: Pain Interference Index; CI: Confidence Interval. N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Program Name: t_pii_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBA

Table 54.3: Anchor-Based Analysis of Meaningful PII Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	22 (46.8%)		22 (37.9%)
Number of Participants Missing the Assessment, n (%)	25 (53.2%)		36 (62.1%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)		6 (10.3%)
95% CI	(5.2, 40.3)		(10.7, 50.2)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	25 (53.2%)		21 (36.2%)
Number of Participants Missing the Assessment, n (%)	22 (46.8%)		37 (63.8%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.8%)		8 (13.8%)
95% CI	(9.4, 45.1)		(18.1, 61.6)

PII: Pain Interference Index; CI: Confidence Interval. N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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MEK-NF-201
GBA

Table 54.3: Anchor-Based Analysis of Meaningful PII Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	17 (36.2%)		16 (27.6%)
Number of Participants Missing the Assessment, n (%)	30 (63.8%)		42 (72.4%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.3%)		4 (6.9%)
95% CI	(1.5, 36.4)		(7.3, 52.4)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	12 (25.5%)		17 (29.3%)
Number of Participants Missing the Assessment, n (%)	35 (74.5%)		41 (70.7%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.3%)		4 (6.9%)
95% CI	(2.1, 48.4)		(6.8, 49.9)

PII: Pain Interference Index; CI: Confidence Interval. N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

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SpringWorks Therapeutics

MEK-NF-201
GBA

Table 54.3: Anchor-Based Analysis of Meaningful PII Score Difference - Non-Responder Imputation: Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	42 (89.4%)		47 (81.0%)
Number of Participants Missing the Assessment, n (%)	5 (10.6%)		11 (19.0%)
Threshold for Meaningful Score Difference	-0.7	n/a	-1.1
Participants with Clinically Meaningful Score Improvement, n (%)	10 (21.3%)		19 (32.8%)
95% CI	(12.1, 39.5)		(26.4, 55.7)

PII: Pain Interference Index; CI: Confidence Interval. N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities. PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Program Name: t_pii_anch_all_nr.sas Output Generated: 2025-05-02T13:35 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.7: Meaningful PII Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	29 (61.7%)	27 (57.4%)	43 (74.1%)	72 (68.6%)
Number of Participants Missing the Assessment, n (%)	18 (38.3%)	20 (42.6%)	15 (25.9%)	33 (31.4%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.4%)	3 (6.4%)	13 (22.4%)	16 (15.2%)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	32 (68.1%)	26 (55.3%)	38 (65.5%)	70 (66.7%)
Number of Participants Missing the Assessment, n (%)	15 (31.9%)	21 (44.7%)	20 (34.5%)	35 (33.3%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)	4 (8.5%)	11 (19.0%)	15 (14.3%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.
 The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.
 PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_impr_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.7: Meaningful PII Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	33 (70.2%)	28 (59.6%)	37 (63.8%)	70 (66.7%)
Number of Participants Missing the Assessment, n (%)	14 (29.8%)	19 (40.4%)	21 (36.2%)	35 (33.3%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.6%)	8 (17.0%)	11 (19.0%)	16 (15.2%)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	31 (66.0%)	26 (55.3%)	36 (62.1%)	67 (63.8%)
Number of Participants Missing the Assessment, n (%)	16 (34.0%)	21 (44.7%)	22 (37.9%)	38 (36.2%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.4%)	4 (8.5%)	12 (20.7%)	15 (14.3%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_impr_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.7: Meaningful PII Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	22 (46.8%)	20 (42.6%)	22 (37.9%)	44 (41.9%)
Number of Participants Missing the Assessment, n (%)	25 (53.2%)	27 (57.4%)	36 (62.1%)	61 (58.1%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)	4 (8.5%)	6 (10.3%)	10 (9.5%)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	25 (53.2%)	20 (42.6%)	21 (36.2%)	46 (43.8%)
Number of Participants Missing the Assessment, n (%)	22 (46.8%)	27 (57.4%)	37 (63.8%)	59 (56.2%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.8%)	6 (12.8%)	9 (15.5%)	15 (14.3%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.
 The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.
 PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_impr_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.7: Meaningful PII Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	17 (36.2%)	14 (29.8%)	16 (27.6%)	33 (31.4%)
Number of Participants Missing the Assessment, n (%)	30 (63.8%)	33 (70.2%)	42 (72.4%)	72 (68.6%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.3%)	2 (4.3%)	5 (8.6%)	7 (6.7%)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	12 (25.5%)	16 (34.0%)	17 (29.3%)	29 (27.6%)
Number of Participants Missing the Assessment, n (%)	35 (74.5%)	31 (66.0%)	41 (70.7%)	76 (72.4%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.3%)	2 (4.3%)	7 (12.1%)	9 (8.6%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.
PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_impr_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 54.7: Meaningful PII Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (-0.9): Full Analysis Set

Visits	Pediatric Self-Report (N=47)	Pediatric Parent Proxy (N=47)	Adult (N=58)	Total (N=105)
Total				
Number of Participants Completed the Assessment, n (%)	42 (89.4%)	37 (78.7%)	47 (81.0%)	89 (84.8%)
Number of Participants Missing the Assessment, n (%)	5 (10.6%)	10 (21.3%)	11 (19.0%)	16 (15.2%)
Threshold for Meaningful Score Difference	-0.9	-0.9	-0.9	-0.9
Participants with Clinically Meaningful Score Improvement, n (%)	10 (21.3%)	10 (21.3%)	23 (39.7%)	33 (31.4%)

PII: Pain Interference Index.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful score improvement if their change from baseline is less than or equal to the corresponding threshold.

The PII assesses the degree which pain has impacted the participants daily activities on a scale from 0 - "Not at all" to 6 - "Completely". Lower scores indicate decreased pain interference with participant's daily activities.

PII assessments were performed on the six days running up to a visit as well as on the visit day, except for the ET visit, which is done on the visit day only. The mean of these seven assessments is taken as the visit score.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pii_impr_all_nr.sas Output Generated: 2025-05-02T13:36 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 18: Compliance Rate for PROMIS by Visit: Full Analysis Set

	Pediatric						Adult	
	PROMIS SF v2.0 - Upper Extremity 8a			PROMIS SF v2.0 - Mobility 8a			PROMIS SF v2.0 - Physical Function 8b	
	Parent Proxy (N=4)		Self (N=3)	Parent Proxy (N=10)		Self (N=7)	Self (N=23)	
Baseline								
PRO Expected	4 (100%)	3 (100%)	3 (100%)	10 (100%)	7 (100%)	7 (100%)	23 (100%)	
PRO Completed	3 (75.0%)	2 (66.7%)	2 (66.7%)	7 (70.0%)	5 (71.4%)	5 (71.4%)	20 (87.0%)	
PRO Not Completed	1 (25.0%)	1 (33.3%)	1 (33.3%)	3 (30.0%)	2 (28.6%)	2 (28.6%)	3 (13.0%)	
C3D15								
PRO Expected	4 (100%)	3 (100%)	3 (100%)	8 (80.0%)	5 (71.4%)	5 (71.4%)	20 (87.0%)	
PRO Completed	2 (50.0%)	1 (33.3%)	1 (33.3%)	4 (50.0%)	3 (60.0%)	3 (60.0%)	17 (85.0%)	
PRO Not Completed	2 (50.0%)	2 (66.7%)	2 (66.7%)	4 (50.0%)	2 (40.0%)	2 (40.0%)	3 (15.0%)	
C5D15								
PRO Expected	4 (100%)	3 (100%)	3 (100%)	8 (80.0%)	5 (71.4%)	5 (71.4%)	20 (87.0%)	
PRO Completed	2 (50.0%)	2 (66.7%)	2 (66.7%)	5 (62.5%)	4 (80.0%)	4 (80.0%)	20 (100%)	
PRO Not Completed	2 (50.0%)	1 (33.3%)	1 (33.3%)	3 (37.5%)	1 (20.0%)	1 (20.0%)	0	
C7D15								
PRO Expected	3 (75.0%)	2 (66.7%)	2 (66.7%)	8 (80.0%)	5 (71.4%)	5 (71.4%)	18 (78.3%)	
PRO Completed	3 (100%)	2 (100%)	2 (100%)	6 (75.0%)	3 (60.0%)	3 (60.0%)	16 (88.9%)	
PRO Not Completed	0	0	0	2 (25.0%)	2 (40.0%)	2 (40.0%)	2 (11.1%)	

PROMIS: Patient-Reported Outcomes Measurement Information System.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_18_promis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 18: Compliance Rate for PROMIS by Visit: Full Analysis Set

	Pediatric						Adult	
	PROMIS SF V2.0 - Upper Extremity 8a			PROMIS SF V2.0 - Mobility 8a			PROMIS SF V2.0 - Physical Function 8b	
	Parent Proxy (N=4)		Self (N=3)	Parent Proxy (N=10)		Self (N=7)	Self (N=23)	
C9D15								
PRO Expected	3 (75.0%)	2 (66.7%)	2 (66.7%)	8 (80.0%)	5 (71.4%)	18 (78.3%)		
PRO Completed	2 (66.7%)	2 (100%)	0	8 (100%)	5 (100%)	15 (83.3%)		
PRO Not Completed	1 (33.3%)	0		0	0	3 (16.7%)		
C13D15								
PRO Expected	3 (75.0%)	2 (66.7%)	2 (66.7%)	6 (60.0%)	3 (42.9%)	15 (65.2%)		
PRO Completed	2 (66.7%)	2 (100%)	0	6 (100%)	3 (100%)	14 (93.3%)		
PRO Not Completed	1 (33.3%)	0		0	0	1 (6.7%)		
C17D15								
PRO Expected	3 (75.0%)	2 (66.7%)	2 (66.7%)	6 (60.0%)	3 (42.9%)	13 (56.5%)		
PRO Completed	2 (66.7%)	2 (100%)	0	4 (66.7%)	3 (100%)	9 (69.2%)		
PRO Not Completed	1 (33.3%)	0		2 (33.3%)	0	4 (30.8%)		
C21D15								
PRO Expected	3 (75.0%)	2 (66.7%)	2 (66.7%)	5 (50.0%)	3 (42.9%)	12 (52.2%)		
PRO Completed	3 (100%)	2 (100%)	0	3 (60.0%)	2 (66.7%)	11 (91.7%)		
PRO Not Completed	0	0		2 (40.0%)	1 (33.3%)	1 (8.3%)		

PROMIS: Patient-Reported Outcomes Measurement Information System.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_18_promis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 18: Compliance Rate for PROMIS by Visit: Full Analysis Set

	Pediatric						Adult	
	PROMIS SF v2.0 - Upper Extremity 8a			PROMIS SF v2.0 - Mobility 8a			PROMIS SF v2.0 - Physical Function 8b	
	Parent Proxy (N=4)		Self (N=3)	Parent Proxy (N=10)		Self (N=7)	Self (N=23)	
C24D21								
PRO Expected	2 (50.0%)	1 (33.3%)	1 (33.3%)	5 (50.0%)	3 (42.9%)	3 (42.9%)	11 (47.8%)	
PRO Completed	2 (100%)	1 (100%)	1 (100%)	2 (40.0%)	1 (33.3%)	1 (33.3%)	10 (90.9%)	
PRO Not Completed	0	0	0	3 (60.0%)	2 (66.7%)	2 (66.7%)	1 (9.1%)	
ET								
PRO Expected	1 (25.0%)	1 (33.3%)	1 (33.3%)	5 (50.0%)	4 (57.1%)	4 (57.1%)	12 (52.2%)	
PRO Completed	0	0	0	2 (40.0%)	1 (25.0%)	1 (25.0%)	4 (33.3%)	
PRO Not Completed	1 (100%)	1 (100%)	1 (100%)	3 (60.0%)	3 (75.0%)	3 (75.0%)	8 (66.7%)	
SFU								
PRO Expected	1 (25.0%)	1 (33.3%)	1 (33.3%)	5 (50.0%)	4 (57.1%)	4 (57.1%)	12 (52.2%)	
PRO Completed	0	0	0	1 (20.0%)	1 (25.0%)	1 (25.0%)	3 (25.0%)	
PRO Not Completed	1 (100%)	1 (100%)	1 (100%)	4 (80.0%)	3 (75.0%)	3 (75.0%)	9 (75.0%)	

PROMIS: Patient-Reported Outcomes Measurement Information System.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_18_promis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 32: PROMIS Physical Function Scale Score: Full Analysis Set		
		Adult (N=23)
Baseline		
n(%)	20 (87.0%)	
Mean (SD)	43.07 (9.513)	
Median	40.55	
Min, Max	27.5, 60.1	
C3D15		
n(%)	17 (73.9%)	
Mean (SD)	43.73 (10.508)	
Median	43.10	
Min, Max	27.5, 60.1	
Change from Baseline at C3D15		
n(%)	15 (65.2%)	
Mean (SD)	1.07 (5.949)	
Median	0	
Min, Max	-7.1, 20.6	
C5D15		
n(%)	20 (87.0%)	
Mean (SD)	44.33 (10.352)	
Median	44.30	
Min, Max	26.0, 60.1	
Change from Baseline at C5D15		
n(%)	18 (78.3%)	
Mean (SD)	1.23 (4.791)	
Median	0	
Min, Max	-5.3, 15.4	
SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.		
Program Name: t_promis_py.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20		

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Table 32: PROMIS Physical Function Scale Score: Full Analysis Set		
		Adult (N=23)
C7D15		
n(%)	18 (78.3%)	
Mean (SD)	45.69 (10.790)	
Median	46.15	
Min, Max	26.0, 60.1	
Change from Baseline at C7D15		
n(%)	16 (69.6%)	
Mean (SD)	4.05 (6.530)	
Median	1.60	
Min, Max	-1.6, 20.6	
C9D15		
n(%)	15 (65.2%)	
Mean (SD)	46.12 (10.016)	
Median	44.70	
Min, Max	30.8, 60.1	
Change from Baseline at C9D15		
n(%)	14 (60.9%)	
Mean (SD)	3.00 (8.489)	
Median	0.35	
Min, Max	-13.8, 20.6	
SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.		
Program Name: t_promis_py.sas Output Generated: 2025-05-02T14:31 Source: ADL, ADQS Data Cutoff Date: 2023-09-20		

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Table 32: PROMIS Physical Function Scale Score: Full Analysis Set		
		Adult (N=23)
C13D15		
n(%)	14 (60.9%)	
Mean (SD)	45.17 (8.452)	
Median	45.20	
Min, Max	31.7, 60.1	
Change from Baseline at C13D15		
n(%)	13 (56.5%)	
Mean (SD)	2.42 (9.447)	
Median	1.00	
Min, Max	-10.9, 20.6	
C17D15		
n(%)	9 (39.1%)	
Mean (SD)	43.43 (8.748)	
Median	43.90	
Min, Max	30.8, 60.1	
Change from Baseline at C17D15		
n(%)	8 (34.8%)	
Mean (SD)	0.43 (2.666)	
Median	0.50	
Min, Max	-3.9, 4.3	
SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.		
Program Name: t_promis_py.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20		

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Table 32: PROMIS Physical Function Scale Score: Full Analysis Set		
		Adult (N=23)
C21D15		
n(%)	11 (47.8%)	
Mean (SD)	47.90 (11.247)	
Median	46.70	
Min, Max	30.8, 60.1	
Change from Baseline at C21D15		
n(%)	10 (43.5%)	
Mean (SD)	1.85 (5.801)	
Median	0	
Min, Max	-7.6, 15.4	
C24D21		
n(%)	10 (43.5%)	
Mean (SD)	45.36 (10.293)	
Median	44.80	
Min, Max	30.8, 60.1	
Change from Baseline at C24D21		
n(%)	9 (39.1%)	
Mean (SD)	0.01 (6.923)	
Median	0	
Min, Max	-9.1, 15.4	
SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.		
Program Name: t_promis_py.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20		

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Table 33: PROMIS Mobility Scale Score: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Baseline		
n(%)	5 (71.4%)	7 (70.0%)
Mean (SD)	41.2 (11.03)	36.6 (6.00)
Median	46.0	38.0
Min, Max	25, 52	26, 42
C3D15		
n(%)	3 (42.9%)	4 (40.0%)
Mean (SD)	45.0 (1.73)	43.3 (3.69)
Median	46.0	43.0
Min, Max	43, 46	39, 48
Change from Baseline at C3D15		
n(%)	2 (28.6%)	4 (40.0%)
Mean (SD)	3.0 (7.07)	7.0 (10.03)
Median	3.0	2.5
Min, Max	-2, 8	1, 22

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.

Program Name: t_promis_mob.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 33: PROMIS Mobility Scale Score: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
C5D15		
n(%)	4 (57.1%)	5 (50.0%)
Mean (SD)	51.5 (8.76)	38.0 (4.53)
Median	52.0	38.0
Min, Max	43, 59	31, 42
Change from Baseline at C5D15		
n(%)	3 (42.9%)	5 (50.0%)
Mean (SD)	8.7 (2.08)	1.4 (3.36)
Median	8.0	0
Min, Max	7, 11	-2, 5
C7D15		
n(%)	3 (42.9%)	6 (60.0%)
Mean (SD)	52.3 (6.51)	41.2 (8.89)
Median	52.0	42.0
Min, Max	46, 59	31, 56
Change from Baseline at C7D15		
n(%)	1 (14.3%)	5 (50.0%)
Mean (SD)	-2.0 (NE)	3.4 (1.82)
Median	-2.0	4.0
Min, Max	-2, -2	1, 5

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.

Program Name: t_promis_mob.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 33: PROMIS Mobility Scale Score: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
C9D15		
n(%)	5 (71.4%)	8 (80.0%)
Mean (SD)	50.2 (8.76)	41.6 (8.78)
Median	48.0	42.5
Min, Max	39, 59	29, 56
Change from Baseline at C9D15		
n(%)	3 (42.9%)	6 (60.0%)
Mean (SD)	3.0 (8.54)	3.0 (3.35)
Median	4.0	2.0
Min, Max	-6, 11	0, 8
C13D15		
n(%)	4 (57.1%)	7 (70.0%)
Mean (SD)	53.8 (10.50)	43.1 (11.17)
Median	59.0	42.0
Min, Max	38, 59	23, 56
Change from Baseline at C13D15		
n(%)	2 (28.6%)	5 (50.0%)
Mean (SD)	7.0 (5.66)	2.8 (5.67)
Median	7.0	3.0
Min, Max	3, 11	-3, 11

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.

Program Name: t_promis_mob.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 33: PROMIS Mobility Scale Score: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
C17D15		
n(%)	3 (42.9%)	5 (50.0%)
Mean (SD)	51.0 (7.00)	42.4 (3.51)
Median	48.0	42.0
Min, Max	46, 59	39, 48
Change from Baseline at C17D15		
n(%)	1 (14.3%)	3 (30.0%)
Mean (SD)	-2.0 (NE)	3.7 (6.66)
Median	-2.0	2.0
Min, Max	-2, -2	-2, 11
C21D15		
n(%)	2 (28.6%)	3 (30.0%)
Mean (SD)	44.5 (2.12)	45.3 (2.52)
Median	44.5	45.0
Min, Max	43, 46	43, 48
Change from Baseline at C21D15		
n(%)	1 (14.3%)	2 (20.0%)
Mean (SD)	-5.0 (NE)	6.0 (7.07)
Median	-5.0	6.0
Min, Max	-5, -5	1, 11

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.

Program Name: t_promis_mob.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 33: PROMIS Mobility Scale Score: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
C24D21		
n(%)	1 (14.3%)	2 (20.0%)
Mean (SD)	43.0 (NE)	49.5 (9.19)
Median	43.0	49.5
Min, Max	43, 43	43, 56
Change from Baseline at C24D21		
n(%)	0	1 (10.0%)
Mean (SD)	NE (NE)	19.0 (NE)
Median	NE	19.0
Min, Max	NE, NE	19, 19
SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable.		
Program Name: t_promis_mob.sas Output Generated: 2025-05-02T14:31 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20		

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Table 34: PROMIS Upper Extremity Scale Score: Full Analysis Set

	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Baseline		
n(%)	2 (66.7%)	3 (75.0%)
Mean (SD)	33.0 (2.83)	31.3 (1.53)
Median	33.0	31.0
Min, Max	31, 35	30, 33
C3D15		
n(%)	1 (33.3%)	2 (50.0%)
Mean (SD)	35.0 (NE)	34.5 (0.71)
Median	35.0	34.5
Min, Max	35, 35	34, 35
Change from Baseline at C3D15		
n(%)	1 (33.3%)	2 (50.0%)
Mean (SD)	0 (NE)	3.0 (2.83)
Median	0	3.0
Min, Max	0, 0	1, 5

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable. Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months, as designated by BICR during the Treatment Phase.

Program Name: t_promis_uext.sas Output Generated: 2025-04-28T10:24 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 34: PROMIS Upper Extremity Scale Score: Full Analysis Set

	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
C5D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	37.0 (7.07)	35.0 (4.24)
Median	37.0	35.0
Min, Max	32, 42	32, 38
Change from Baseline at C5D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	4.0 (4.24)	4.5 (3.54)
Median	4.0	4.5
Min, Max	1, 7	2, 7
C7D15		
n(%)	2 (66.7%)	3 (75.0%)
Mean (SD)	36.0 (4.24)	36.0 (3.61)
Median	36.0	35.0
Min, Max	33, 39	33, 40
Change from Baseline at C7D15		
n(%)	2 (66.7%)	3 (75.0%)
Mean (SD)	3.0 (1.41)	4.7 (2.52)
Median	3.0	5.0
Min, Max	2, 4	2, 7

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable. Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months, as designated by BICR during the Treatment Phase.

Program Name: t_promis_uext.sas Output Generated: 2025-04-28T10:24 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 34: PROMIS Upper Extremity Scale Score: Full Analysis Set

	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
C9D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	49.5 (10.61)	42.5 (3.54)
Median	49.5	42.5
Min, Max	42, 57	40, 45
Change from Baseline at C9D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	16.5 (7.78)	12.0 (4.24)
Median	16.5	12.0
Min, Max	11, 22	9, 15
C13D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	44.5 (6.36)	40.0 (2.83)
Median	44.5	40.0
Min, Max	40, 49	38, 42
Change from Baseline at C13D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	11.5 (3.54)	9.5 (3.54)
Median	11.5	9.5
Min, Max	9, 14	7, 12

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable. Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months, as designated by BICR during the Treatment Phase.

Program Name: t_promis_uext.sas Output Generated: 2025-04-28T10:24 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 34: PROMIS Upper Extremity Scale Score: Full Analysis Set

	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
C17D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	33.5 (9.19)	40.0 (0)
Median	33.5	40.0
Min, Max	27, 40	40, 40
Change from Baseline at C17D15		
n(%)	2 (66.7%)	2 (50.0%)
Mean (SD)	0.5 (6.36)	9.5 (0.71)
Median	0.5	9.5
Min, Max	-4, 5	9, 10
C21D15		
n(%)	2 (66.7%)	3 (75.0%)
Mean (SD)	44.0 (18.38)	36.3 (5.13)
Median	44.0	35.0
Min, Max	31, 57	32, 42
Change from Baseline at C21D15		
n(%)	2 (66.7%)	3 (75.0%)
Mean (SD)	11.0 (15.56)	5.0 (6.56)
Median	11.0	4.0
Min, Max	0, 22	-1, 12

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable. Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months, as designated by BICR during the Treatment Phase.

Program Name: t_promis_uext.sas Output Generated: 2025-04-28T10:24 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 34: PROMIS Upper Extremity Scale Score: Full Analysis Set

		Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
C24D21	n(%)	1 (33.3%)	2 (50.0%)
	Mean (SD)	32.0 (NE)	42.5 (3.54)
	Median	32.0	42.5
	Min, Max	32, 32	40, 45
Change from Baseline at C24D21	n(%)	1 (33.3%)	2 (50.0%)
	Mean (SD)	1.0 (NE)	10.5 (2.12)
	Median	1.0	10.5
	Min, Max	1, 1	9, 12

SD: Standard deviation; Min: Minimum; Max: Maximum; PROMIS: Patient-Reported Outcomes Measurement Information System. PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean. Overall visit scores are calculated as the mean of the individual question scores. NE: Not Evaluable. Confirmed objective response is defined as two consecutive assessments of PR or CR within 2-6 months, as designated by BICR during the Treatment Phase.

Program Name: t_promis_uext.sas Output Generated: 2025-04-28T10:24 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Baseline			
Strength Assessment MRC Grading			
n (%)	14 (93.3%)	22 (95.7%)	36 (94.7%)
Mean (SD)	4.2 (0.82)	4.4 (0.62)	4.3 (0.70)
Median	4.4	4.5	4.5
Min, Max	2, 5	3, 5	2, 5
Strength Assessment Dynamometer (LBS)			
n (%)	14 (93.3%)	22 (95.7%)	36 (94.7%)
Mean (SD)	90.0 (92.39)	143.0 (126.04)	122.4 (115.71)
Median	39.1	106.5	89.2
Min, Max	13, 272	15, 516	13, 516
C5D15			
Strength Assessment MRC Grading			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	4.5 (0.55)	4.5 (0.68)	4.5 (0.62)
Median	4.7	4.8	4.8
Min, Max	3, 5	3, 5	3, 5
Strength Assessment Dynamometer (LBS)			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	93.5 (107.65)	180.0 (162.32)	144.2 (146.58)
Median	44.2	139.4	92.3
Min, Max	10, 325	13, 554	10, 554

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Change from Baseline at C5D15			
Strength Assessment MRC Grading			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	0.2 (0.44)	0.1 (0.40)	0.2 (0.42)
Median	0.0	0.0	0.0
Min, Max	0, 1	-1, 1	-1, 1
Strength Assessment Dynamometer (LBS)			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	13.7 (30.65)	20.4 (48.45)	17.6 (41.49)
Median	3.1	2.9	2.9
Min, Max	-33, 69	-28, 156	-33, 156
Percentage Change from Baseline at C5D15			
Strength Assessment MRC Grading			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	8.7 (19.51)	3.7 (11.13)	5.8 (15.06)
Median	0.0	0.0	0.0
Min, Max	-6, 67	-14, 33	-14, 67
Strength Assessment Dynamometer (LBS)			
n (%)	12 (80.0%)	17 (73.9%)	29 (76.3%)
Mean (SD)	6.7 (33.77)	11.6 (28.75)	9.5 (30.44)
Median	10.3	3.1	3.1
Min, Max	-76, 43	-15, 103	-76, 103

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C9D15			
Strength Assessment MRC Grading			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	4.3 (0.94)	4.5 (0.71)	4.4 (0.78)
Median	4.5	4.9	4.7
Min, Max	2, 5	3, 5	2, 5
Strength Assessment Dynamometer (LBS)			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	70.7 (73.15)	202.5 (223.61)	156.9 (194.44)
Median	43.5	134.1	86.4
Min, Max	19, 245	22, 884	19, 884
Change from Baseline at C9D15			
Strength Assessment MRC Grading			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	0.2 (0.39)	0.2 (0.58)	0.2 (0.51)
Median	0.0	0.0	0.0
Min, Max	0, 1	-2, 1	-2, 1
Strength Assessment Dynamometer (LBS)			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	16.9 (29.55)	54.8 (101.11)	41.7 (84.63)
Median	7.7	14.8	10.0
Min, Max	-4, 94	-17, 368	-17, 368

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Percentage Change from Baseline at C9D15			
Strength Assessment MRC Grading			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	5.9 (10.19)	4.6 (14.01)	5.1 (12.62)
Median	0.0	0.0	0.0
Min, Max	-6, 23	-36, 33	-36, 33
Strength Assessment Dynamometer (LBS)			
n (%)	9 (60.0%)	17 (73.9%)	26 (68.4%)
Mean (SD)	28.0 (23.50)	28.4 (37.66)	28.3 (32.93)
Median	34.5	17.5	22.3
Min, Max	-10, 62	-30, 101	-30, 101
C13D15			
Strength Assessment MRC Grading			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	4.6 (0.42)	4.6 (0.56)	4.6 (0.51)
Median	4.7	5.0	4.8
Min, Max	4, 5	4, 5	4, 5
Strength Assessment Dynamometer (LBS)			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	79.4 (89.88)	217.7 (258.49)	169.6 (222.78)
Median	49.9	130.2	88.0
Min, Max	14, 285	22, 984	14, 984

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Change from Baseline at C13D15			
Strength Assessment MRC Grading			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	0.3 (0.35)	0.3 (0.46)	0.3 (0.42)
Median	0.1	0.0	0.0
Min, Max	0, 1	0, 1	0, 1
Strength Assessment Dynamometer (LBS)			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	18.8 (31.93)	68.5 (130.33)	51.2 (108.25)
Median	4.7	14.5	12.8
Min, Max	1, 95	-31, 468	-31, 468
Percentage Change from Baseline at C13D15			
Strength Assessment MRC Grading			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	6.8 (9.70)	7.5 (13.09)	7.3 (11.80)
Median	1.7	0.0	0.0
Min, Max	0, 23	-8, 39	-8, 39
Strength Assessment Dynamometer (LBS)			
n (%)	8 (53.3%)	15 (65.2%)	23 (60.5%)
Mean (SD)	26.2 (21.85)	36.1 (51.42)	32.7 (43.10)
Median	20.4	20.7	20.7
Min, Max	1, 52	-30, 127	-30, 127

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C17D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	4.6 (0.50)	4.6 (0.66)	4.5 (0.57)
Median	4.6	5.0	4.8
Min, Max	4, 5	4, 5	4, 5
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	84.8 (101.23)	199.0 (321.31)	145.7 (243.90)
Median	47.1	80.9	75.4
Min, Max	11, 300	23, 984	11, 984
Change from Baseline at C17D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	0.2 (0.38)	0.2 (0.31)	0.2 (0.33)
Median	0.0	0.0	0.0
Min, Max	0, 1	0, 1	0, 1
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	21.8 (40.76)	65.6 (163.42)	45.1 (120.73)
Median	7.6	10.5	7.6
Min, Max	-6, 110	-15, 468	-15, 468

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Percentage Change from Baseline at C17D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	5.3 (9.70)	5.9 (10.13)	5.6 (9.58)
Median	0.0	0.0	0.0
Min, Max	-6, 21	0, 29	-6, 29
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	28.2 (39.47)	36.7 (54.28)	32.8 (46.48)
Median	28.8	16.4	28.8
Min, Max	-36, 81	-16, 135	-36, 135
C21D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	4.7 (0.40)	4.5 (0.59)	4.6 (0.50)
Median	4.8	4.7	4.8
Min, Max	4, 5	4, 5	4, 5
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	86.6 (98.01)	241.4 (331.50)	169.1 (255.84)
Median	43.7	106.0	73.4
Min, Max	13, 286	21, 982	13, 982

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Change from Baseline at C21D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	0.4 (0.49)	0.2 (0.29)	0.3 (0.40)
Median	0.3	0.0	0.0
Min, Max	0, 1	0, 1	0, 1
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	23.6 (33.67)	71.7 (168.36)	49.2 (123.60)
Median	13.3	-0.2	7.2
Min, Max	-5, 96	-37, 466	-37, 466
Percentage Change from Baseline at C21D15			
Strength Assessment MRC Grading			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	10.0 (12.82)	5.2 (10.03)	7.4 (11.26)
Median	7.1	0.0	0.0
Min, Max	-6, 25	-1, 29	-6, 29
Strength Assessment Dynamometer (LBS)			
n (%)	7 (46.7%)	8 (34.8%)	15 (39.5%)
Mean (SD)	34.0 (34.68)	13.2 (37.60)	22.9 (36.58)
Median	50.6	-1.4	18.3
Min, Max	-27, 71	-21, 90	-27, 90

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

Program Name: t_stre.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADMK Data Cutoff Date: 2023-09-20

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C24D21			
Strength Assessment MRC Grading			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	4.6 (0.42)	4.5 (0.53)	4.5 (0.48)
Median	4.6	4.7	4.7
Min, Max	4, 5	4, 5	4, 5
Strength Assessment Dynamometer (LBS)			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	50.0 (47.80)	194.4 (282.19)	143.4 (235.67)
Median	35.2	97.7	69.6
Min, Max	13, 139	21, 972	13, 972
Change from Baseline at C24D21			
Strength Assessment MRC Grading			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	0.2 (0.57)	0.2 (0.45)	0.2 (0.48)
Median	0.0	0.0	0.0
Min, Max	0, 1	0, 1	0, 1
Strength Assessment Dynamometer (LBS)			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	8.2 (11.33)	56.8 (136.15)	39.7 (110.45)
Median	4.4	12.9	7.0
Min, Max	-4, 26	-14, 456	-14, 456

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments. For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.

Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.

MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.

For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.

The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 50: Strength Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
Percentage Change from Baseline at C24D21			
Strength Assessment MRC Grading			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	5.4 (16.76)	7.1 (15.31)	6.5 (15.33)
Median	0.0	0.0	0.0
Min, Max	-9, 38	-3, 50	-9, 50
Strength Assessment Dynamometer (LBS)			
n (%)	6 (40.0%)	11 (47.8%)	17 (44.7%)
Mean (SD)	15.7 (29.29)	26.1 (41.59)	22.4 (37.08)
Median	14.3	14.6	14.6
Min, Max	-23, 67	-19, 101	-23, 101

SD: Standard deviation; Min: Minimum; Max: Maximum.
All participants with a target PN causing motor dysfunction or weakness at baseline undergo strength assessments.
For each of the individual strength assessments, to assess the change from baseline at a visit, a participant will need assessments in which all the following categories, as assessed at baseline, match at that visit: side affected, position during assessment (sitting/supine/lateral decubitus), muscle group assessed.
Measurements will be obtained using Medical Research Council (MRC) grading followed by quantitative assessments using the sponsor provided MicroFET2 dynamometer.
MRC Grading is assessed on a scale of 0 to 5, with 0 representing no movement being observed, and 5 representing the muscle contracting normally against full resistance.
For each participant, the sum of the dynamometer scores for the muscle groups tested will be taken as an overall score for each visit.
The MRC Grade visit score is calculated for each participant separately, and these scores are then averaged for this summary.
Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C1D1			
Range of Motion Assessment (Degrees)			
n (%)	15 (100%)	21 (91.3%)	36 (94.7%)
Mean (SD)	552.7 (353.09)	449.7 (344.20)	492.6 (346.73)
Median	472.0	309.0	422.0
Min, Max	45, 1246	45, 1273	45, 1273
C5D15			
Range of Motion Assessment (Degrees)			
n (%)	12 (80.0%)	14 (60.9%)	26 (68.4%)
Mean (SD)	587.9 (355.78)	551.1 (367.11)	568.1 (355.14)
Median	501.5	387.0	459.0
Min, Max	34, 1262	220, 1437	34, 1437
Change from Baseline at C5D15			
Range of Motion Assessment (Degrees)			
n (%)	12 (80.0%)	14 (60.9%)	26 (68.4%)
Mean (SD)	11.1 (31.42)	49.1 (63.66)	31.6 (54.06)
Median	2.5	35.0	13.0
Min, Max	-30, 92	-42, 164	-42, 164
Percentage Change from Baseline at C5D15			
Range of Motion Assessment			
n (%)	12 (80.0%)	14 (60.9%)	26 (68.4%)
Mean (SD)	0.6 (9.45)	11.6 (18.47)	6.5 (15.73)
Median	0.6	7.7	3.3
Min, Max	-24, 13	-10, 65	-24, 65

SD: Standard deviation; Min: Minimum; Max: Maximum.
 All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.
 To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).
 For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit.
 Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C9D15			
Range of Motion Assessment (Degrees)			
n (%)	9 (60.0%)	14 (60.9%)	23 (60.5%)
Mean (SD)	540.0 (337.05)	513.8 (376.87)	524.0 (354.13)
Median	520.0	371.5	439.0
Min, Max	24, 1050	139, 1447	24, 1447
Change from Baseline at C9D15			
Range of Motion Assessment (Degrees)			
n (%)	9 (60.0%)	14 (60.9%)	23 (60.5%)
Mean (SD)	15.9 (39.90)	30.6 (63.28)	24.9 (54.77)
Median	10.0	15.5	15.0
Min, Max	-30, 81	-42, 174	-42, 174
Percentage Change from Baseline at C9D15			
Range of Motion Assessment			
n (%)	9 (60.0%)	14 (60.9%)	23 (60.5%)
Mean (SD)	-1.9 (17.68)	7.2 (19.62)	3.7 (19.02)
Median	2.5	3.5	2.5
Min, Max	-47, 11	-16, 62	-47, 62

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.

To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).

For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C13D15			
Range of Motion Assessment (Degrees)			
n (%)	8 (53.3%)	12 (52.2%)	20 (52.6%)
Mean (SD)	553.1 (297.71)	496.5 (390.06)	519.2 (348.64)
Median	463.5	306.5	428.0
Min, Max	175, 1050	140, 1371	140, 1371
Change from Baseline at C13D15			
Range of Motion Assessment (Degrees)			
n (%)	8 (53.3%)	12 (52.2%)	20 (52.6%)
Mean (SD)	-6.1 (82.06)	17.7 (51.28)	8.2 (64.39)
Median	15.0	9.5	10.0
Min, Max	-189, 70	-49, 102	-189, 102
Percentage Change from Baseline at C13D15			
Range of Motion Assessment			
n (%)	8 (53.3%)	12 (52.2%)	20 (52.6%)
Mean (SD)	0.7 (15.24)	4.9 (19.85)	3.2 (17.84)
Median	4.0	3.7	4.0
Min, Max	-32, 17	-25, 51	-32, 51

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.

To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).

For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C17D15			
Range of Motion Assessment (Degrees)			
n (%)	7 (46.7%)	6 (26.1%)	13 (34.2%)
Mean (SD)	574.7 (337.17)	475.0 (403.10)	528.7 (356.68)
Median	477.0	346.0	452.0
Min, Max	160, 1050	144, 1186	144, 1186
Change from Baseline at C17D15			
Range of Motion Assessment (Degrees)			
n (%)	7 (46.7%)	6 (26.1%)	13 (34.2%)
Mean (SD)	20.6 (69.38)	29.7 (76.20)	24.8 (69.63)
Median	5.0	10.0	5.0
Min, Max	-59, 129	-42, 144	-59, 144
Percentage Change from Baseline at C17D15			
Range of Motion Assessment			
n (%)	7 (46.7%)	6 (26.1%)	13 (34.2%)
Mean (SD)	3.3 (12.27)	2.4 (17.61)	2.9 (14.31)
Median	1.1	1.2	1.1
Min, Max	-14, 22	-21, 27	-21, 27

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.

To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).

For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C21D15			
Range of Motion Assessment (Degrees)			
n (%)	7 (46.7%)	5 (21.7%)	12 (31.6%)
Mean (SD)	559.1 (328.42)	659.0 (298.40)	600.8 (306.36)
Median	458.0	660.0	467.5
Min, Max	118, 1050	350, 1121	118, 1121
Change from Baseline at C21D15			
Range of Motion Assessment (Degrees)			
n (%)	7 (46.7%)	5 (21.7%)	12 (31.6%)
Mean (SD)	5.0 (36.18)	19.8 (71.87)	11.2 (51.48)
Median	-8.0	25.0	-1.5
Min, Max	-32, 72	-45, 131	-45, 131
Percentage Change from Baseline at C21D15			
Range of Motion Assessment			
n (%)	7 (46.7%)	5 (21.7%)	12 (31.6%)
Mean (SD)	-1.5 (9.84)	4.1 (13.29)	0.8 (11.20)
Median	-1.9	2.8	-0.4
Min, Max	-21, 8	-9, 25	-21, 25

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.

To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).

For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 51: Range of Motion Assessments by Visit: Full Analysis Set

	Pediatric (N=15)	Adult (N=23)	Total (N=38)
C24D21			
Range of Motion Assessment (Degrees)			
n (%)	6 (40.0%)	8 (34.8%)	14 (36.8%)
Mean (SD)	482.7 (259.71)	493.0 (349.32)	488.6 (302.78)
Median	440.0	393.0	435.0
Min, Max	145, 944	147, 1165	145, 1165
Change from Baseline at C24D21			
Range of Motion Assessment (Degrees)			
n (%)	6 (40.0%)	8 (34.8%)	14 (36.8%)
Mean (SD)	12.8 (34.00)	23.4 (70.01)	18.9 (55.80)
Median	3.0	4.0	3.0
Min, Max	-31, 58	-46, 162	-46, 162
Percentage Change from Baseline at C24D21			
Range of Motion Assessment			
n (%)	6 (40.0%)	8 (34.8%)	14 (36.8%)
Mean (SD)	1.5 (6.21)	4.0 (16.19)	2.9 (12.55)
Median	0.7	0.3	0.7
Min, Max	-6, 10	-16, 31	-16, 31

SD: Standard deviation; Min: Minimum; Max: Maximum.

All participants with a target PN causing motor dysfunction or weakness at baseline will undergo a focused evaluation of range of motion of the affected joints.

To assess the change from baseline at a visit, a participant will need assessments in which all three categories, as assessed at baseline, match at that visit: joint assessed, motion tested, type (passive/active).

For each participant, range of motion results will be summed, and this will be taken as an overall score for each visit. Participants are only considered at a post-baseline timepoint if they have an identical assessment at baseline and that timepoint.

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Table 56.3: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Improvement by >=15% (5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C3D15	
Number of Participants Completed the Assessment, n (%)	15 (65.2%)
Number of Participants Missing the Assessment, n (%)	8 (34.8%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	1 (4.3%)
Visit C5D15	
Number of Participants Completed the Assessment, n (%)	18 (78.3%)
Number of Participants Missing the Assessment, n (%)	5 (21.7%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	2 (8.7%)
Visit C7D15	
Number of Participants Completed the Assessment, n (%)	16 (69.6%)
Number of Participants Missing the Assessment, n (%)	7 (30.4%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	4 (17.4%)

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

Table 56.3: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Improvement by >=15% (5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C9D15	
Number of Participants Completed the Assessment, n (%)	14 (60.9%)
Number of Participants Missing the Assessment, n (%)	9 (39.1%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	4 (17.4%)
Visit C13D15	
Number of Participants Completed the Assessment, n (%)	13 (56.5%)
Number of Participants Missing the Assessment, n (%)	10 (43.5%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	4 (17.4%)
Visit C17D15	
Number of Participants Completed the Assessment, n (%)	8 (34.8%)
Number of Participants Missing the Assessment, n (%)	15 (65.2%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	0

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 56.3: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Improvement by >=15% (5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C21D15	
Number of Participants Completed the Assessment, n (%)	10 (43.5%)
Number of Participants Missing the Assessment, n (%)	13 (56.5%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	1 (4.3%)
Visit C24D21	
Number of Participants Completed the Assessment, n (%)	9 (39.1%)
Number of Participants Missing the Assessment, n (%)	14 (60.9%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	1 (4.3%)
Total	
Number of Participants Completed the Assessment, n (%)	18 (78.3%)
Number of Participants Missing the Assessment, n (%)	5 (21.7%)
Threshold for Meaningful Score Difference	5.97
Participants with Clinically Meaningful Score Improvement, n (%)	4 (17.4%)

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 56.7: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Worsening by >=15% (-5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C3D15	
Number of Participants Completed the Assessment, n (%)	15 (65.2%)
Number of Participants Missing the Assessment, n (%)	8 (34.8%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	1 (4.3%)
Visit C5D15	
Number of Participants Completed the Assessment, n (%)	18 (78.3%)
Number of Participants Missing the Assessment, n (%)	5 (21.7%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	0
Visit C7D15	
Number of Participants Completed the Assessment, n (%)	16 (69.6%)
Number of Participants Missing the Assessment, n (%)	7 (30.4%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	0

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 56.7: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Worsening by >=15% (-5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C9D15	
Number of Participants Completed the Assessment, n (%)	14 (60.9%)
Number of Participants Missing the Assessment, n (%)	9 (39.1%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	1 (4.3%)
Visit C13D15	
Number of Participants Completed the Assessment, n (%)	13 (56.5%)
Number of Participants Missing the Assessment, n (%)	10 (43.5%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	3 (13.0%)
Visit C17D15	
Number of Participants Completed the Assessment, n (%)	8 (34.8%)
Number of Participants Missing the Assessment, n (%)	15 (65.2%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	0

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

Table 56.7: Meaningful PROMIS Physical Function Score Difference - Non-Responder Imputation - Worsening by >=15% (-5.97) : Full Analysis Set

Visits	Adult (N=23)
Visit C21D15	
Number of Participants Completed the Assessment, n (%)	10 (43.5%)
Number of Participants Missing the Assessment, n (%)	13 (56.5%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	1 (4.3%)
Visit C24D21	
Number of Participants Completed the Assessment, n (%)	9 (39.1%)
Number of Participants Missing the Assessment, n (%)	14 (60.9%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	2 (8.7%)
Total	
Number of Participants Completed the Assessment, n (%)	18 (78.3%)
Number of Participants Missing the Assessment, n (%)	5 (21.7%)
Threshold for Meaningful Score Difference	-5.97
Participants with Clinically Meaningful Score Worsening, n (%)	3 (13.0%)

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_py_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.3: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C3D15		
Number of Participants Completed the Assessment, n (%)	1 (33.3%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)	2 (66.7%)	2 (50.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	0	0
Visit C5D15		
Number of Participants Completed the Assessment, n (%)	2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)	1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	0	1 (25.0%)
Visit C7D15		
Number of Participants Completed the Assessment, n (%)	2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)	1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	0	1 (25.0%)

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.3: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits		Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		2 (66.7%)	2 (50.0%)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		2 (66.7%)	2 (50.0%)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		0	2 (50.0%)

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.3: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits	Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C21D15		
Number of Participants Completed the Assessment, n (%)	2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)	1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	1 (33.3%)	1 (25.0%)
Visit C24D21		
Number of Participants Completed the Assessment, n (%)	1 (33.3%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)	2 (66.7%)	2 (50.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	0	2 (50.0%)
Total		
Number of Participants Completed the Assessment, n (%)	2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)	1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference	7.05	6.3
Participants with Clinically Meaningful Score Improvement, n (%)	2 (66.7%)	3 (75.0%)

PROMIS: Patient-Reported Outcomes Measurement Information System.
 PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
 Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_impr_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.7: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Worsening by >=15% Full Analysis Set

Visits		Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Visit C5D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Visit C7D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.7: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Worsening by >=15% Full Analysis Set

Visits		Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Visit C13D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Visit C17D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 57.7: Meaningful PROMIS Upper Extremity Score Difference - Non-Responder Imputation - Worsening by >=15% Full Analysis Set

Visits		Pediatric Self-Report (N=3)	Pediatric Parent Proxy (N=4)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Visit C24D21			
Number of Participants Completed the Assessment, n (%)		1 (33.3%)	2 (50.0%)
Number of Participants Missing the Assessment, n (%)		2 (66.7%)	2 (50.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0
Total			
Number of Participants Completed the Assessment, n (%)		2 (66.7%)	3 (75.0%)
Number of Participants Missing the Assessment, n (%)		1 (33.3%)	1 (25.0%)
Threshold for Meaningful Score Difference		-7.05	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)		0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_uext_wrsn_nr_c24.sas Output Generated: 2025-05-02T13:38 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 58.3: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits		Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)		2 (28.6%)	4 (40.0%)
Number of Participants Missing the Assessment, n (%)		5 (71.4%)	6 (60.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		1 (14.3%)	1 (10.0%)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)		3 (42.9%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)		4 (57.1%)	5 (50.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		3 (42.9%)	0
Visit C7D15			
Number of Participants Completed the Assessment, n (%)		1 (14.3%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)		6 (85.7%)	5 (50.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_impr_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

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Table 58.3: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits		Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)		3 (42.9%)	6 (60.0%)
Number of Participants Missing the Assessment, n (%)		4 (57.1%)	4 (40.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		1 (14.3%)	1 (10.0%)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)		2 (28.6%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)		5 (71.4%)	5 (50.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		1 (14.3%)	1 (10.0%)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)		1 (14.3%)	3 (30.0%)
Number of Participants Missing the Assessment, n (%)		6 (85.7%)	7 (70.0%)
Threshold for Meaningful Score Difference		6.75	6.3
Participants with Clinically Meaningful Score Improvement, n (%)		0	1 (10.0%)

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_impr_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

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Table 58.3: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Improvement by >=15%: Full Analysis Set

Visits	Pediatric Self-Report (N=7)		Pediatric Parent Proxy (N=10)	
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	1 (14.3%)		2 (20.0%)	
Number of Participants Missing the Assessment, n (%)	6 (85.7%)		8 (80.0%)	
Threshold for Meaningful Score Difference	6.75		6.3	
Participants with Clinically Meaningful Score Improvement, n (%)	0		1 (10.0%)	
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	0		1 (10.0%)	
Number of Participants Missing the Assessment, n (%)	0		9 (90.0%)	
Threshold for Meaningful Score Difference	6.75		6.3	
Participants with Clinically Meaningful Score Improvement, n (%)	0		1 (10.0%)	
Total				
Number of Participants Completed the Assessment, n (%)	3 (42.9%)		6 (60.0%)	
Number of Participants Missing the Assessment, n (%)	4 (57.1%)		4 (40.0%)	
Threshold for Meaningful Score Difference	6.75		6.3	
Participants with Clinically Meaningful Score Improvement, n (%)	3 (42.9%)		4 (40.0%)	

PROMIS: Patient-Reported Outcomes Measurement Information System.
PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.
Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_impr_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

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Table 58.7: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Worsening by >=15%: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Visit C3D15		
Number of Participants Completed the Assessment, n (%)	2 (28.6%)	4 (40.0%)
Number of Participants Missing the Assessment, n (%)	5 (71.4%)	6 (60.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Visit C5D15		
Number of Participants Completed the Assessment, n (%)	3 (42.9%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)	4 (57.1%)	5 (50.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Visit C7D15		
Number of Participants Completed the Assessment, n (%)	1 (14.3%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)	6 (85.7%)	5 (50.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_wrsn_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

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Table 58.7: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Worsening by >=15%: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Visit C9D15		
Number of Participants Completed the Assessment, n (%)	3 (42.9%)	6 (60.0%)
Number of Participants Missing the Assessment, n (%)	4 (57.1%)	4 (40.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Visit C13D15		
Number of Participants Completed the Assessment, n (%)	2 (28.6%)	5 (50.0%)
Number of Participants Missing the Assessment, n (%)	5 (71.4%)	5 (50.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Visit C17D15		
Number of Participants Completed the Assessment, n (%)	1 (14.3%)	3 (30.0%)
Number of Participants Missing the Assessment, n (%)	6 (85.7%)	7 (70.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0

PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_wrsn_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

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Table 58.7: Meaningful PROMIS Mobility Score Difference - Non-Responder Imputation - Worsening by >=15%: Full Analysis Set

	Pediatric Self-Report (N=7)	Pediatric Parent Proxy (N=10)
Visit C21D15		
Number of Participants Completed the Assessment, n (%)	1 (14.3%)	2 (20.0%)
Number of Participants Missing the Assessment, n (%)	6 (85.7%)	8 (80.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Visit C24D21		
Number of Participants Completed the Assessment, n (%)	0	1 (10.0%)
Number of Participants Missing the Assessment, n (%)	0	9 (90.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0
Total		
Number of Participants Completed the Assessment, n (%)	3 (42.9%)	6 (60.0%)
Number of Participants Missing the Assessment, n (%)	4 (57.1%)	4 (40.0%)
Threshold for Meaningful Score Difference	-6.75	-6.3
Participants with Clinically Meaningful Score Worsening, n (%)	0	0

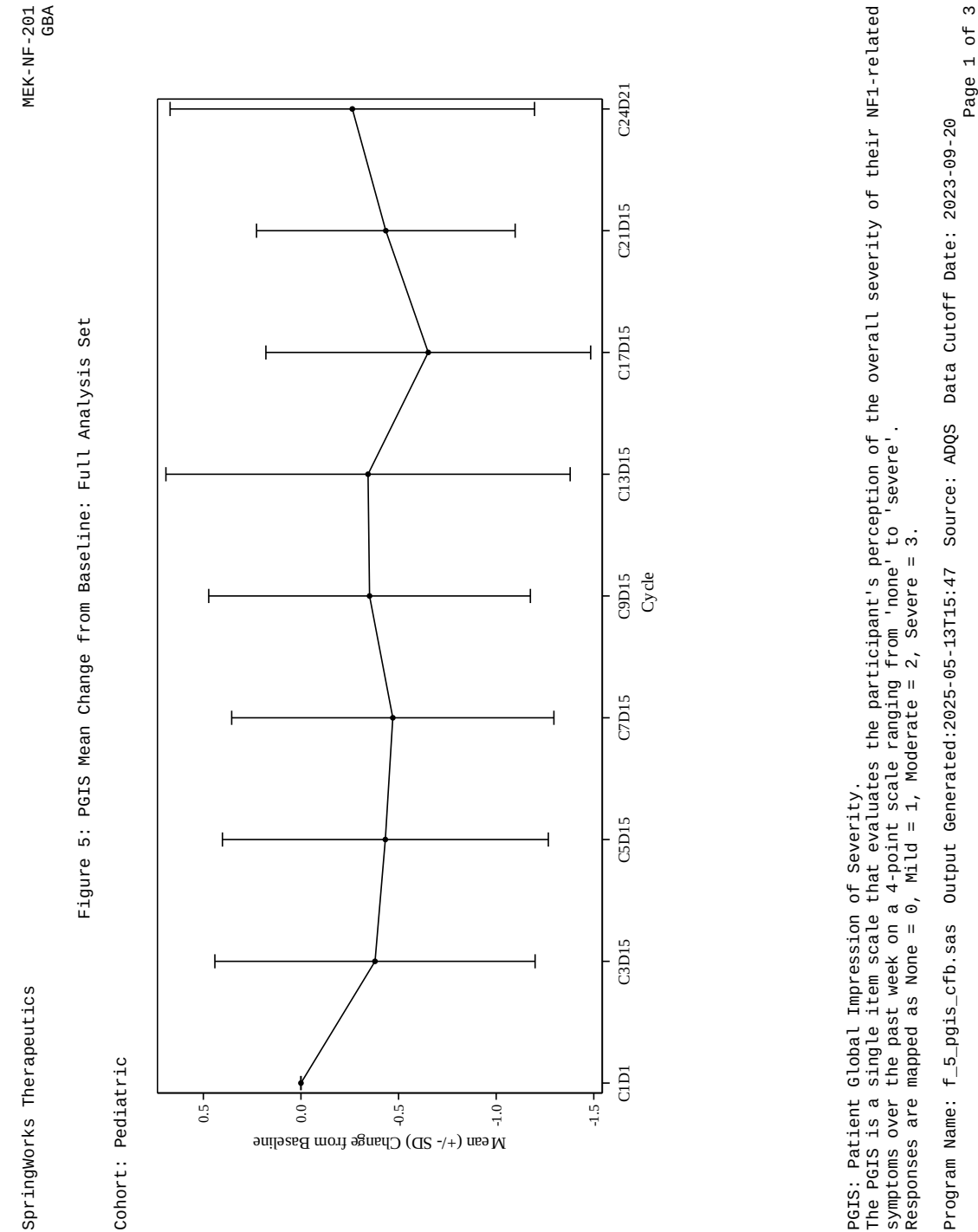
PROMIS: Patient-Reported Outcomes Measurement Information System.

PROMIS items are answered Likert scale with responses ranging from 1 to 5. The total raw scores for the measure will be converted to T-scores using the applicable score conversion table in the user manual and scoring instructions. A higher T-score indicates better reported physical functioning. A T-score of 50 represents the population mean.

Overall visit scores are calculated as the mean of the individual question scores.

Program Name: t_promis_mob_obj_wrsn_nr_a.sas Output Generated: 2025-05-02T13:39 Source: ADSL,ADQS Data Cutoff Date: 2023-09-20

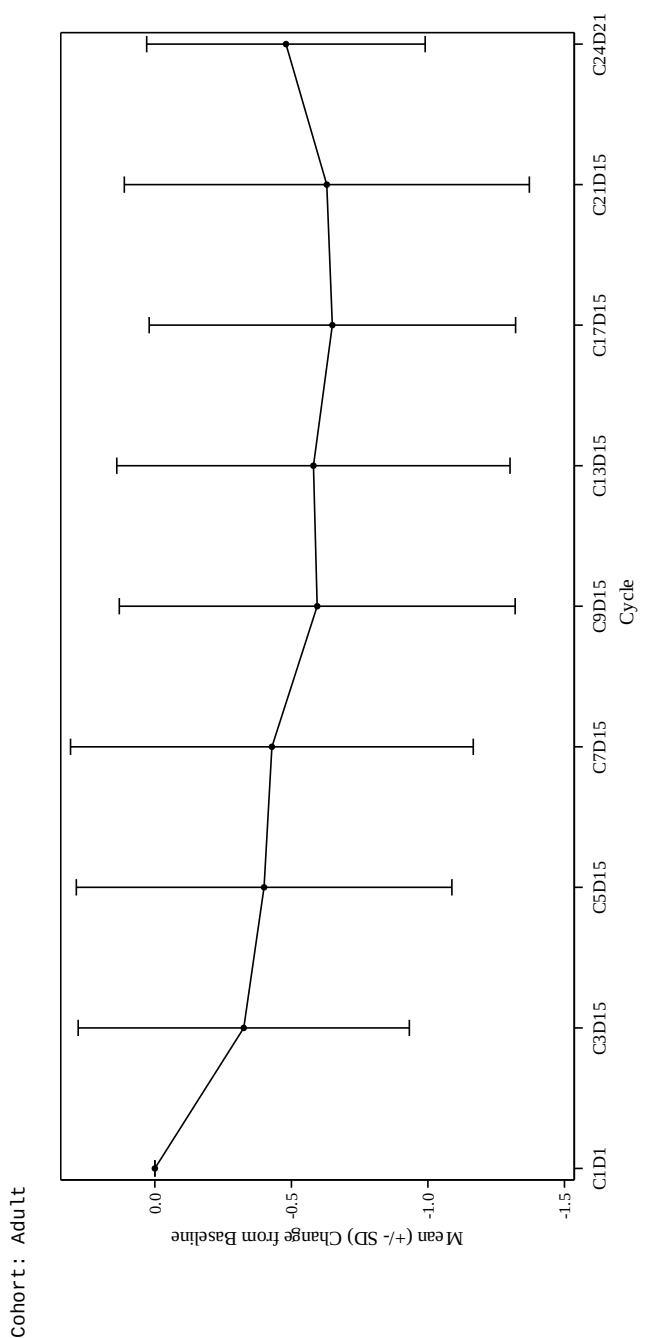
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Figure 5: PGIS Mean Change from Baseline: Full Analysis Set



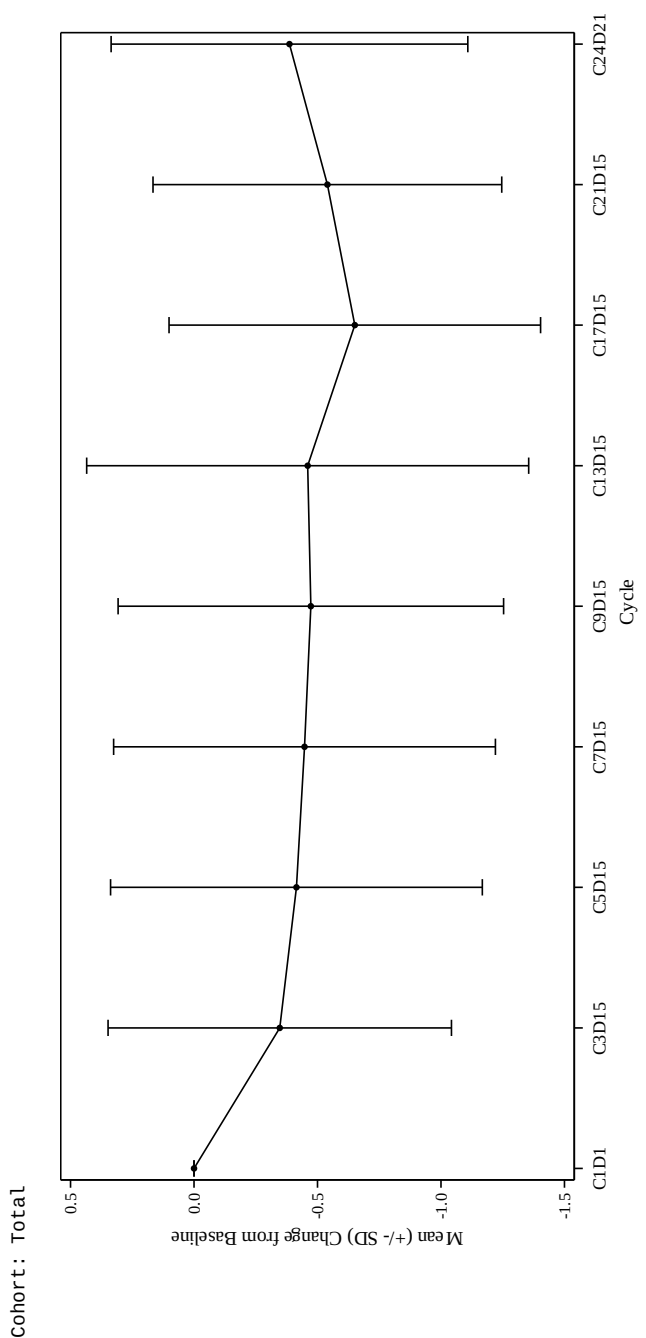
PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from 'none' to 'severe'. Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3.

Program Name: f_5_pgis_cfb.sas Output Generated: 2025-05-13T15:47 Source: ADQS Data Cutoff Date: 2023-09-20 Page 2 of 3

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Figure 5: PGIS Mean Change from Baseline: Full Analysis Set



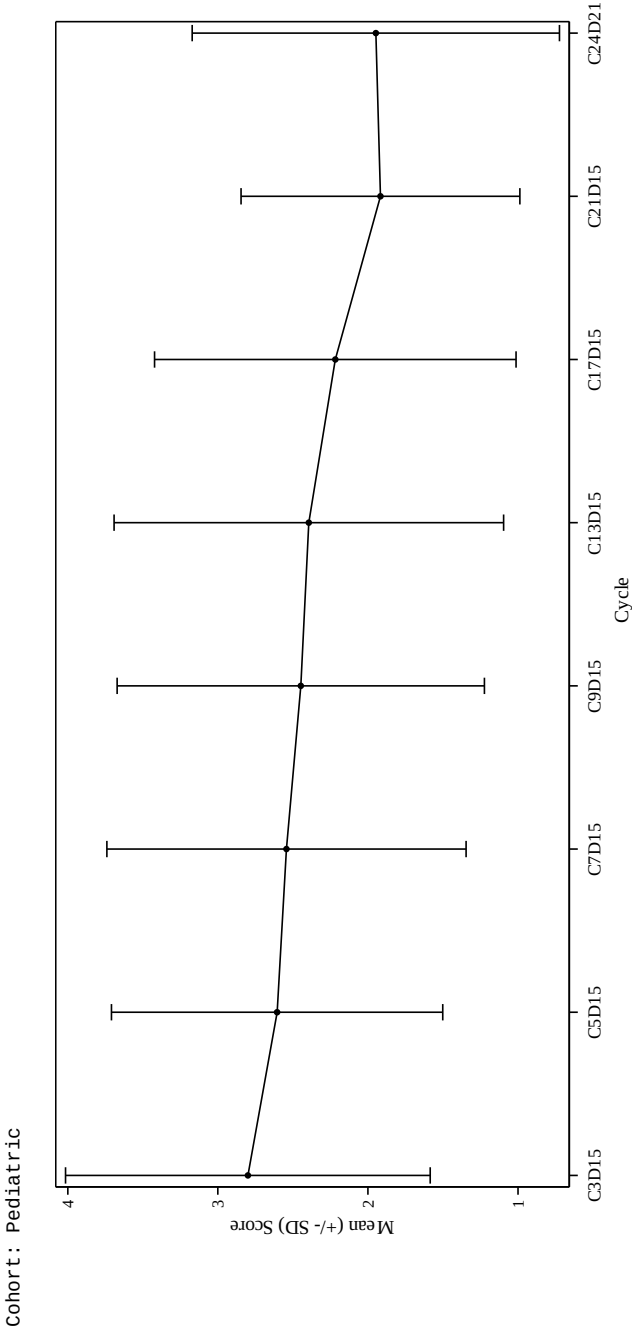
PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from 'none' to 'severe'. Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3.

Program Name: f_5_pgis_cfb.sas Output Generated: 2025-05-13T15:47 Source: ADQS Data Cutoff Date: 2023-09-20 Page 3 of 3

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Figure 6: PGIC Mean Score: Full Analysis Set



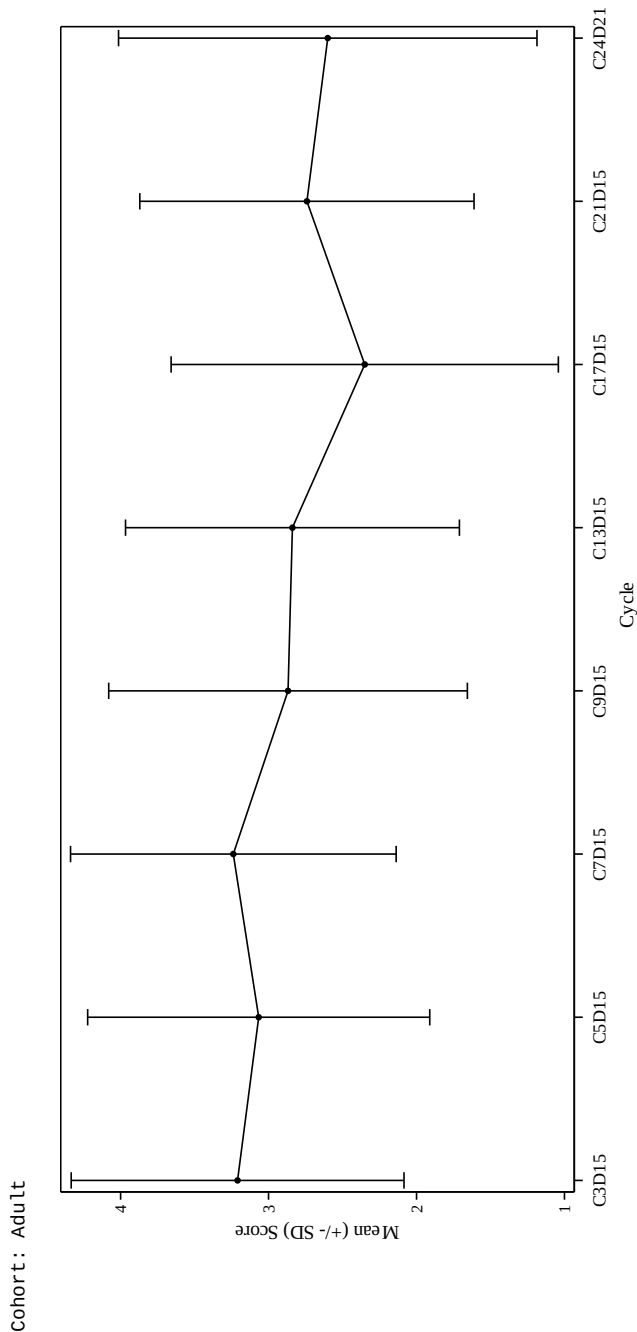
PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from 'very much better' to 'very much worse'. Responses are mapped as Very Much Better =1, Moderately Better = 2, A Little Better = 3, No Change = 4, A Little Worse = 5, Moderately Worse = 6, Very Much Worse = 7.

Program Name: f_6_pgic_cfb.sas Output Generated: 2025-05-13T15:57 Source: ADQS Data Cutoff Date: 2023-09-20 Page 1 of 3

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Figure 6: PGIC Mean Score: Full Analysis Set



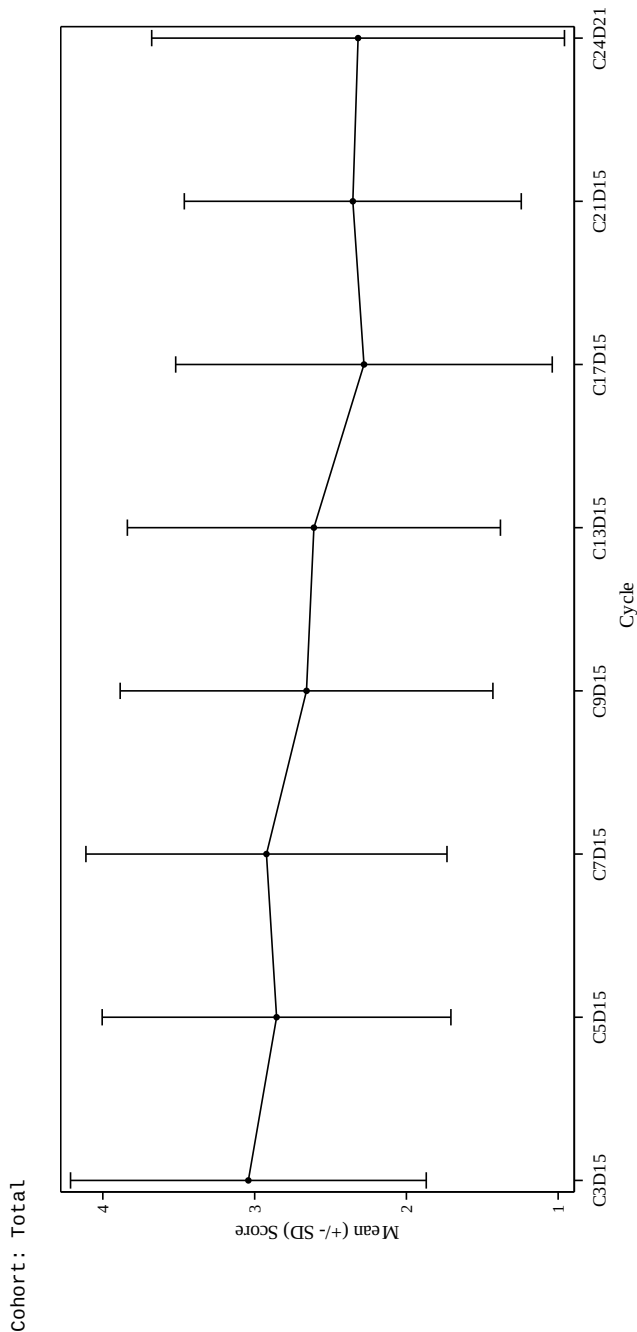
PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from 'very much better' to 'very much worse'. Responses are mapped as Very Much Better = 1, Moderately Better = 2, A Little Better = 3, No Change = 4, A Little Worse = 5, Moderately Worse = 6, Very Much Worse = 7.

Program Name: f_6_pgic_cfb.sas Output Generated: 2025-05-13T15:57 Source: ADQS Data Cutoff Date: 2023-09-20 Page 2 of 3

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Figure 6: PGIC Mean Score: Full Analysis Set



PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from 'very much better' to 'very much worse'. Responses are mapped as Very Much Better =1, Moderately Better =2, A Little Better =3, No Change =4, A Little Worse =5, Moderately Worse =6, Very Much Worse =7.

Program Name: f_6_pgic_cfb.sas Output Generated:2025-05-13T15:57 Source: ADQS Data Cutoff Date: 2023-09-20 Page 3 of 3

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Table 16: Compliance Rate for PGIS by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
Baseline			
PRO Expected	47 (100%)	58 (100%)	105 (100%)
PRO Completed	46 (97.9%)	57 (98.3%)	103 (98.1%)
PRO Not Completed	1 (2.1%)	1 (1.7%)	2 (1.9%)
C3D15			
PRO Expected	45 (95.7%)	51 (87.9%)	96 (91.4%)
PRO Completed	30 (66.7%)	42 (82.4%)	72 (75.0%)
PRO Not Completed	15 (33.3%)	9 (17.6%)	24 (25.0%)
C5D15			
PRO Expected	45 (95.7%)	50 (86.2%)	95 (90.5%)
PRO Completed	38 (84.4%)	45 (90.0%)	83 (87.4%)
PRO Not Completed	7 (15.6%)	5 (10.0%)	12 (12.6%)
C7D15			
PRO Expected	41 (87.2%)	46 (79.3%)	87 (82.9%)
PRO Completed	35 (85.4%)	40 (87.0%)	75 (86.2%)
PRO Not Completed	6 (14.6%)	6 (13.0%)	12 (13.8%)

PGIS: Patient Global Impression of Severity.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_16_pgis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 16: Compliance Rate for PGIS by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C9D15			
PRO Expected	40 (85.1%)	45 (77.6%)	85 (81.0%)
PRO Completed	37 (92.5%)	37 (82.2%)	74 (87.1%)
PRO Not Completed	3 (7.5%)	8 (17.8%)	11 (12.9%)
C13D15			
PRO Expected	34 (72.3%)	36 (62.1%)	70 (66.7%)
PRO Completed	31 (91.2%)	31 (86.1%)	62 (88.6%)
PRO Not Completed	3 (8.8%)	5 (13.9%)	8 (11.4%)
C17D15			
PRO Expected	33 (70.2%)	34 (58.6%)	67 (63.8%)
PRO Completed	23 (69.7%)	20 (58.8%)	43 (64.2%)
PRO Not Completed	10 (30.3%)	14 (41.2%)	24 (35.8%)
C21D15			
PRO Expected	30 (63.8%)	32 (55.2%)	62 (59.0%)
PRO Completed	24 (80.0%)	27 (84.4%)	51 (82.3%)
PRO Not Completed	6 (20.0%)	5 (15.6%)	11 (17.7%)

PGIS: Patient Global Impression of Severity.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_16_pgis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 16: Compliance Rate for PGIS by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C24D21			
PRO Expected	27 (57.4%)	31 (53.4%)	58 (55.2%)
PRO Completed	19 (70.4%)	25 (80.6%)	44 (75.9%)
PRO Not Completed	8 (29.6%)	6 (19.4%)	14 (24.1%)
ET			
PRO Expected	17 (36.2%)	27 (46.6%)	44 (41.9%)
PRO Completed	7 (41.2%)	8 (29.6%)	15 (34.1%)
PRO Not Completed	10 (58.8%)	19 (70.4%)	29 (65.9%)
SFU			
PRO Expected	17 (36.2%)	27 (46.6%)	44 (41.9%)
PRO Completed	5 (29.4%)	6 (22.2%)	11 (25.0%)
PRO Not Completed	12 (70.6%)	21 (77.8%)	33 (75.0%)

PGIS: Patient Global Impression of Severity.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_16_pgis_comp.sas Output Generated: 2025-05-02T13:33 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 17: Compliance Rate for PGIC by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15			
PRO Expected	45 (95.7%)	51 (87.9%)	96 (91.4%)
PRO Completed	30 (66.7%)	42 (82.4%)	72 (75.0%)
PRO Not Completed	15 (33.3%)	9 (17.6%)	24 (25.0%)
C5D15			
PRO Expected	45 (95.7%)	50 (86.2%)	95 (90.5%)
PRO Completed	38 (84.4%)	45 (90.0%)	83 (87.4%)
PRO Not Completed	7 (15.6%)	5 (10.0%)	12 (12.6%)
C7D15			
PRO Expected	41 (87.2%)	46 (79.3%)	87 (82.9%)
PRO Completed	35 (85.4%)	40 (87.0%)	75 (86.2%)
PRO Not Completed	6 (14.6%)	6 (13.0%)	12 (13.8%)
C9D15			
PRO Expected	40 (85.1%)	45 (77.6%)	85 (81.0%)
PRO Completed	37 (92.5%)	37 (82.2%)	74 (87.1%)
PRO Not Completed	3 (7.5%)	8 (17.8%)	11 (12.9%)

PGIC: Patient Global Impression of Change.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_17_pgic_comp.sas Output Generated: 2025-05-02T13:33 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 17: Compliance Rate for PGIC by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C13D15			
PRO Expected	34 (72.3%)	36 (62.1%)	70 (66.7%)
PRO Completed	31 (91.2%)	31 (86.1%)	62 (88.6%)
PRO Not Completed	3 (8.8%)	5 (13.9%)	8 (11.4%)
C17D15			
PRO Expected	33 (70.2%)	34 (58.6%)	67 (63.8%)
PRO Completed	22 (66.7%)	20 (58.8%)	42 (62.7%)
PRO Not Completed	11 (33.3%)	14 (41.2%)	25 (37.3%)
C21D15			
PRO Expected	30 (63.8%)	32 (55.2%)	62 (59.0%)
PRO Completed	24 (80.0%)	27 (84.4%)	51 (82.3%)
PRO Not Completed	6 (20.0%)	5 (15.6%)	11 (17.7%)
C24D21			
PRO Expected	27 (57.4%)	31 (53.4%)	58 (55.2%)
PRO Completed	19 (70.4%)	25 (80.6%)	44 (75.9%)
PRO Not Completed	8 (29.6%)	6 (19.4%)	14 (24.1%)

PGIC: Patient Global Impression of Change.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_17_pgic_comp.sas Output Generated: 2025-05-02T13:33 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 17: Compliance Rate for PGIC by Visit: Full Analysis Set

	Pediatric (N=47)	Adult (N=58)	Total (N=105)
ET			
PRO Expected	17 (36.2%)	27 (46.6%)	44 (41.9%)
PRO Completed	7 (41.2%)	8 (29.6%)	15 (34.1%)
PRO Not Completed	10 (58.8%)	19 (70.4%)	29 (65.9%)
SFU			
PRO Expected	17 (36.2%)	27 (46.6%)	44 (41.9%)
PRO Completed	5 (29.4%)	6 (22.2%)	11 (25.0%)
PRO Not Completed	12 (70.6%)	21 (77.8%)	33 (75.0%)

PGIC: Patient Global Impression of Change.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Program Name: t_17_pgic_comp.sas Output Generated: 2025-05-02T13:33 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 52: 6-Minute Walk Test by Visit: Full Analysis Set

	Pediatric (N=11)	Adult (N=16)	Total (N=27)
Baseline			
6-Minute Walk Test Distance (m)			
n (%)	11 (100%)	16 (100%)	27 (100%)
Mean (SD)	417.4 (124.44)	410.1 (94.63)	413.0 (105.52)
Median	428.0	434.0	433.0
Min, Max	111, 588	197, 526	111, 588
CSD15			
6-Minute Walk Test Distance (m)			
n (%)	8 (72.7%)	12 (75.0%)	20 (74.1%)
Mean (SD)	424.6 (76.35)	408.5 (117.18)	415.0 (100.81)
Median	433.5	403.5	406.5
Min, Max	312, 508	134, 590	134, 590
Change from Baseline in 6-Minute Walk Test (m)			
n (%)	8 (72.7%)	12 (75.0%)	20 (74.1%)
Mean (SD)	-24.6 (47.81)	18.2 (113.94)	1.1 (93.92)
Median	-19.0	-7.0	-14.0
Min, Max	-103, 30	-134, 336	-134, 336

SD: Standard deviation; Min: Minimum; Max: Maximum; PN: Plexiform Neurofibroma.

Participants with a target PN causing airway or lower extremity motor dysfunction at baseline will be assessed for change in 6-minute walk test distance.

The object of this test is to walk as far as possible over 6 minutes. After completing the test, participants will be instructed to rest for 5 minutes, after which time vital signs are repeated. The total meters walked will be captured.

Program Name: t_walkt.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADFT Data Cutoff Date: 2023-09-20

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Table 52: 6-Minute Walk Test by Visit: Full Analysis Set

	Pediatric (N=11)	Adult (N=16)	Total (N=27)
C9D15			
6-Minute Walk Test Distance (m)			
n (%)	8 (72.7%)	11 (68.8%)	19 (70.4%)
Mean (SD)	442.3 (88.41)	423.9 (72.48)	431.6 (77.75)
Median	464.0	428.0	428.0
Min, Max	291, 527	277, 580	277, 580
Change from Baseline in 6-Minute Walk Test (m)			
n (%)	8 (72.7%)	11 (68.8%)	19 (70.4%)
Mean (SD)	1.9 (75.18)	-6.5 (57.14)	-3.0 (63.49)
Median	-2.5	0.0	0.0
Min, Max	-100, 119	-91, 74	-100, 119
C13D15			
6-Minute Walk Test Distance (m)			
n (%)	6 (54.5%)	10 (62.5%)	16 (59.3%)
Mean (SD)	441.8 (55.16)	423.1 (77.05)	430.1 (68.30)
Median	446.5	416.5	425.5
Min, Max	369, 509	320, 586	320, 586
Change from Baseline in 6-Minute Walk Test (m)			
n (%)	6 (54.5%)	10 (62.5%)	16 (59.3%)
Mean (SD)	-6.8 (60.76)	2.2 (70.41)	-1.2 (65.00)
Median	7.5	5.5	7.5
Min, Max	-99, 55	-161, 79	-161, 79

SD: Standard deviation; Min: Minimum; Max: Maximum; PN: Plexiform Neurofibroma.
 Participants with a target PN causing airway or lower extremity motor dysfunction at baseline will be assessed for change in 6-minute walk test distance.
 The object of this test is to walk as far as possible over 6 minutes. After completing the test, participants will be instructed to rest for 5 minutes, after which time vital signs are repeated. The total meters walked will be captured.

Program Name: t_walkt.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADFT Data Cutoff Date: 2023-09-20

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Table 52: 6-Minute Walk Test by Visit: Full Analysis Set

	Pediatric (N=11)	Adult (N=16)	Total (N=27)
C17D15			
6-Minute Walk Test Distance (m)			
n (%)	6 (54.5%)	5 (31.3%)	11 (40.7%)
Mean (SD)	492.0 (79.69)	428.2 (52.82)	463.0 (73.49)
Median	485.5	438.0	461.0
Min, Max	372, 610	348, 495	348, 610
Change from Baseline in 6-Minute Walk Test (m)			
n (%)	6 (54.5%)	5 (31.3%)	11 (40.7%)
Mean (SD)	36.0 (82.38)	-19.2 (28.17)	10.9 (67.46)
Median	49.5	-6.0	4.0
Min, Max	-91, 148	-54, 5	-91, 148
C21D15			
6-Minute Walk Test Distance (m)			
n (%)	6 (54.5%)	4 (25.0%)	10 (37.0%)
Mean (SD)	453.3 (91.49)	448.8 (81.80)	451.5 (82.98)
Median	460.0	439.0	439.0
Min, Max	318, 556	360, 557	318, 557
Change from Baseline in 6-Minute Walk Test (m)			
n (%)	6 (54.5%)	4 (25.0%)	10 (37.0%)
Mean (SD)	-2.7 (75.68)	-3.8 (37.29)	-3.1 (60.38)
Median	-11.0	-16.0	-16.0
Min, Max	-88, 97	-33, 50	-88, 97

SD: Standard deviation; Min: Minimum; Max: Maximum; PN: Plexiform Neurofibroma.
 Participants with a target PN causing airway or lower extremity motor dysfunction at baseline will be assessed for change in 6-minute walk test distance.
 The object of this test is to walk as far as possible over 6 minutes. After completing the test, participants will be instructed to rest for 5 minutes, after which time vital signs are repeated. The total meters walked will be captured.

Program Name: t_walkt.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADFT Data Cutoff Date: 2023-09-20

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Table 52: 6-Minute Walk Test by Visit: Full Analysis Set

	Pediatric (N=11)	Adult (N=16)	Total (N=27)
C24D21			
6-Minute Walk Test Distance (m)			
n (%)			
Mean (SD)	5 (45.5%)	7 (43.8%)	12 (44.4%)
Median	437.6 (94.96)	406.7 (73.56)	419.6 (80.52)
Min, Max	449.0 315, 532	430.0 284, 494	434.0 284, 532
Change from Baseline in 6-Minute Walk Test (m)			
n (%)			
Mean (SD)	5 (45.5%)	7 (43.8%)	12 (44.4%)
Median	-17.2 (106.83)	-24.4 (26.30)	-21.4 (67.39)
Min, Max	-59.0 -139, 115	-13.0 -64, 10	-25.0 -139, 115

SD: Standard deviation; Min: Minimum; Max: Maximum; PN: Plexiform Neurofibroma.
 Participants with a target PN causing airway or lower extremity motor dysfunction at baseline will be assessed for change in 6-minute walk test distance.
 The object of this test is to walk as far as possible over 6 minutes. After completing the test, participants will be instructed to rest for 5 minutes, after which time vital signs are repeated. The total meters walked will be captured.

Program Name: t_walkt.sas Output Generated: 2025-05-02T13:34 Source: ADL, ADFT Data Cutoff Date: 2023-09-20

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Table 59.3: Improvement of PGIS Scores from Any Category to None - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15	Number of Participants Completed the Assessment, n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
	Number of Participants Missing the Assessment, n (%)	17 (36.2%)	15 (25.9%)	32 (30.5%)
	Participants with Clinically Meaningful Score Improvement, n (%)	9 (19.1%)	6 (10.3%)	15 (14.3%)
C5D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	13 (22.4%)	22 (21.0%)
	Participants with Clinically Meaningful Score Improvement, n (%)	11 (23.4%)	7 (12.1%)	18 (17.1%)
C7D15	Number of Participants Completed the Assessment, n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
	Number of Participants Missing the Assessment, n (%)	12 (25.5%)	16 (27.6%)	28 (26.7%)
	Participants with Clinically Meaningful Score Improvement, n (%)	10 (21.3%)	10 (17.2%)	20 (19.0%)
C9D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	20 (34.5%)	29 (27.6%)
	Participants with Clinically Meaningful Score Improvement, n (%)	12 (25.5%)	10 (17.2%)	22 (21.0%)
C13D15	Number of Participants Completed the Assessment, n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
	Number of Participants Missing the Assessment, n (%)	14 (29.8%)	27 (46.6%)	41 (39.0%)
	Participants with Clinically Meaningful Score Improvement, n (%)	11 (23.4%)	9 (15.5%)	20 (19.0%)

PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".

Program Name: t_59_3_pgis_improve_nr.sas Output Generated: 2025-05-02T13:39 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 59.3: Improvement of PGIS Scores from Any Category to None - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	20 (34.5%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	38 (65.5%)	61 (58.1%)
	Participants with Clinically Meaningful Score Improvement, n (%)	9 (19.1%)	8 (13.8%)	17 (16.2%)
C21D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	31 (53.4%)	54 (51.4%)
	Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.6%)	6 (10.3%)	11 (10.5%)
C24D21	Number of Participants Completed the Assessment, n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	28 (59.6%)	33 (56.9%)	61 (58.1%)
	Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.5%)	5 (8.6%)	9 (8.6%)
Total	Number of Participants Completed the Assessment, n (%)	45 (95.7%)	51 (87.9%)	96 (91.4%)
	Number of Participants Missing the Assessment, n (%)	2 (4.3%)	7 (12.1%)	9 (8.6%)
	Participants with Clinically Meaningful Score Improvement, n (%)	22 (46.8%)	19 (32.8%)	41 (39.0%)

PGIS: Patient Global Impression of Severity.

The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".

Program Name: t_59_3_pgis_improve_nr.sas Output Generated: 2025-05-02T13:39 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 59.7: Worsening of PGIS Scores from Any Category to Moderate or Severe - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15	Number of Participants Completed the Assessment, n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
	Number of Participants Missing the Assessment, n (%)	17 (36.2%)	15 (25.9%)	32 (30.5%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	3 (5.2%)	3 (2.9%)
C5D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	13 (22.4%)	22 (21.0%)
	Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	2 (3.4%)	3 (2.9%)
C7D15	Number of Participants Completed the Assessment, n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
	Number of Participants Missing the Assessment, n (%)	12 (25.5%)	16 (27.6%)	28 (26.7%)
	Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	2 (3.4%)	3 (2.9%)
C9D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	20 (34.5%)	29 (27.6%)
	Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	1 (1.7%)	2 (1.9%)
C13D15	Number of Participants Completed the Assessment, n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
	Number of Participants Missing the Assessment, n (%)	14 (29.8%)	27 (46.6%)	41 (39.0%)
	Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.3%)	1 (1.7%)	3 (2.9%)

PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".

Program Name: t_59_7_pgis_worsen_nr.sas Output Generated: 2025-05-02T13:39 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 59.7: Worsening of PGIS Scores from Any Category to Moderate or Severe - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	20 (34.5%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	38 (65.5%)	61 (58.1%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
C21D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	31 (53.4%)	54 (51.4%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.7%)	1 (1.0%)
C24D21	Number of Participants Completed the Assessment, n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	28 (59.6%)	33 (56.9%)	61 (58.1%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
Total	Number of Participants Completed the Assessment, n (%)	45 (95.7%)	51 (87.9%)	96 (91.4%)
	Number of Participants Missing the Assessment, n (%)	2 (4.3%)	7 (12.1%)	9 (8.6%)
	Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.4%)	6 (10.3%)	9 (8.6%)

PGIS: Patient Global Impression of Severity.

The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".

Program Name: t_59_7_pgis_worsen_nr.sas Output Generated: 2025-05-02T13:39 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 60.2: Improvement of PGIC Scores to Very Much or Moderately Better - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15	Number of Participants Completed the Assessment, n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
	Number of Participants Missing the Assessment, n (%)	17 (36.2%)	15 (25.9%)	32 (30.5%)
	Participants with Clinically Meaningful Score Improvement, n (%)	10 (21.3%)	11 (19.0%)	21 (20.0%)
C5D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	13 (22.4%)	22 (21.0%)
	Participants with Clinically Meaningful Score Improvement, n (%)	16 (34.0%)	14 (24.1%)	30 (28.6%)
C7D15	Number of Participants Completed the Assessment, n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
	Number of Participants Missing the Assessment, n (%)	12 (25.5%)	16 (27.6%)	28 (26.7%)
	Participants with Clinically Meaningful Score Improvement, n (%)	17 (36.2%)	11 (19.0%)	28 (26.7%)
C9D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	20 (34.5%)	29 (27.6%)
	Participants with Clinically Meaningful Score Improvement, n (%)	20 (42.6%)	17 (29.3%)	37 (35.2%)
C13D15	Number of Participants Completed the Assessment, n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
	Number of Participants Missing the Assessment, n (%)	14 (29.8%)	27 (46.6%)	41 (39.0%)
	Participants with Clinically Meaningful Score Improvement, n (%)	17 (36.2%)	12 (20.7%)	29 (27.6%)

PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Program Name: t_60_2_pgic_improve_nr.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 60.2: Improvement of PGIC Scores to Very Much or Moderately Better - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15	Number of Participants Completed the Assessment, n (%)	23 (48.9%)	20 (34.5%)	43 (41.0%)
	Number of Participants Missing the Assessment, n (%)	24 (51.1%)	38 (65.5%)	62 (59.0%)
	Participants with Clinically Meaningful Score Improvement, n (%)	13 (27.7%)	13 (22.4%)	26 (24.8%)
C21D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	31 (53.4%)	54 (51.4%)
	Participants with Clinically Meaningful Score Improvement, n (%)	17 (36.2%)	12 (20.7%)	29 (27.6%)
C24D21	Number of Participants Completed the Assessment, n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	28 (59.6%)	33 (56.9%)	61 (58.1%)
	Participants with Clinically Meaningful Score Improvement, n (%)	15 (31.9%)	13 (22.4%)	28 (26.7%)
Total	Number of Participants Completed the Assessment, n (%)	45 (95.7%)	51 (87.9%)	96 (91.4%)
	Number of Participants Missing the Assessment, n (%)	2 (4.3%)	7 (12.1%)	9 (8.6%)
	Participants with Clinically Meaningful Score Improvement, n (%)	37 (78.7%)	27 (46.6%)	64 (61.0%)

PGIC: Patient Global Impression of Change.

The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Program Name: t_60_2_pgic_improve_nr.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 60.4: Worsening of PGIC Scores to Moderately or Very Much Worse - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15	Number of Participants Completed the Assessment, n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
	Number of Participants Missing the Assessment, n (%)	17 (36.2%)	15 (25.9%)	32 (30.5%)
	Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	0	1 (1.0%)
C5D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	13 (22.4%)	22 (21.0%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.7%)	1 (1.0%)
C7D15	Number of Participants Completed the Assessment, n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
	Number of Participants Missing the Assessment, n (%)	12 (25.5%)	16 (27.6%)	28 (26.7%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.7%)	1 (1.0%)
C9D15	Number of Participants Completed the Assessment, n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
	Number of Participants Missing the Assessment, n (%)	9 (19.1%)	20 (34.5%)	29 (27.6%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.7%)	1 (1.0%)
C13D15	Number of Participants Completed the Assessment, n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
	Number of Participants Missing the Assessment, n (%)	14 (29.8%)	27 (46.6%)	41 (39.0%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0

PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Program Name: t_60_4_pgic_worsen_nr.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 60.4: Worsening of PGIC Scores to Moderately or Very Much Worse - Non-Responder Imputation: Full Analysis Set

Visit		Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15	Number of Participants Completed the Assessment, n (%)	23 (48.9%)	20 (34.5%)	43 (41.0%)
	Number of Participants Missing the Assessment, n (%)	24 (51.1%)	38 (65.5%)	62 (59.0%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
C21D15	Number of Participants Completed the Assessment, n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
	Number of Participants Missing the Assessment, n (%)	23 (48.9%)	31 (53.4%)	54 (51.4%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
C24D21	Number of Participants Completed the Assessment, n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
	Number of Participants Missing the Assessment, n (%)	28 (59.6%)	33 (56.9%)	61 (58.1%)
	Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0
Total	Number of Participants Completed the Assessment, n (%)	45 (95.7%)	51 (87.9%)	96 (91.4%)
	Number of Participants Missing the Assessment, n (%)	2 (4.3%)	7 (12.1%)	9 (8.6%)
	Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.1%)	2 (3.4%)	3 (2.9%)

PGIC: Patient Global Impression of Change.

The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Program Name: t_60_4_pgic_worsen_nr.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 61: PGIS Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
Baseline			
n (%)	46 (97.9%)	57 (98.3%)	103 (98.1%)
Mean (SD)	0.9 (0.90)	1.5 (0.80)	1.3 (0.90)
Median	1.0	2.0	1.0
Min, Max	0, 3	0, 3	0, 3
C3D15			
n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
Mean (SD)	0.5 (0.57)	1.2 (0.93)	0.9 (0.87)
Median	0.0	1.0	1.0
Min, Max	0, 2	0, 3	0, 3
Change from Baseline at C3D15			
n (%)	29 (61.7%)	43 (74.1%)	72 (68.6%)
Mean (SD)	-0.4 (0.82)	-0.3 (0.61)	-0.3 (0.70)
Median	0.0	0.0	0.0
Min, Max	-2, 1	-1, 1	-2, 1

PGIS: Patient Global Impression of Severity.

The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".

Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3

Program Name: t_61_pgis_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 61: PGIS Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C5D15			
n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
Mean (SD)	0.4 (0.59)	1.1 (0.89)	0.8 (0.85)
Median	0.0	1.0	1.0
Min, Max	0, 2	0, 3	0, 3
Change from Baseline at C5D15			
n (%)	37 (78.7%)	45 (77.6%)	82 (78.1%)
Mean (SD)	-0.4 (0.83)	-0.4 (0.69)	-0.4 (0.75)
Median	0.0	0.0	0.0
Min, Max	-2, 2	-2, 1	-2, 2
C7D15			
n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
Mean (SD)	0.5 (0.70)	1.0 (0.96)	0.8 (0.90)
Median	0.0	1.0	1.0
Min, Max	0, 3	0, 3	0, 3
Change from Baseline at C7D15			
n (%)	34 (72.3%)	42 (72.4%)	76 (72.4%)
Mean (SD)	-0.5 (0.83)	-0.4 (0.74)	-0.4 (0.77)
Median	0.0	0.0	0.0
Min, Max	-3, 1	-2, 1	-3, 1

PGIS: Patient Global Impression of Severity.

The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe". Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3

Program Name: t_61_pgis_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 61: PGIS Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C9D15			
n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
Mean (SD)	0.5 (0.76)	1.0 (0.93)	0.8 (0.88)
Median	0.0	1.0	1.0
Min, Max	0, 3	0, 3	0, 3
Change from Baseline at C9D15			
n (%)	37 (78.7%)	37 (63.8%)	74 (70.5%)
Mean (SD)	-0.4 (0.82)	-0.6 (0.72)	-0.5 (0.78)
Median	0.0	-1.0	0.0
Min, Max	-2, 2	-2, 1	-2, 2
C13D15			
n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
Mean (SD)	0.5 (0.79)	0.8 (0.80)	0.7 (0.80)
Median	0.0	1.0	0.0
Min, Max	0, 3	0, 3	0, 3
Change from Baseline at C13D15			
n (%)	32 (68.1%)	31 (53.4%)	63 (60.0%)
Mean (SD)	-0.3 (1.04)	-0.6 (0.72)	-0.5 (0.89)
Median	0.0	-1.0	0.0
Min, Max	-3, 2	-2, 1	-3, 2

PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".
Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3

Program Name: t_61_pgis_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 61: PGIS Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C17D15			
n (%)	24 (51.1%)	20 (34.5%)	44 (41.9%)
Mean (SD)	0.3 (0.48)	0.6 (0.82)	0.5 (0.66)
Median	0.0	0.0	0.0
Min, Max	0, 1	0, 2	0, 2
Change from Baseline at C17D15			
n (%)	23 (48.9%)	20 (34.5%)	43 (41.0%)
Mean (SD)	-0.7 (0.83)	-0.7 (0.67)	-0.7 (0.75)
Median	-1.0	-1.0	-1.0
Min, Max	-3, 1	-2, 0	-3, 1
C21D15			
n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
Mean (SD)	0.5 (0.59)	0.9 (0.80)	0.7 (0.72)
Median	0.5	1.0	1.0
Min, Max	0, 2	0, 3	0, 3
Change from Baseline at C21D15			
n (%)	23 (48.9%)	27 (46.6%)	50 (47.6%)
Mean (SD)	-0.4 (0.66)	-0.6 (0.74)	-0.5 (0.71)
Median	0.0	-1.0	-1.0
Min, Max	-2, 1	-2, 2	-2, 2

PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".
Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3

Program Name: t_61_pgis_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 61: PGIS Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C24D21			
n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
Mean (SD)	0.6 (0.60)	0.9 (0.81)	0.8 (0.73)
Median	1.0	1.0	1.0
Min, Max	0, 2	0, 2	0, 2
Change from Baseline at C24D21			
n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
Mean (SD)	-0.3 (0.93)	-0.5 (0.51)	-0.4 (0.72)
Median	0.0	0.0	0.0
Min, Max	-2, 1	-1, 0	-2, 1

PGIS: Patient Global Impression of Severity.
The PGIS is a single item scale that evaluates the participant's perception of the overall severity of their NF1-related symptoms over the past week on a 4-point scale ranging from "none" to "severe".
Responses are mapped as None = 0, Mild = 1, Moderate = 2, Severe = 3

Program Name: t_61_pgis_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 62: PGIC Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C3D15			
n (%)	30 (63.8%)	43 (74.1%)	73 (69.5%)
Mean (SD)	2.8 (1.21)	3.2 (1.12)	3.0 (1.17)
Median	3.0	3.0	3.0
Min, Max	1, 6	1, 5	1, 6
C5D15			
n (%)	38 (80.9%)	45 (77.6%)	83 (79.0%)
Mean (SD)	2.6 (1.10)	3.1 (1.16)	2.9 (1.15)
Median	3.0	3.0	3.0
Min, Max	1, 5	1, 6	1, 6
C7D15			
n (%)	35 (74.5%)	42 (72.4%)	77 (73.3%)
Mean (SD)	2.5 (1.20)	3.2 (1.10)	2.9 (1.19)
Median	3.0	3.0	3.0
Min, Max	1, 5	1, 6	1, 6

PGIC: Patient Global Impression of Change.

The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Responses are mapped as Very Much Better = 2, A Little Better = 3, No Change = 4, A Little Worse = 5, Moderately worse = 6, Very much worse = 7.

Program Name: t_62_pgic_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 62: PGIC Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C9D15			
n (%)	38 (80.9%)	38 (65.5%)	76 (72.4%)
Mean (SD)	2.4 (1.22)	2.9 (1.21)	2.7 (1.23)
Median	2.0	3.0	3.0
Min, Max	1, 5	1, 6	1, 6
C13D15			
n (%)	33 (70.2%)	31 (53.4%)	64 (61.0%)
Mean (SD)	2.4 (1.30)	2.8 (1.13)	2.6 (1.23)
Median	2.0	3.0	3.0
Min, Max	1, 5	1, 5	1, 5
C17D15			
n (%)	23 (48.9%)	20 (34.5%)	43 (41.0%)
Mean (SD)	2.2 (1.20)	2.4 (1.31)	2.3 (1.24)
Median	2.0	2.0	2.0
Min, Max	1, 5	1, 5	1, 5
C21D15			
n (%)	24 (51.1%)	27 (46.6%)	51 (48.6%)
Mean (SD)	1.9 (0.93)	2.7 (1.13)	2.4 (1.11)
Median	2.0	3.0	2.0
Min, Max	1, 4	1, 5	1, 5

PGIC: Patient Global Impression of Change.

The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".

Responses are mapped as Very Much Better =1, Moderately Better =2, A Little Better =3, No Change =4, A Little Worse =5, Moderately Worse =6, Very much Worse =7.

Program Name: t_62_pgic_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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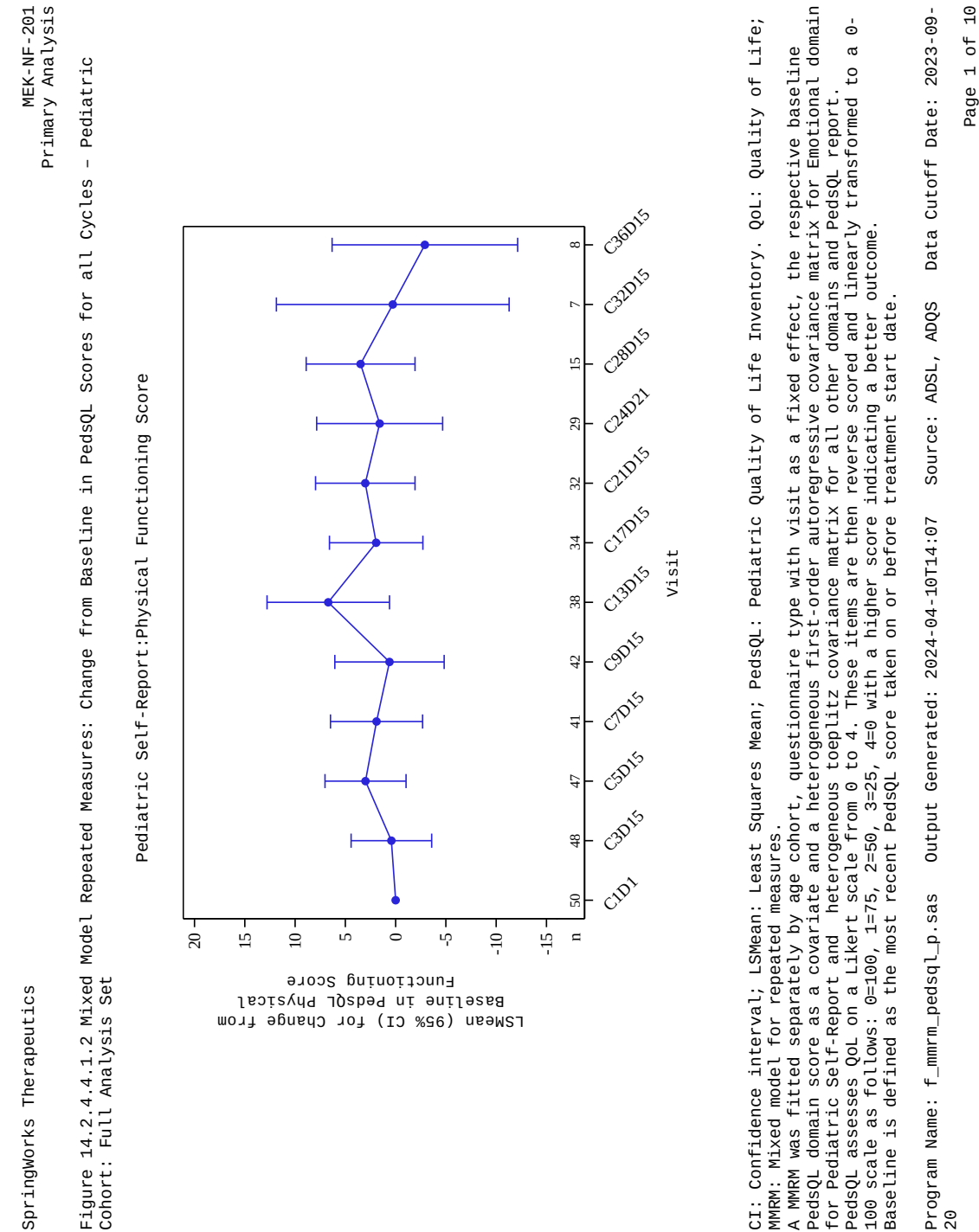
Table 62: PGIC Summary by Visit: Full Analysis Set

Visit	Pediatric (N=47)	Adult (N=58)	Total (N=105)
C24D21			
n (%)	19 (40.4%)	25 (43.1%)	44 (41.9%)
Mean (SD)	1.9 (1.22)	2.6 (1.41)	2.3 (1.36)
Median	2.0	2.0	2.0
Min, Max	1, 5	1, 5	1, 5

PGIC: Patient Global Impression of Change.
The PGIC is a single item scale that evaluates the participant's perception of the overall change in their overall status since the start of the study treatment on a 7-point scale ranging from "very much better" to "very much worse".
Responses are mapped as Very Much Better =1, Moderately Better = 2, A Little Better = 3, No Change = 4, A Little Worse = 5, Moderately worse = 6, Very much Worse = 7.

Program Name: t_62_pgic_cfb.sas Output Generated: 2025-05-02T13:40 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

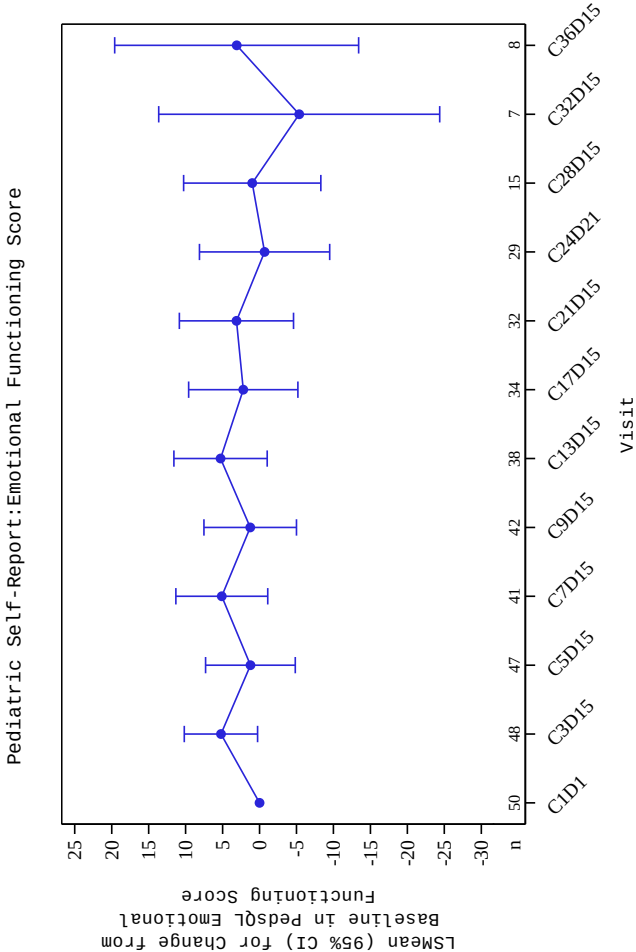
6 Gesundheitsbezogene Lebensqualität



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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



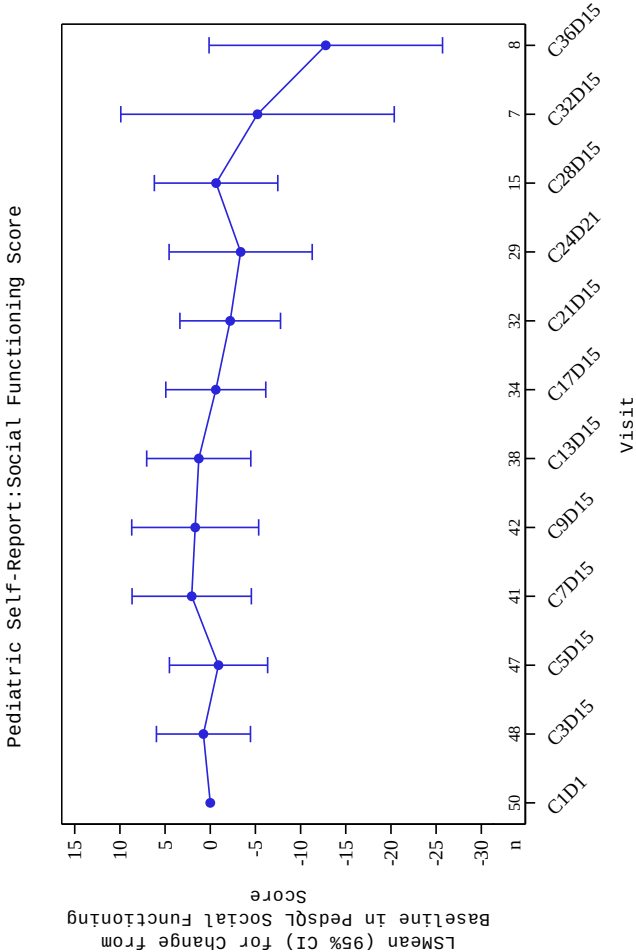
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures.
A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrp_pedsq_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set

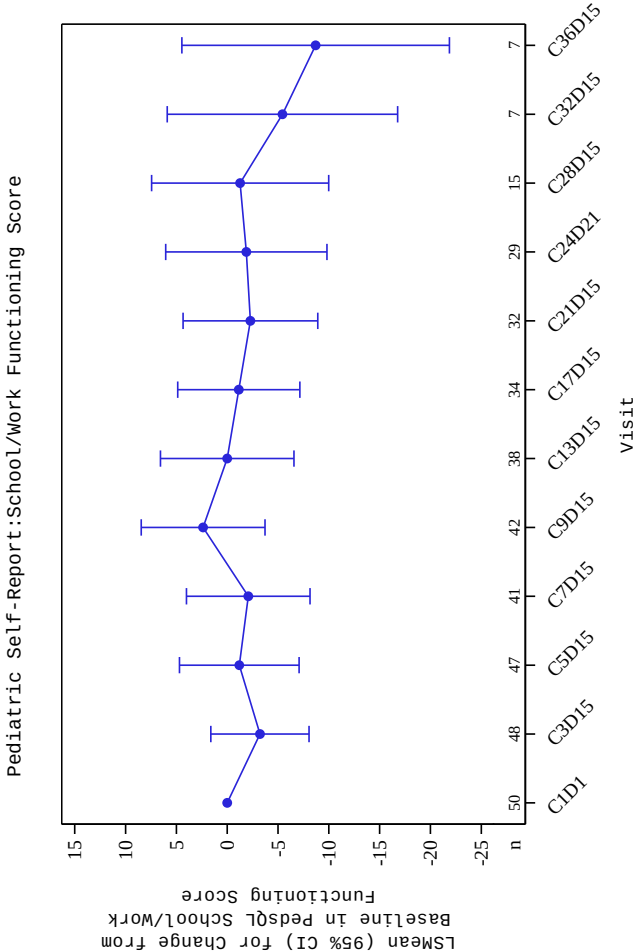


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



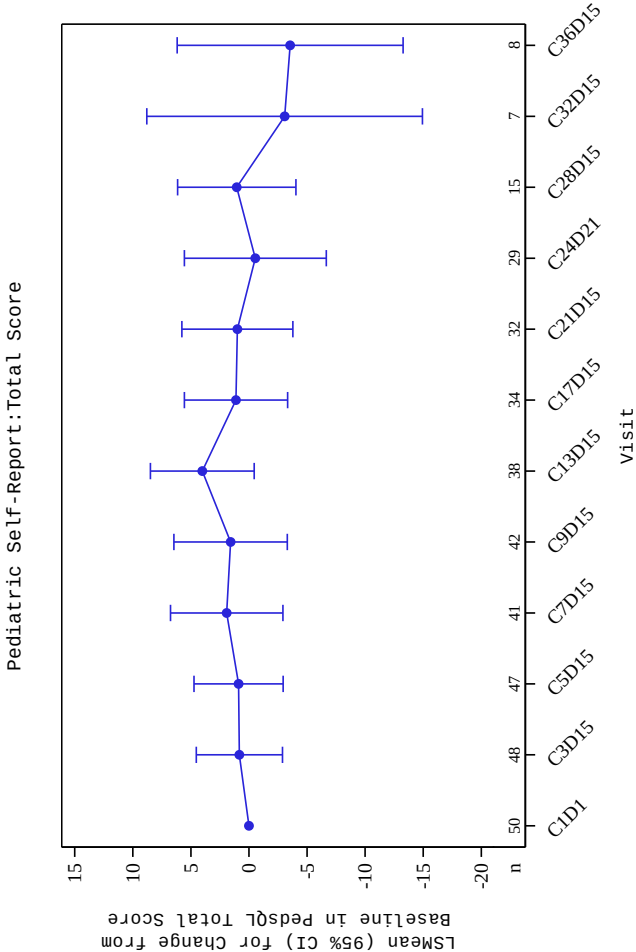
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrp_pedsq_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



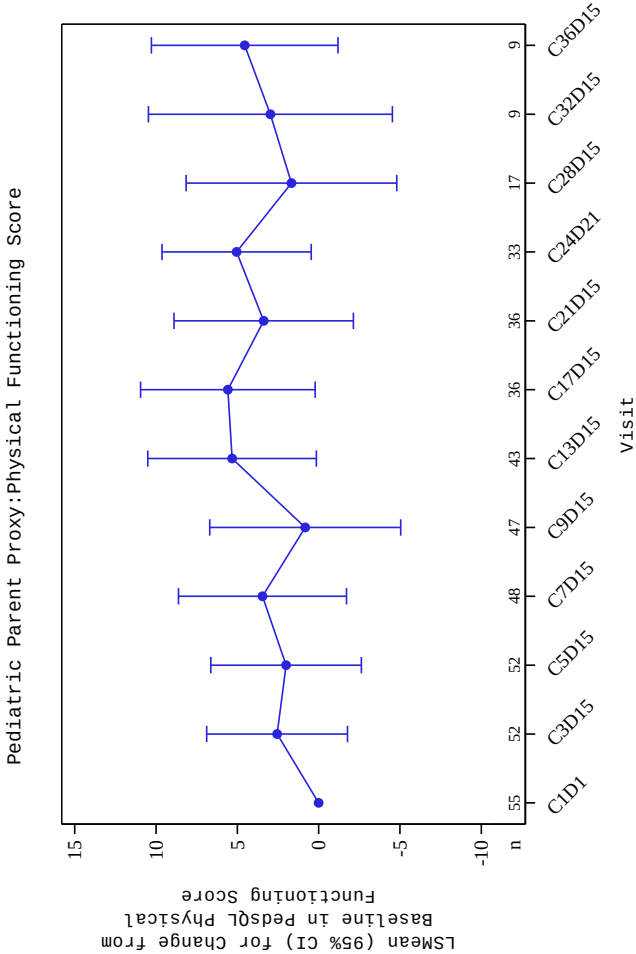
CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrmm_pedsqll_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



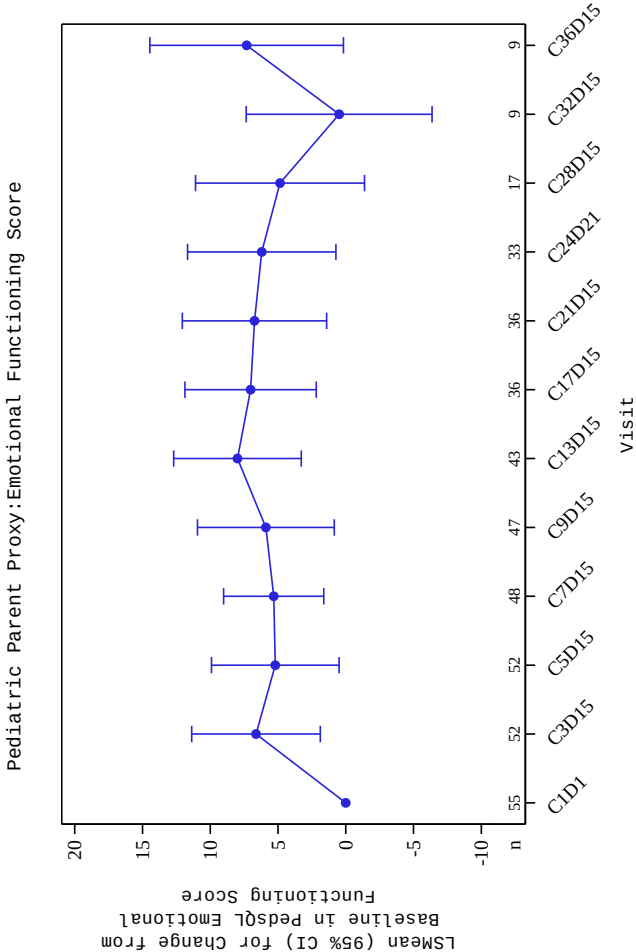
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrmm_pedsqll_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



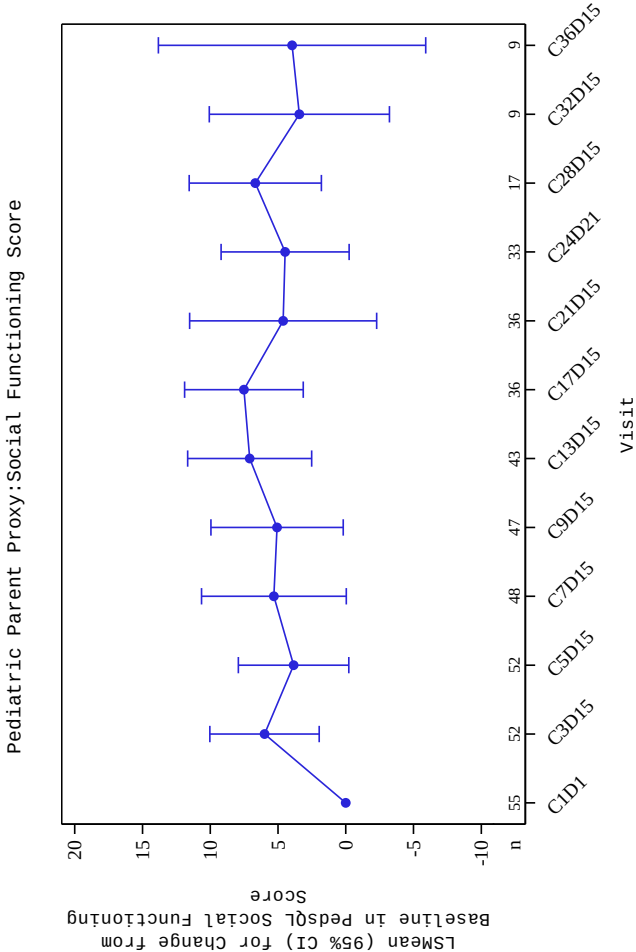
CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrp_pedsq_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



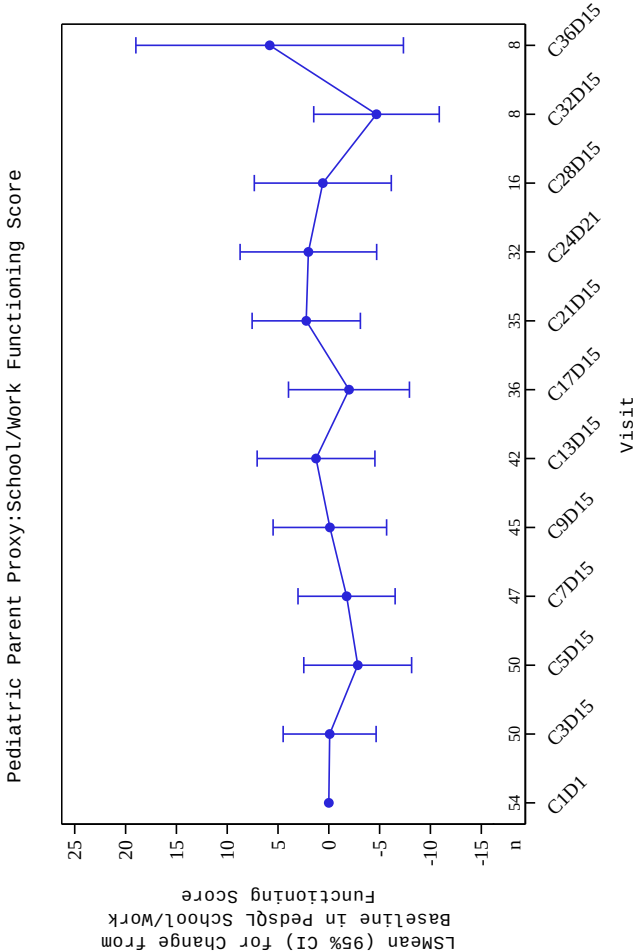
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrp_pedsq_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

MEK-NF-201
Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



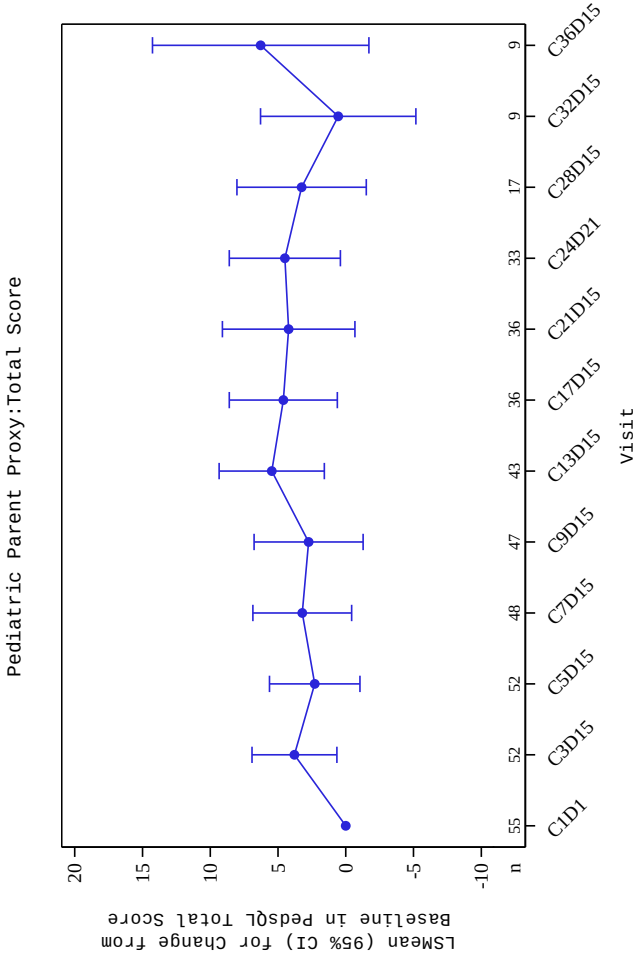
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toeplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrmm_pedsqll_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Primary Analysis

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Figure 14.2.4.4.1.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles – Pediatric Cohort: Full Analysis Set



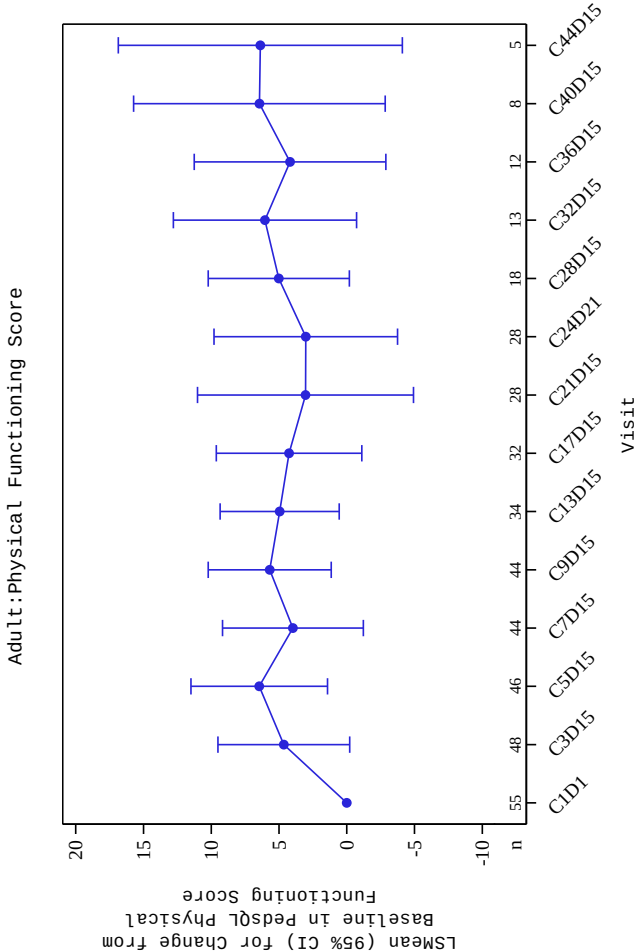
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous first-order autoregressive covariance matrix for Emotional domain for Pediatric Self-Report and heterogeneous toepplitz covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_mmrmm_pedsqll_p.sas Output Generated: 2024-04-10T14:07 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Figure 14.2.4.4.2.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for All Cycles – Adult Cohort: Full Analysis Set

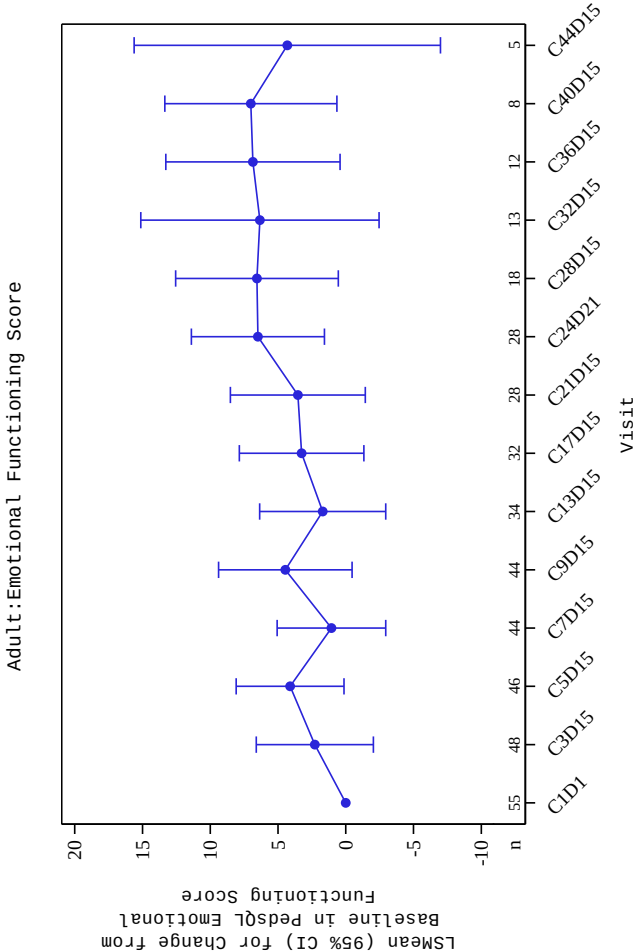


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous toeplitz covariance matrix for School/Work domain and heterogeneous first-order autoregressive covariance matrix for all other domains. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Priamry Analysis

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Figure 14.2.4.4.2.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for All Cycles – Adult Cohort: Full Analysis Set

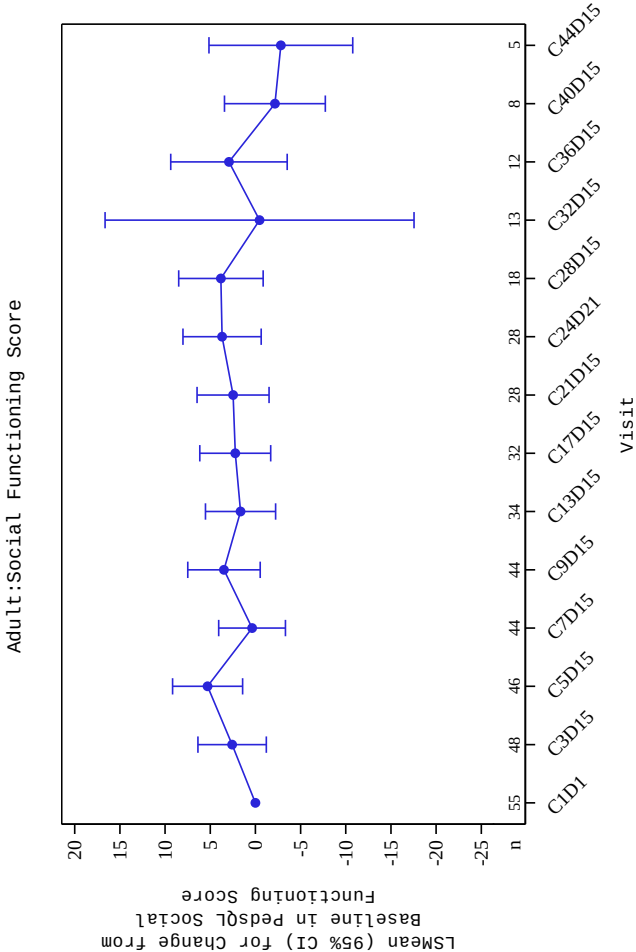


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous toeplitz covariance matrix for School/Work domain and heterogeneous first-order autoregressive covariance matrix for all other domains. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 14.2.4.4.2.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for All Cycles – Adult Cohort: Full Analysis Set

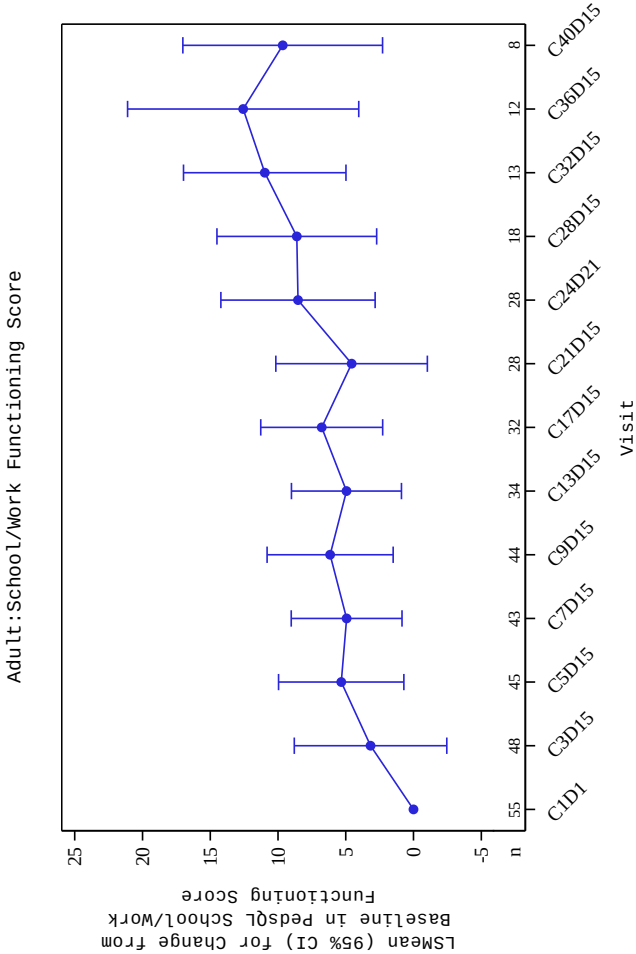


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous toeplitz covariance matrix for School/Work domain and heterogeneous first-order autoregressive covariance matrix for all other domains. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Priamry Analysis

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Figure 14.2.4.4.2.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for All Cycles – Adult Cohort: Full Analysis Set

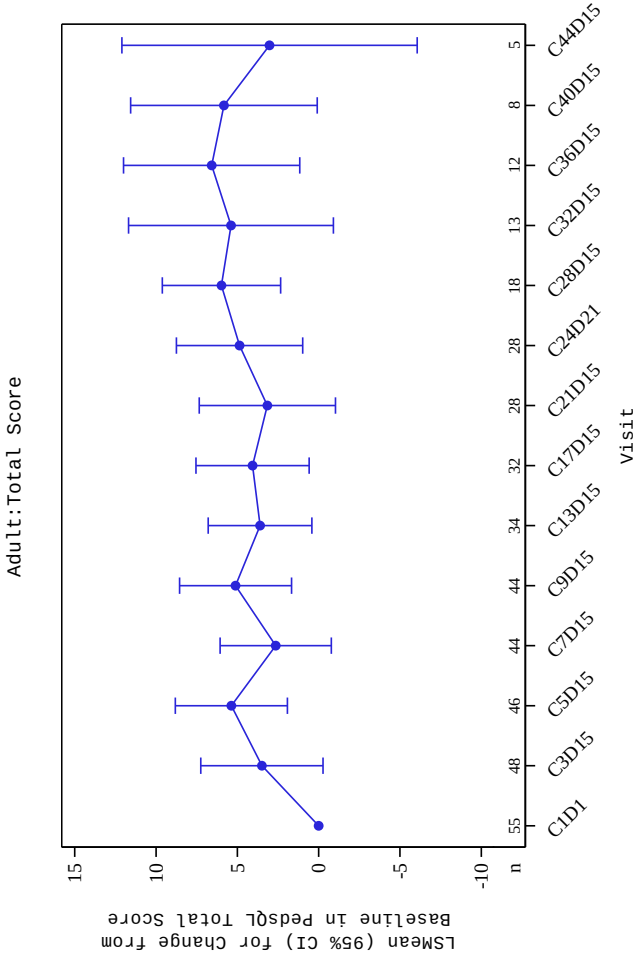


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous toeplitz covariance matrix for School/Work domain and heterogeneous first-order autoregressive covariance matrix for all other domains. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Priamry Analysis

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Figure 14.2.4.4.2.2 Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for All Cycles – Adult Cohort: Full Analysis Set

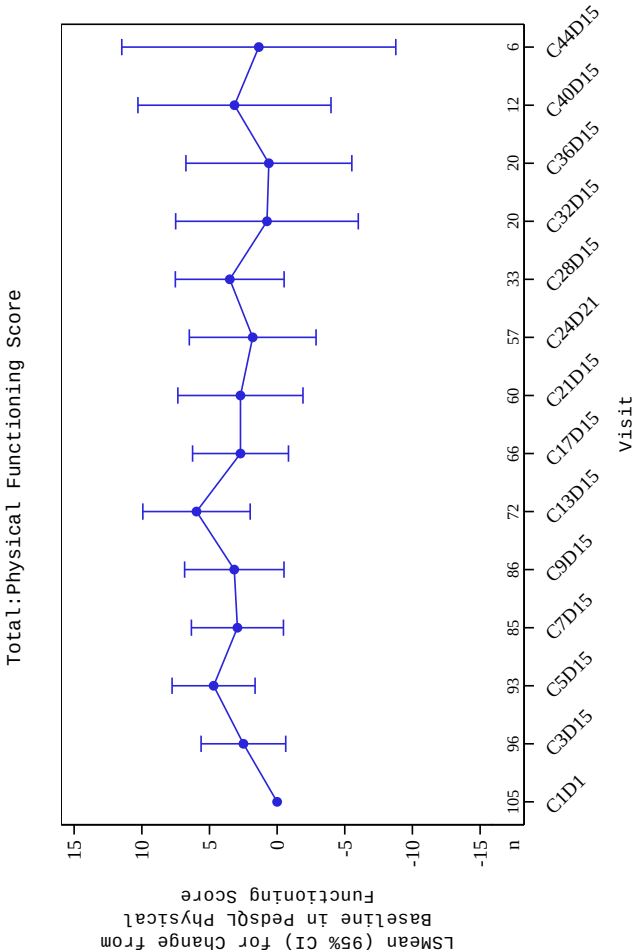


CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted separately by age cohort, questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score as a covariate and a heterogeneous toeplitz covariance matrix for School/Work domain and heterogeneous first-order autoregressive covariance matrix for all other domains. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 7: Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles: Full Analysis Set

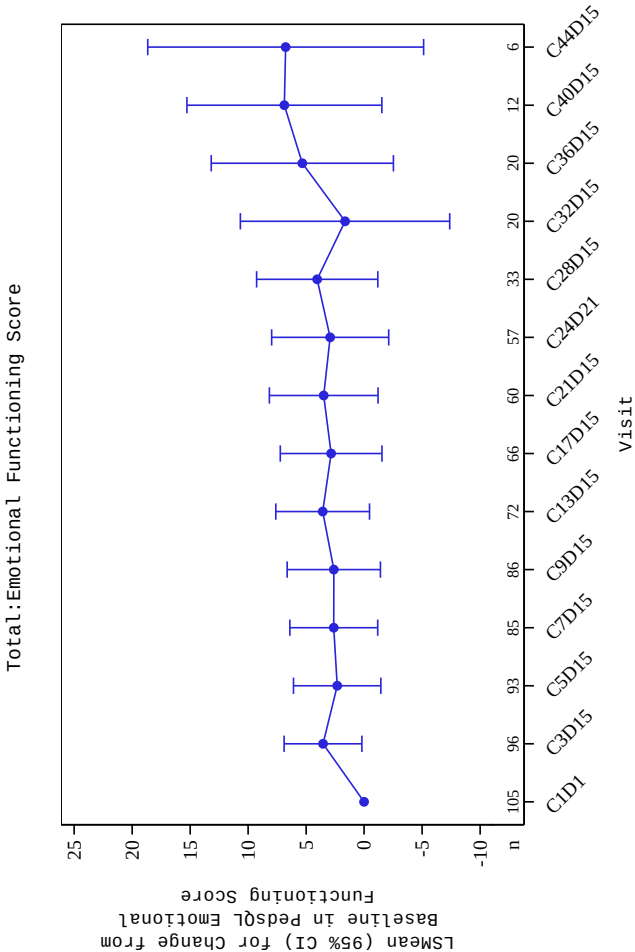


CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted by questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score and age cohort as covariates and a heterogeneous toepplitz covariance matrix for Social domain and heterogeneous first-order autoregressive covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 7: Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles: Full Analysis Set

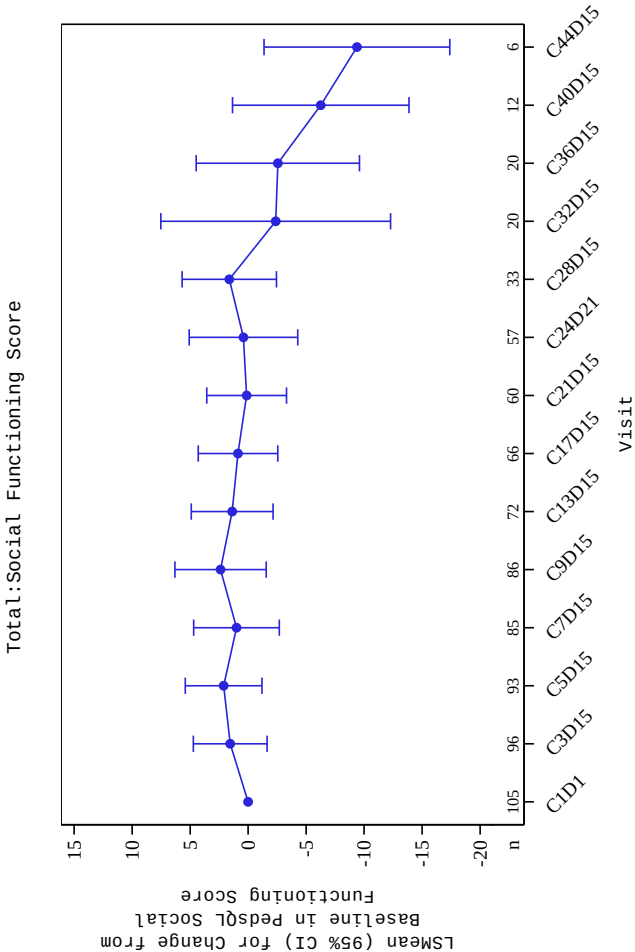


CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted by questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score and age cohort as covariates and a heterogeneous toepplitz covariance matrix for Social domain and heterogeneous first-order autoregressive covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 7: Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles: Full Analysis Set

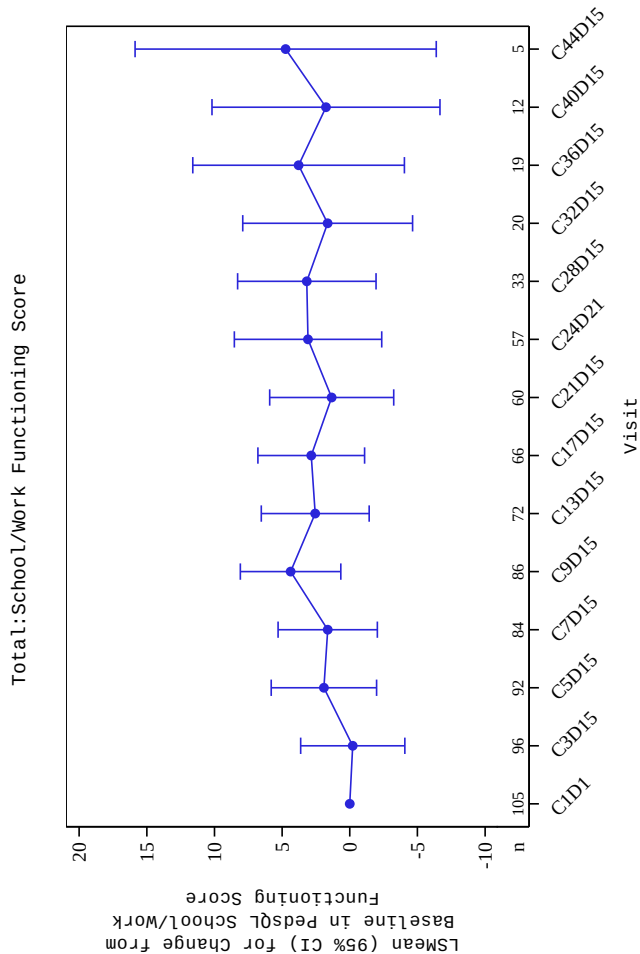


CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted by questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score and age cohort as covariates and a heterogeneous toeplitz covariance matrix for Social domain and heterogeneous first-order autoregressive covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 7: Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles: Full Analysis Set



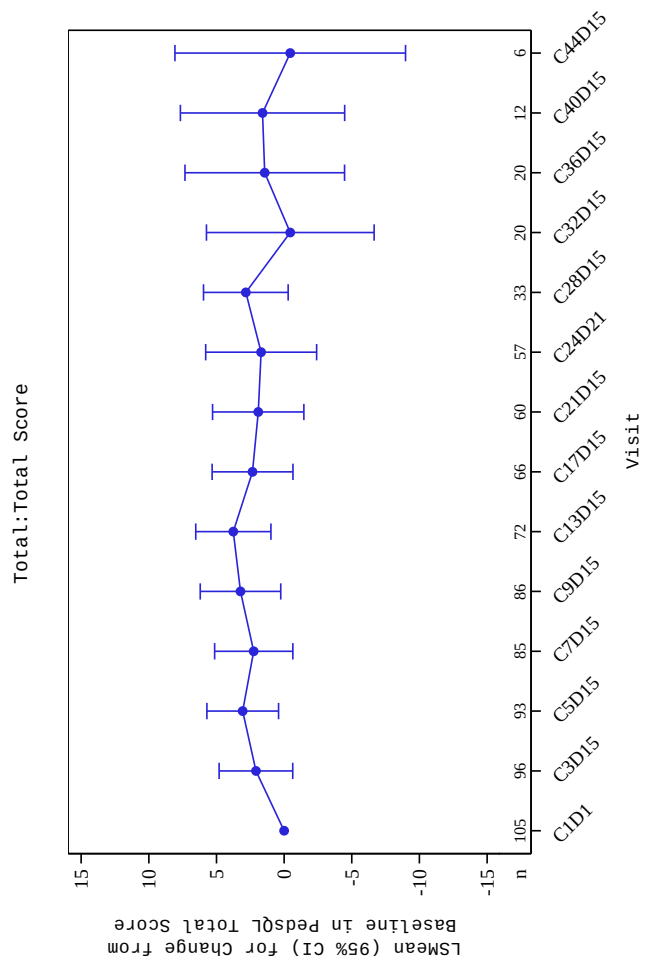
CI: Confidence interval; LS Mean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted by questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score and age cohort as covariates and a heterogeneous toplitz covariance matrix for Social domain and heterogeneous first-order autoregressive covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

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Figure 7: Mixed Model Repeated Measures: Change from Baseline in PedsQL Scores for all Cycles: Full Analysis Set



CI: Confidence interval; LSMean: Least Squares Mean; PedsQL: Pediatric Quality of Life Inventory. QoL: Quality of Life; MMRM: Mixed model for repeated measures. A MMRM was fitted by questionnaire type with visit as a fixed effect, the respective baseline PedsQL domain score and age cohort as covariates and a heterogeneous toeplitz covariance matrix for Social domain and heterogeneous first-order autoregressive covariance matrix for all other domains and PedsQL report. PedsQL assesses QoL on a Likert scale from 0 to 4. These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with a higher score indicating a better outcome. Baseline is defined as the most recent PedsQL score taken on or before treatment start date.

Program Name: f_7_pedsq_mmrn.t.sas Output Generated: 2025-05-12T15:01 Source: ADQS Data Cutoff Date: 2023-09-20
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GBA

Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
PRO Expected	50 (100%)	56 (100%)	58 (100%)	108 (100%)
PRO Completed	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
PRO Not Completed	0	1 (1.8%)	3 (5.2%)	3 (2.8%)
C3D15				
PRO Expected	48 (96.0%)	54 (96.4%)	51 (87.9%)	99 (91.7%)
PRO Completed	47 (97.9%)	51 (94.4%)	47 (92.2%)	94 (94.9%)
PRO Not Completed	1 (2.1%)	3 (5.6%)	4 (7.8%)	5 (5.1%)
C5D15				
PRO Expected	48 (96.0%)	54 (96.4%)	50 (86.2%)	98 (90.7%)
PRO Completed	46 (95.8%)	52 (96.3%)	48 (96.0%)	94 (95.9%)
PRO Not Completed	2 (4.2%)	2 (3.7%)	2 (4.0%)	4 (4.1%)
C7D15				
PRO Expected	45 (90.0%)	50 (89.3%)	46 (79.3%)	91 (84.3%)
PRO Completed	41 (91.1%)	47 (94.0%)	44 (95.7%)	85 (93.4%)
PRO Not Completed	4 (8.9%)	3 (6.0%)	2 (4.3%)	6 (6.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBA

Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
PRO Expected	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
PRO Completed	41 (95.3%)	45 (93.8%)	38 (82.6%)	79 (88.8%)
PRO Not Completed	2 (4.7%)	3 (6.3%)	8 (17.4%)	10 (11.2%)
C13D15				
PRO Expected	38 (76.0%)	42 (75.0%)	36 (62.1%)	74 (68.5%)
PRO Completed	36 (94.7%)	41 (97.6%)	36 (100%)	72 (97.3%)
PRO Not Completed	2 (5.3%)	1 (2.4%)	0	2 (2.7%)
C17D15				
PRO Expected	36 (72.0%)	40 (71.4%)	34 (58.6%)	70 (64.8%)
PRO Completed	33 (91.7%)	35 (87.5%)	32 (94.1%)	65 (92.9%)
PRO Not Completed	3 (8.3%)	5 (12.5%)	2 (5.9%)	5 (7.1%)
C21D15				
PRO Expected	33 (66.0%)	37 (66.1%)	32 (55.2%)	65 (60.2%)
PRO Completed	32 (97.0%)	36 (97.3%)	29 (90.6%)	61 (93.8%)
PRO Not Completed	1 (3.0%)	1 (2.7%)	3 (9.4%)	4 (6.2%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
PRO Expected	30 (60.0%)	34 (60.7%)	31 (53.4%)	61 (56.5%)
PRO Completed	29 (96.7%)	33 (97.1%)	30 (96.8%)	59 (96.7%)
PRO Not Completed	1 (3.3%)	1 (2.9%)	1 (3.2%)	2 (3.3%)
C28D15				
PRO Expected	19 (38.0%)	21 (37.5%)	25 (43.1%)	44 (40.7%)
PRO Completed	15 (78.9%)	17 (81.0%)	20 (80.0%)	35 (79.5%)
PRO Not Completed	4 (21.1%)	4 (19.0%)	5 (20.0%)	9 (20.5%)
C32D15				
PRO Expected	8 (16.0%)	10 (17.9%)	14 (24.1%)	22 (20.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	14 (100%)	21 (95.5%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.5%)
C36D15				
PRO Expected	8 (16.0%)	10 (17.9%)	13 (22.4%)	21 (19.4%)
PRO Completed	8 (100%)	9 (90.0%)	13 (100%)	21 (100%)
PRO Not Completed	0	1 (10.0%)	0	0

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
PRO Expected	6 (12.0%)	6 (10.7%)	9 (15.5%)	15 (13.9%)
PRO Completed	4 (8.0%)	4 (6.6%)	8 (88.9%)	12 (80.0%)
PRO Not Completed	2 (33.3%)	2 (33.3%)	1 (11.1%)	3 (20.0%)
C44D15				
PRO Expected	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
PRO Completed	1 (100%)	1 (100%)	5 (100%)	6 (100%)
PRO Not Completed	0	0	0	0
C48D15				
PRO Expected	0	0	1 (1.7%)	1 (0.9%)
PRO Completed	0	0	1 (100%)	1 (100%)
PRO Not Completed	0	0	0	0
ET				
PRO Expected	20 (40.0%)	22 (39.3%)	28 (48.3%)	48 (44.4%)
PRO Completed	11 (55.0%)	12 (54.5%)	19 (67.9%)	30 (62.5%)
PRO Not Completed	9 (45.0%)	10 (45.5%)	9 (32.1%)	18 (37.5%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
SFU				
PRO Expected	26 (52.0%)	29 (51.8%)	39 (67.2%)	65 (60.2%)
PRO Completed	15 (57.7%)	17 (58.6%)	16 (41.0%)	31 (47.7%)
PRO Not Completed	11 (42.3%)	12 (41.4%)	23 (59.0%)	34 (52.3%)
LTFU				
PRO Expected	3 (6.0%)	3 (5.4%)	4 (6.9%)	7 (6.5%)
PRO Completed	2 (66.7%)	2 (66.7%)	3 (75.0%)	5 (71.4%)
PRO Not Completed	1 (33.3%)	1 (33.3%)	1 (25.0%)	2 (28.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected. Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria. Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed. Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
PRO Expected	50 (100%)	56 (100%)	58 (100%)	108 (100%)
PRO Completed	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
PRO Not Completed	0	1 (1.8%)	3 (5.2%)	3 (2.8%)
C3D15				
PRO Expected	48 (96.0%)	54 (96.4%)	51 (87.9%)	99 (91.7%)
PRO Completed	47 (97.9%)	51 (94.4%)	47 (92.2%)	94 (94.9%)
PRO Not Completed	1 (2.1%)	3 (5.6%)	4 (7.8%)	5 (5.1%)
C5D15				
PRO Expected	48 (96.0%)	54 (96.4%)	50 (86.2%)	98 (90.7%)
PRO Completed	46 (95.8%)	52 (96.3%)	48 (96.0%)	94 (95.9%)
PRO Not Completed	2 (4.2%)	2 (3.7%)	2 (4.0%)	4 (4.1%)
C7D15				
PRO Expected	45 (90.0%)	50 (89.3%)	46 (79.3%)	91 (84.3%)
PRO Completed	41 (91.1%)	47 (94.0%)	44 (95.7%)	85 (93.4%)
PRO Not Completed	4 (8.9%)	3 (6.0%)	2 (4.3%)	6 (6.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
PRO Expected	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
PRO Completed	41 (95.3%)	45 (93.8%)	38 (82.6%)	79 (88.8%)
PRO Not Completed	2 (4.7%)	3 (6.3%)	8 (17.4%)	10 (11.2%)
C13D15				
PRO Expected	38 (76.0%)	42 (75.0%)	36 (62.1%)	74 (68.5%)
PRO Completed	36 (94.7%)	41 (97.6%)	36 (100%)	72 (97.3%)
PRO Not Completed	2 (5.3%)	1 (2.4%)	0	2 (2.7%)
C17D15				
PRO Expected	36 (72.0%)	40 (71.4%)	34 (58.6%)	70 (64.8%)
PRO Completed	33 (91.7%)	35 (87.5%)	32 (94.1%)	65 (92.9%)
PRO Not Completed	3 (8.3%)	5 (12.5%)	2 (5.9%)	5 (7.1%)
C21D15				
PRO Expected	33 (66.0%)	37 (66.1%)	32 (55.2%)	65 (60.2%)
PRO Completed	32 (97.0%)	36 (97.3%)	29 (98.6%)	61 (93.8%)
PRO Not Completed	1 (3.0%)	1 (2.7%)	3 (9.4%)	4 (6.2%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
PRO Expected	30 (60.0%)	34 (60.7%)	31 (53.4%)	61 (56.5%)
PRO Completed	29 (96.7%)	33 (97.1%)	30 (96.8%)	59 (96.7%)
PRO Not Completed	1 (3.3%)	1 (2.9%)	1 (3.2%)	2 (3.3%)
C28D15				
PRO Expected	19 (38.0%)	21 (37.5%)	25 (43.1%)	44 (40.7%)
PRO Completed	15 (78.9%)	17 (81.0%)	20 (80.0%)	35 (79.5%)
PRO Not Completed	4 (21.1%)	4 (19.0%)	5 (20.0%)	9 (20.5%)
C32D15				
PRO Expected	8 (16.0%)	10 (17.9%)	14 (24.1%)	22 (20.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	14 (100%)	21 (95.5%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.5%)
C36D15				
PRO Expected	8 (16.0%)	10 (17.9%)	13 (22.4%)	21 (19.4%)
PRO Completed	8 (100%)	9 (90.0%)	13 (100%)	21 (100%)
PRO Not Completed	0	1 (10.0%)	0	0

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
PRO Expected	6 (12.0%)	6 (10.7%)	9 (15.5%)	15 (13.9%)
PRO Completed	4 (8.0%)	4 (6.6%)	8 (88.9%)	12 (80.0%)
PRO Not Completed	2 (3.3%)	2 (3.3%)	1 (1.1%)	3 (2.0%)
C44D15				
PRO Expected	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
PRO Completed	1 (100%)	1 (100%)	5 (100%)	6 (100%)
PRO Not Completed	0	0	0	0
C48D15				
PRO Expected	0	0	1 (1.7%)	1 (0.9%)
PRO Completed	0	0	1 (100%)	1 (100%)
PRO Not Completed	0	0	0	0
ET				
PRO Expected	20 (40.0%)	22 (39.3%)	28 (48.3%)	48 (44.4%)
PRO Completed	11 (55.0%)	12 (54.5%)	19 (67.9%)	30 (62.5%)
PRO Not Completed	9 (45.0%)	10 (45.5%)	9 (32.1%)	18 (37.5%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
SFU				
PRO Expected	26 (52.0%)	29 (51.8%)	39 (67.2%)	65 (60.2%)
PRO Completed	15 (57.7%)	17 (58.6%)	16 (41.0%)	31 (47.7%)
PRO Not Completed	11 (42.3%)	12 (41.4%)	23 (59.0%)	34 (52.3%)
LTFU				
PRO Expected	3 (6.0%)	3 (5.4%)	4 (6.9%)	7 (6.5%)
PRO Completed	2 (66.7%)	2 (66.7%)	3 (75.0%)	5 (71.4%)
PRO Not Completed	1 (33.3%)	1 (33.3%)	1 (25.0%)	2 (28.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected. Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria. Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit. Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed. Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
PRO Expected	50 (100%)	56 (100%)	58 (100%)	108 (100%)
PRO Completed	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
PRO Not Completed	0	1 (1.8%)	3 (5.2%)	3 (2.8%)
C3D15				
PRO Expected	48 (96.0%)	54 (96.4%)	51 (87.9%)	99 (91.7%)
PRO Completed	47 (97.9%)	51 (94.4%)	47 (92.2%)	94 (94.9%)
PRO Not Completed	1 (2.1%)	3 (5.6%)	4 (7.8%)	5 (5.1%)
C5D15				
PRO Expected	48 (96.0%)	54 (96.4%)	50 (86.2%)	98 (90.7%)
PRO Completed	46 (95.8%)	52 (96.3%)	48 (96.0%)	94 (95.9%)
PRO Not Completed	2 (4.2%)	2 (3.7%)	2 (4.0%)	4 (4.1%)
C7D15				
PRO Expected	45 (90.0%)	50 (89.3%)	46 (79.3%)	91 (84.3%)
PRO Completed	41 (91.1%)	47 (94.0%)	44 (95.7%)	85 (93.4%)
PRO Not Completed	4 (8.9%)	3 (6.0%)	2 (4.3%)	6 (6.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
PRO Expected	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
PRO Completed	41 (95.3%)	45 (93.8%)	38 (82.6%)	79 (88.8%)
PRO Not Completed	2 (4.7%)	3 (6.3%)	8 (17.4%)	10 (11.2%)
C13D15				
PRO Expected	38 (76.0%)	42 (75.0%)	36 (62.1%)	74 (68.5%)
PRO Completed	36 (94.7%)	41 (97.6%)	36 (100%)	72 (97.3%)
PRO Not Completed	2 (5.3%)	1 (2.4%)	0	2 (2.7%)
C17D15				
PRO Expected	36 (72.0%)	40 (71.4%)	34 (58.6%)	70 (64.8%)
PRO Completed	33 (91.7%)	35 (87.5%)	32 (94.1%)	65 (92.9%)
PRO Not Completed	3 (8.3%)	5 (12.5%)	2 (5.9%)	5 (7.1%)
C21D15				
PRO Expected	33 (66.0%)	37 (66.1%)	32 (55.2%)	65 (60.2%)
PRO Completed	32 (97.0%)	36 (97.3%)	29 (90.6%)	61 (93.8%)
PRO Not Completed	1 (3.0%)	1 (2.7%)	3 (9.4%)	4 (6.2%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
PRO Expected	30 (60.0%)	34 (60.7%)	31 (53.4%)	61 (56.5%)
PRO Completed	29 (96.7%)	33 (97.1%)	30 (96.8%)	59 (96.7%)
PRO Not Completed	1 (3.3%)	1 (2.9%)	1 (3.2%)	2 (3.3%)
C28D15				
PRO Expected	19 (38.0%)	21 (37.5%)	25 (43.1%)	44 (40.7%)
PRO Completed	15 (78.9%)	17 (81.0%)	20 (80.0%)	35 (79.5%)
PRO Not Completed	4 (21.1%)	4 (19.0%)	5 (20.0%)	9 (20.5%)
C32D15				
PRO Expected	8 (16.0%)	10 (17.9%)	14 (24.1%)	22 (20.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	14 (100%)	21 (95.5%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.5%)
C36D15				
PRO Expected	8 (16.0%)	10 (17.9%)	13 (22.4%)	21 (19.4%)
PRO Completed	8 (100%)	9 (90.0%)	13 (100%)	21 (100%)
PRO Not Completed	0	1 (10.0%)	0	0

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
PRO Expected	6 (12.0%)	6 (10.7%)	9 (15.5%)	15 (13.9%)
PRO Completed	4 (8.0%)	4 (6.6%)	8 (88.9%)	12 (80.0%)
PRO Not Completed	2 (3.3%)	2 (3.3%)	1 (1.1%)	3 (2.0%)
C44D15				
PRO Expected	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
PRO Completed	1 (100%)	1 (100%)	5 (100%)	6 (100%)
PRO Not Completed	0	0	0	0
C48D15				
PRO Expected	0	0	1 (1.7%)	1 (0.9%)
PRO Completed	0	0	1 (100%)	1 (100%)
PRO Not Completed	0	0	0	0
ET				
PRO Expected	20 (40.0%)	22 (39.3%)	28 (48.3%)	48 (44.4%)
PRO Completed	11 (55.0%)	12 (54.5%)	19 (67.9%)	30 (62.5%)
PRO Not Completed	9 (45.0%)	10 (45.5%)	9 (32.1%)	18 (37.5%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
SFU				
PRO Expected	26 (52.0%)	29 (51.8%)	39 (67.2%)	65 (60.2%)
PRO Completed	15 (57.7%)	17 (58.6%)	16 (41.0%)	31 (47.7%)
PRO Not Completed	11 (42.3%)	12 (41.4%)	23 (59.0%)	34 (52.3%)
LTFU				
PRO Expected	3 (6.0%)	3 (5.4%)	4 (6.9%)	7 (6.5%)
PRO Completed	2 (66.7%)	2 (66.7%)	3 (75.0%)	5 (71.4%)
PRO Not Completed	1 (33.3%)	1 (33.3%)	1 (25.0%)	2 (28.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
PRO Expected	50 (100%)	56 (100%)	58 (100%)	108 (100%)
PRO Completed	50 (100%)	54 (96.4%)	55 (94.8%)	105 (97.2%)
PRO Not Completed	0	2 (3.6%)	3 (5.2%)	3 (2.8%)
C3D15				
PRO Expected	48 (96.0%)	54 (96.4%)	51 (87.9%)	99 (91.7%)
PRO Completed	47 (97.9%)	50 (92.6%)	47 (92.2%)	94 (94.9%)
PRO Not Completed	1 (2.1%)	4 (7.4%)	4 (7.8%)	5 (5.1%)
C5D15				
PRO Expected	48 (96.0%)	54 (96.4%)	50 (86.2%)	98 (90.7%)
PRO Completed	46 (95.8%)	50 (92.6%)	47 (94.0%)	93 (94.9%)
PRO Not Completed	2 (4.2%)	4 (7.4%)	3 (6.0%)	5 (5.1%)
C7D15				
PRO Expected	45 (90.0%)	50 (89.3%)	46 (79.3%)	91 (84.3%)
PRO Completed	41 (91.1%)	46 (92.0%)	43 (93.5%)	84 (92.3%)
PRO Not Completed	4 (8.9%)	4 (8.0%)	3 (6.5%)	7 (7.7%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
PRO Expected	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
PRO Completed	41 (95.3%)	44 (91.7%)	38 (82.6%)	79 (88.8%)
PRO Not Completed	2 (4.7%)	4 (8.3%)	8 (17.4%)	10 (11.2%)
C13D15				
PRO Expected	38 (76.0%)	42 (75.0%)	36 (62.1%)	74 (68.5%)
PRO Completed	36 (94.7%)	41 (97.6%)	36 (100%)	72 (97.3%)
PRO Not Completed	2 (5.3%)	1 (2.4%)	0	2 (2.7%)
C17D15				
PRO Expected	36 (72.0%)	40 (71.4%)	34 (58.6%)	70 (64.8%)
PRO Completed	33 (91.7%)	35 (87.5%)	32 (94.1%)	65 (92.9%)
PRO Not Completed	3 (8.3%)	5 (12.5%)	2 (5.9%)	5 (7.1%)
C21D15				
PRO Expected	33 (66.0%)	37 (66.1%)	32 (55.2%)	65 (60.2%)
PRO Completed	32 (97.0%)	36 (97.3%)	29 (98.6%)	61 (93.8%)
PRO Not Completed	1 (3.0%)	1 (2.7%)	3 (9.4%)	4 (6.2%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
PRO Expected	30 (60.0%)	34 (60.7%)	31 (53.4%)	61 (56.5%)
PRO Completed	29 (96.7%)	33 (97.1%)	30 (96.8%)	59 (96.7%)
PRO Not Completed	1 (3.3%)	1 (2.9%)	1 (3.2%)	2 (3.3%)
C28D15				
PRO Expected	19 (38.0%)	21 (37.5%)	25 (43.1%)	44 (40.7%)
PRO Completed	15 (78.9%)	17 (81.0%)	20 (80.0%)	35 (79.5%)
PRO Not Completed	4 (21.1%)	4 (19.0%)	5 (20.0%)	9 (20.5%)
C32D15				
PRO Expected	8 (16.0%)	10 (17.9%)	14 (24.1%)	22 (20.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	14 (100%)	21 (95.5%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.5%)
C36D15				
PRO Expected	8 (16.0%)	10 (17.9%)	13 (22.4%)	21 (19.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	13 (100%)	20 (95.2%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.8%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.

Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
PRO Expected	6 (12.0%)	6 (10.7%)	9 (15.5%)	15 (13.9%)
PRO Completed	4 (8.0%)	4 (6.6%)	8 (88.9%)	12 (80.0%)
PRO Not Completed	2 (33.3%)	2 (33.3%)	1 (11.1%)	3 (20.0%)
C44D15				
PRO Expected	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
PRO Completed	1 (100%)	1 (100%)	4 (80.0%)	5 (83.3%)
PRO Not Completed	0	0	1 (20.0%)	1 (16.7%)
C48D15				
PRO Expected	0	0	1 (1.7%)	1 (0.9%)
PRO Completed	0	0	1 (100%)	1 (100%)
PRO Not Completed	0	0	0	0
ET				
PRO Expected	20 (40.0%)	22 (39.3%)	28 (48.3%)	48 (44.4%)
PRO Completed	11 (55.0%)	11 (50.0%)	19 (67.9%)	30 (62.5%)
PRO Not Completed	9 (45.0%)	11 (50.0%)	9 (32.1%)	18 (37.5%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
SFU				
PRO Expected	26 (52.0%)	29 (51.8%)	39 (67.2%)	65 (60.2%)
PRO Completed	15 (57.7%)	16 (55.2%)	16 (41.0%)	31 (47.7%)
PRO Not Completed	11 (42.3%)	13 (44.8%)	23 (59.0%)	34 (52.3%)
LTFU				
PRO Expected	3 (6.0%)	3 (5.4%)	4 (6.9%)	7 (6.5%)
PRO Completed	2 (66.7%)	2 (66.7%)	3 (75.0%)	5 (71.4%)
PRO Not Completed	1 (33.3%)	1 (33.3%)	1 (25.0%)	2 (28.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Total PedsQL Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
PRO Expected	50 (100%)	56 (100%)	58 (100%)	108 (100%)
PRO Completed	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
PRO Not Completed	0	1 (1.8%)	3 (5.2%)	3 (2.8%)
C3D15				
PRO Expected	48 (96.0%)	54 (96.4%)	51 (87.9%)	99 (91.7%)
PRO Completed	47 (97.9%)	51 (94.4%)	47 (92.2%)	94 (94.9%)
PRO Not Completed	1 (2.1%)	3 (5.6%)	4 (7.8%)	5 (5.1%)
C5D15				
PRO Expected	48 (96.0%)	54 (96.4%)	50 (86.2%)	98 (90.7%)
PRO Completed	46 (95.8%)	52 (96.3%)	48 (96.0%)	94 (95.9%)
PRO Not Completed	2 (4.2%)	2 (3.7%)	2 (4.0%)	4 (4.1%)
C7D15				
PRO Expected	45 (90.0%)	50 (89.3%)	46 (79.3%)	91 (84.3%)
PRO Completed	41 (91.1%)	47 (94.0%)	44 (95.7%)	85 (93.4%)
PRO Not Completed	4 (8.9%)	3 (6.0%)	2 (4.3%)	6 (6.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Total PedsQL Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
PRO Expected	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
PRO Completed	41 (95.3%)	45 (93.8%)	38 (82.6%)	79 (88.8%)
PRO Not Completed	2 (4.7%)	3 (6.3%)	8 (17.4%)	10 (11.2%)
C13D15				
PRO Expected	38 (76.0%)	42 (75.0%)	36 (62.1%)	74 (68.5%)
PRO Completed	36 (94.7%)	41 (97.6%)	36 (100%)	72 (97.3%)
PRO Not Completed	2 (5.3%)	1 (2.4%)	0	2 (2.7%)
C17D15				
PRO Expected	36 (72.0%)	40 (71.4%)	34 (58.6%)	70 (64.8%)
PRO Completed	33 (91.7%)	35 (87.5%)	32 (94.1%)	65 (92.9%)
PRO Not Completed	3 (8.3%)	5 (12.5%)	2 (5.9%)	5 (7.1%)
C21D15				
PRO Expected	33 (66.0%)	37 (66.1%)	32 (55.2%)	65 (60.2%)
PRO Completed	32 (97.0%)	36 (97.3%)	29 (90.6%)	61 (93.8%)
PRO Not Completed	1 (3.0%)	1 (2.7%)	3 (9.4%)	4 (6.2%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Total PedsQL Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
PRO Expected	30 (60.0%)	34 (60.7%)	31 (53.4%)	61 (56.5%)
PRO Completed	29 (96.7%)	33 (97.1%)	30 (96.8%)	59 (96.7%)
PRO Not Completed	1 (3.3%)	1 (2.9%)	1 (3.2%)	2 (3.3%)
C28D15				
PRO Expected	19 (38.0%)	21 (37.5%)	25 (43.1%)	44 (40.7%)
PRO Completed	15 (78.9%)	17 (81.0%)	20 (80.0%)	35 (79.5%)
PRO Not Completed	4 (21.1%)	4 (19.0%)	5 (20.0%)	9 (20.5%)
C32D15				
PRO Expected	8 (16.0%)	10 (17.9%)	14 (24.1%)	22 (20.4%)
PRO Completed	7 (87.5%)	9 (90.0%)	14 (100%)	21 (95.5%)
PRO Not Completed	1 (12.5%)	1 (10.0%)	0	1 (4.5%)
C36D15				
PRO Expected	8 (16.0%)	10 (17.9%)	13 (22.4%)	21 (19.4%)
PRO Completed	8 (100%)	9 (90.0%)	13 (100%)	21 (100%)
PRO Not Completed	0	1 (10.0%)	0	0

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.

N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire. Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.

Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.

Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.

Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Total PedsQL Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
PRO Expected	6 (12.0%)	6 (10.7%)	9 (15.5%)	15 (13.9%)
PRO Completed	4 (8.0%)	4 (6.6%)	8 (88.9%)	12 (80.0%)
PRO Not Completed	2 (33.3%)	2 (33.3%)	1 (11.1%)	3 (20.0%)
C44D15				
PRO Expected	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
PRO Completed	1 (100%)	1 (100%)	5 (100%)	6 (100%)
PRO Not Completed	0	0	0	0
C48D15				
PRO Expected	0	0	1 (1.7%)	1 (0.9%)
PRO Completed	0	0	1 (100%)	1 (100%)
PRO Not Completed	0	0	0	0
ET				
PRO Expected	20 (40.0%)	22 (39.3%)	28 (48.3%)	48 (44.4%)
PRO Completed	11 (55.0%)	12 (54.5%)	19 (67.9%)	30 (62.5%)
PRO Not Completed	9 (45.0%)	10 (45.5%)	9 (32.1%)	18 (37.5%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 14: Compliance Rate for PedsQL by Visit: Full Analysis Set

Domain: Total PedsQL Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
SFU				
PRO Expected	26 (52.0%)	29 (51.8%)	39 (67.2%)	65 (60.2%)
PRO Completed	15 (57.7%)	17 (58.6%)	16 (41.0%)	31 (47.7%)
PRO Not Completed	11 (42.3%)	12 (41.4%)	23 (59.0%)	34 (52.3%)
LTFU				
PRO Expected	3 (6.0%)	3 (5.4%)	4 (6.9%)	7 (6.5%)
PRO Completed	2 (66.7%)	2 (66.7%)	3 (75.0%)	5 (71.4%)
PRO Not Completed	1 (33.3%)	1 (33.3%)	1 (25.0%)	2 (28.6%)

PedsQL: Pediatric Quality of Life Inventory; PRO: Patient Reported Outcome; ET: Early Termination; SFU: Safety Follow-Up; LTFU: Long-Term Follow-Up.
 N represents the number of participants in the Full Analysis Set eligible for the corresponding questionnaire.
 Compliance rates are calculated as participants with minimum requirements for scoring divided by the number of participants with PRO assessments expected.
 Participants were expected to complete a PRO assessment as long as they were alive and had not discontinued study at the given cycle and satisfied the age eligibility criteria.
 Participants are considered as having minimum requirements for scoring a PedsQL domain at a given visit if <=50% of the questions in that domain are missing at that visit.
 Percentages completed/not completed are calculated out of those expected, and percentages for reasons not completed are calculated out of the total not completed.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_pedcomp.sas Output Generated: 2025-05-12T17:52 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
n (%)	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
Mean (SD)	77.50 (22.106)	73.81 (23.765)	57.73 (25.093)	67.14 (25.605)
Median	82.81	78.13	59.38	71.88
Min, Max	12.5, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	78.39 (21.697)	76.92 (23.156)	61.00 (26.509)	69.69 (25.630)
Median	84.38	85.94	64.06	75.00
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0
Change from Baseline at				
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	0.59 (15.044)	3.25 (19.003)	5.47 (15.757)	3.03 (15.519)
Median	0.00	3.13	4.69	0.00
Min, Max	-37.5, 40.6	-59.4, 65.6	-37.5, 37.5	-37.5, 40.6
LS Mean (SE)	0.42 (2.038)	2.56 (2.200)	4.64 (2.471)	2.49 (1.592)
95% CI	(-3.59, 4.43)	(-1.77, 6.88)	(-0.22, 9.51)	(-0.63, 5.62)
p-value	0.836	0.246	0.061	0.118

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	81.91 (20.646)	77.91 (20.843)	64.11 (27.381)	73.11 (25.689)
Median	90.63	84.38	68.75	78.13
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0
Change from Baseline at				
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	3.06 (13.769)	3.03 (19.328)	7.11 (15.100)	5.06 (14.508)
Median	3.13	3.13	6.25	3.13
Min, Max	-31.3, 43.8	-50.0, 68.8	-34.4, 43.8	-34.4, 43.8
LS Mean (SE)	2.99 (2.047)	2.00 (2.352)	6.46 (2.559)	4.69 (1.562)
95% CI	(-1.03, 7.02)	(-2.63, 6.63)	(1.42, 11.50)	(1.63, 7.76)
p-value	0.145	0.395	0.012	0.003

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	80.95 (19.712)	79.04 (21.273)	61.87 (27.852)	71.07 (25.963)
Median	87.50	82.81	64.06	75.00
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0
Change from Baseline at				
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	1.98 (17.198)	3.97 (19.088)	3.92 (17.429)	2.98 (17.242)
Median	0.00	0.00	3.13	3.13
Min, Max	-34.4, 62.5	-56.3, 53.1	-34.4, 40.6	-34.4, 62.5
LS Mean (SE)	1.90 (2.327)	3.45 (2.626)	3.98 (2.640)	2.93 (1.734)
95% CI	(-2.68, 6.48)	(-1.71, 8.62)	(-1.22, 9.17)	(-0.47, 6.34)
p-value	0.415	0.190	0.133	0.091

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	79.24 (22.448)	76.53 (22.581)	64.63 (26.506)	71.77 (25.543)
Median	85.94	78.13	65.63	75.00
Min, Max	0.0, 100.0	15.6, 100.0	3.1, 100.0	0.0, 100.0
Change from Baseline at				
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	0.82 (20.288)	1.53 (24.380)	5.61 (16.857)	3.27 (18.657)
Median	0.00	3.13	3.13	0.00
Min, Max	-75.0, 37.5	-68.8, 59.4	-25.0, 43.8	-75.0, 43.8
LS Mean (SE)	0.61 (2.762)	0.83 (2.984)	5.68 (2.307)	3.17 (1.870)
95% CI	(-4.83, 6.05)	(-5.04, 6.70)	(1.14, 10.22)	(-0.51, 6.84)
p-value	0.826	0.781	0.014	0.091

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	84.35 (18.397)	80.16 (21.477)	68.29 (21.965)	76.77 (21.583)
Median	93.30	87.50	67.19	81.25
Min, Max	31.3, 100.0	0.0, 100.0	25.0, 100.0	25.0, 100.0
Change from Baseline at				
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	6.56 (23.363)	5.74 (22.254)	4.60 (16.414)	5.63 (20.264)
Median	0.00	3.13	3.13	1.56
Min, Max	-31.3, 87.5	-62.5, 71.9	-25.0, 46.9	-31.3, 87.5
LS Mean (SE)	6.70 (3.093)	5.32 (2.635)	4.95 (2.232)	5.96 (2.021)
95% CI	(0.61, 12.79)	(0.14, 10.51)	(0.56, 9.34)	(1.99, 9.93)
p-value	0.031	0.044	0.027	0.003

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	80.51 (17.695)	82.55 (19.910)	67.68 (24.253)	74.29 (21.939)
Median	85.94	87.50	65.63	81.25
Min, Max	43.8, 100.0	21.9, 100.0	18.8, 100.0	18.8, 100.0
Change from Baseline at				
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	1.93 (18.141)	4.77 (20.695)	1.95 (16.106)	1.94 (17.053)
Median	0.00	3.13	0.00	0.00
Min, Max	-46.9, 37.5	-65.6, 43.8	-28.1, 34.4	-46.9, 37.5
LS Mean (SE)	1.94 (2.360)	5.58 (2.729)	4.26 (2.729)	2.71 (1.804)
95% CI	(-2.71, 6.58)	(0.22, 10.95)	(-1.11, 9.63)	(-0.84, 6.25)
p-value	0.412	0.042	0.120	0.134

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	80.76 (17.301)	79.43 (21.094)	67.63 (26.259)	74.64 (22.726)
Median	82.81	87.50	73.44	78.13
Min, Max	50.0, 100.0	25.0, 100.0	15.6, 100.0	15.6, 100.0
Change from Baseline at				
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	3.13 (20.330)	0.69 (20.309)	1.12 (22.793)	2.19 (21.353)
Median	4.69	3.13	3.13	3.13
Min, Max	-43.8, 37.5	-75.0, 28.1	-65.6, 31.3	-65.6, 37.5
LS Mean (SE)	3.02 (2.513)	3.38 (2.802)	3.04 (4.050)	2.71 (2.355)
95% CI	(-1.93, 7.97)	(-2.13, 8.89)	(-4.92, 11.01)	(-1.91, 7.34)
p-value	0.231	0.229	0.453	0.250

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	78.34 (23.369)	81.06 (19.136)	66.52 (26.144)	72.53 (25.262)
Median	81.25	87.50	68.75	75.00
Min, Max	21.9, 100.0	37.5, 100.0	6.3, 100.0	6.3, 100.0
Change from Baseline at				
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	0.54 (21.571)	2.65 (15.569)	1.90 (18.987)	1.21 (20.173)
Median	0.00	3.13	3.13	0.00
Min, Max	-46.9, 43.8	-34.4, 37.5	-34.4, 34.4	-46.9, 43.8
LS Mean (SE)	1.59 (3.183)	5.05 (2.333)	3.02 (3.441)	1.81 (2.384)
95% CI	(-4.68, 7.85)	(0.46, 9.64)	(-3.75, 9.79)	(-2.88, 6.49)
p-value	0.618	0.031	0.380	0.449

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	81.04 (18.430)	78.49 (20.725)	68.06 (24.805)	73.96 (22.773)
Median	81.25	84.38	68.75	78.13
Min, Max	28.1, 100.0	37.5, 100.0	9.4, 100.0	9.4, 100.0
Change from Baseline at				
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	-0.63 (16.117)	-1.47 (15.433)	3.13 (12.592)	1.42 (14.194)
Median	-3.13	0.00	0.00	0.00
Min, Max	-28.1, 34.4	-28.1, 34.4	-15.6, 34.4	-28.1, 34.4
LS Mean (SE)	3.48 (2.750)	1.67 (3.291)	5.01 (2.646)	3.50 (2.045)
95% CI	(-1.93, 8.90)	(-4.80, 8.15)	(-0.19, 10.22)	(-0.51, 7.52)
p-value	0.206	0.611	0.059	0.087

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	76.34 (19.420)	81.25 (19.073)	63.56 (25.062)	68.04 (23.556)
Median	81.25	87.50	60.71	68.75
Min, Max	37.5, 100.0	46.9, 100.0	21.9, 100.0	21.9, 100.0
Change from Baseline at				
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	-11.16 (20.952)	-1.04 (14.987)	3.95 (17.055)	-1.34 (19.417)
Median	-3.13	0.00	3.13	3.13
Min, Max	-53.1, 6.3	-28.1, 25.0	-31.3, 34.4	-53.1, 34.4
LS Mean (SE)	0.28 (5.879)	2.97 (3.812)	6.04 (3.436)	0.75 (3.436)
95% CI	(-11.29, 11.86)	(-4.53, 10.47)	(-0.72, 12.80)	(-6.00, 7.50)
p-value	0.962	0.437	0.080	0.827

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	82.03 (15.195)	82.64 (19.016)	61.98 (26.777)	70.00 (24.531)
Median	82.81	90.63	57.81	70.31
Min, Max	56.3, 100.0	43.8, 100.0	25.0, 100.0	25.0, 100.0
Change from Baseline at				
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	-5.08 (17.111)	0.35 (14.014)	2.86 (16.721)	-0.31 (16.902)
Median	-12.50	0.00	4.69	-1.56
Min, Max	-25.0, 21.9	-31.3, 21.9	-25.0, 34.4	-25.0, 34.4
LS Mean (SE)	-2.91 (4.687)	4.55 (2.916)	4.18 (3.593)	0.61 (3.122)
95% CI	(-12.14, 6.31)	(-1.19, 10.29)	(-2.89, 11.25)	(-5.52, 6.74)
p-value	0.535	0.120	0.245	0.845

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	81.25 (10.520)	70.31 (20.650)	59.38 (30.160)	66.67 (26.926)
Median	81.25	71.88	57.81	68.75
Min, Max	68.8, 93.8	43.8, 93.8	21.9, 100.0	21.9, 100.0
Change from Baseline at				
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	-6.25 (5.103)	-3.91 (7.813)	7.42 (21.322)	2.86 (18.486)
Median	-6.25	0.00	7.81	0.00
Min, Max	-12.5, 0.0	-15.6, 0.0	-34.4, 34.4	-34.4, 34.4
LS Mean (SE)	NA	NA	6.45 (4.717)	3.15 (3.634)
95% CI	(NA, NA)	(NA, NA)	(-2.84, 15.73)	(-3.98, 10.29)
p-value	NA	NA	0.173	0.386

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	71.88	59.38	65.63 (36.039)	66.67 (32.335)
Median	71.88	59.38	68.75	70.31
Min, Max	71.9, 71.9	59.4, 59.4	18.8, 100.0	18.8, 100.0
Change from Baseline at				
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	-12.50	-15.63	10.63 (13.729)	6.77 (15.489)
Median	-12.50	-15.63	6.25	4.69
Min, Max	-12.5, -12.5	-15.6, -15.6	0.0, 34.4	-12.5, 34.4
LS Mean (SE)	NA	NA	6.38 (5.326)	1.35 (5.157)
95% CI	(NA, NA)	(NA, NA)	(-4.10, 16.86)	(-8.77, 11.48)
p-value	NA	NA	0.232	0.793

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Physical Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	40.63	40.63
Median	NA	NA	40.63	40.63
Min, Max	(NA, NA)	(NA, NA)	40.6, 40.6	40.6, 40.6
Change from Baseline at				
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	6.25	6.25
Median	NA	NA	6.25	6.25
Min, Max	(NA, NA)	(NA, NA)	6.3, 6.3	6.3, 6.3
LS Mean (SE)	NA	NA	NA	NA
95% CI	(NA, NA)	(NA, NA)	(NA, NA)	(NA, NA)
p-value	NA	NA	NA	NA

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
n (%)	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
Mean (SD)	74.90 (21.818)	73.27 (19.418)	68.27 (21.240)	71.43 (21.670)
Median	80.00	75.00	70.00	70.00
Min, Max	5.0, 100.0	35.0, 100.0	5.0, 100.0	5.0, 100.0

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	80.10 (20.460)	79.62 (17.955)	70.42 (21.997)	75.26 (21.684)
Median	87.50	85.00	70.00	80.00
Min, Max	25.0, 100.0	35.0, 100.0	15.0, 100.0	15.0, 100.0
Change from Baseline at				
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	5.21 (21.536)	6.15 (19.418)	3.54 (14.802)	4.38 (18.400)
Median	0.00	5.00	5.00	0.00
Min, Max	-50.0, 70.0	-45.0, 45.0	-35.0, 35.0	-50.0, 70.0
LS Mean (SE)	5.22 (2.518)	6.62 (2.411)	2.28 (2.196)	3.54 (1.707)
95% CI	(0.26, 10.18)	(1.88, 11.37)	(-2.04, 6.60)	(0.19, 6.90)
p-value	0.039	0.006	0.300	0.038

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	75.96 (22.999)	78.65 (20.198)	73.51 (19.097)	74.74 (21.080)
Median	80.00	82.50	75.00	80.00
Min, Max	15.0, 100.0	25.0, 100.0	30.0, 100.0	15.0, 100.0
Change from Baseline at				
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	0.32 (25.905)	5.48 (18.949)	5.14 (14.357)	2.70 (21.029)
Median	0.00	5.00	5.00	5.00
Min, Max	-80.0, 60.0	-35.0, 55.0	-35.0, 35.0	-80.0, 60.0
LS Mean (SE)	1.23 (3.081)	5.20 (2.393)	4.11 (2.020)	2.32 (1.918)
95% CI	(-4.84, 7.29)	(0.49, 9.91)	(0.13, 8.08)	(-1.44, 6.09)
p-value	0.690	0.030	0.043	0.227

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	80.12 (23.116)	78.75 (17.760)	71.14 (19.703)	75.47 (21.762)
Median	90.00	80.00	70.00	80.00
Min, Max	0.0, 100.0	35.0, 100.0	30.0, 100.0	0.0, 100.0
Change from Baseline at				
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	3.41 (27.121)	5.21 (16.534)	1.93 (14.516)	2.65 (21.417)
Median	0.00	5.00	0.00	0.00
Min, Max	-100.0, 60.0	-30.0, 45.0	-25.0, 40.0	-100.0, 60.0
LS Mean (SE)	5.11 (3.155)	5.32 (1.878)	1.06 (2.036)	2.62 (1.929)
95% CI	(-1.10, 11.32)	(1.62, 9.01)	(-2.95, 5.06)	(-1.17, 6.40)
p-value	0.107	0.005	0.605	0.176

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	76.19 (23.107)	79.44 (20.562)	74.55 (19.878)	75.35 (21.404)
Median	80.00	80.00	75.00	77.50
Min, Max	0.0, 100.0	25.0, 100.0	30.0, 100.0	0.0, 100.0
Change from Baseline at				
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	0.24 (26.479)	6.04 (21.085)	4.43 (17.294)	2.38 (22.225)
Median	0.00	5.00	0.00	0.00
Min, Max	-100.0, 50.0	-40.0, 55.0	-35.0, 50.0	-100.0, 50.0
LS Mean (SE)	1.26 (3.180)	5.89 (2.565)	4.46 (2.503)	2.61 (2.048)
95% CI	(-5.00, 7.52)	(0.85, 10.94)	(-0.46, 9.39)	(-1.41, 6.64)
p-value	0.692	0.022	0.076	0.203

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	79.61 (22.037)	81.28 (16.442)	74.08 (19.568)	77.00 (20.947)
Median	87.50	85.00	72.50	82.50
Min, Max	30.0, 100.0	45.0, 100.0	30.0, 100.0	30.0, 100.0
Change from Baseline at				
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	5.13 (24.891)	7.21 (19.127)	0.70 (13.676)	3.04 (20.366)
Median	0.00	5.00	0.00	0.00
Min, Max	-50.0, 60.0	-50.0, 50.0	-35.0, 25.0	-50.0, 60.0
LS Mean (SE)	5.27 (3.205)	7.99 (2.392)	1.70 (2.364)	3.57 (2.057)
95% CI	(-1.03, 11.58)	(3.28, 12.70)	(-2.95, 6.35)	(-0.47, 7.61)
p-value	0.101	<0.001	0.473	0.083

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	76.91 (24.215)	81.81 (18.942)	76.72 (20.344)	76.82 (22.251)
Median	82.50	87.50	80.00	82.50
Min, Max	10.0, 100.0	40.0, 100.0	45.0, 100.0	10.0, 100.0
Change from Baseline at				
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	1.91 (25.376)	7.78 (16.144)	2.19 (14.139)	2.05 (20.550)
Median	0.00	5.00	0.00	0.00
Min, Max	-80.0, 45.0	-25.0, 45.0	-20.0, 30.0	-80.0, 45.0
LS Mean (SE)	2.21 (3.754)	7.02 (2.465)	3.26 (2.334)	2.84 (2.232)
95% CI	(-5.18, 9.59)	(2.17, 11.87)	(-1.33, 7.85)	(-1.54, 7.23)
p-value	0.557	0.005	0.164	0.203

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	79.06 (21.419)	80.28 (17.806)	78.13 (20.846)	78.63 (20.979)
Median	82.50	77.50	85.00	85.00
Min, Max	25.0, 100.0	40.0, 100.0	30.0, 100.0	25.0, 100.0
Change from Baseline at				
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	3.28 (26.323)	5.69 (21.783)	2.59 (14.711)	2.96 (21.523)
Median	7.50	10.00	0.00	0.00
Min, Max	-60.0, 60.0	-40.0, 45.0	-35.0, 40.0	-60.0, 60.0
LS Mean (SE)	3.12 (3.925)	6.74 (2.707)	3.53 (2.530)	3.49 (2.384)
95% CI	(-4.60, 10.85)	(1.41, 12.06)	(-1.44, 8.51)	(-1.20, 8.17)
p-value	0.427	0.013	0.163	0.144

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	74.31 (24.558)	80.15 (21.560)	79.64 (18.605)	76.93 (21.810)
Median	80.00	90.00	85.00	80.00
Min, Max	10.0, 100.0	30.0, 100.0	35.0, 100.0	10.0, 100.0
Change from Baseline at				
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	-2.24 (25.863)	5.00 (22.638)	5.71 (16.085)	1.67 (21.801)
Median	0.00	5.00	5.00	0.00
Min, Max	-90.0, 35.0	-40.0, 45.0	-30.0, 40.0	-90.0, 40.0
LS Mean (SE)	-0.68 (4.478)	6.20 (2.783)	6.48 (2.496)	2.93 (2.569)
95% CI	(-9.50, 8.13)	(0.73, 11.68)	(1.57, 11.39)	(-2.12, 7.97)
p-value	0.879	0.027	0.010	0.255

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	72.67 (21.619)	78.53 (21.122)	76.39 (19.986)	74.70 (20.499)
Median	65.00	85.00	80.00	80.00
Min, Max	35.0, 100.0	40.0, 100.0	35.0, 100.0	35.0, 100.0
Change from Baseline at				
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	2.67 (18.212)	6.47 (16.934)	5.00 (18.231)	3.94 (17.974)
Median	0.00	5.00	2.50	0.00
Min, Max	-20.0, 50.0	-30.0, 30.0	-30.0, 45.0	-30.0, 50.0
LS Mean (SE)	0.99 (4.717)	4.85 (3.168)	6.55 (3.051)	4.04 (2.662)
95% CI	(-8.30, 10.27)	(-1.38, 11.08)	(0.55, 12.56)	(-1.18, 9.27)
p-value	0.834	0.127	0.032	0.129

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	59.29 (30.198)	72.78 (27.285)	74.23 (23.704)	69.00 (26.388)
Median	55.00	70.00	75.00	70.00
Min, Max	20.0, 100.0	40.0, 100.0	25.0, 100.0	20.0, 100.0
Change from Baseline at				
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	-10.00 (28.431)	0.56 (9.167)	6.15 (19.701)	0.50 (23.725)
Median	0.00	0.00	0.00	0.00
Min, Max	-65.0, 20.0	-10.0, 15.0	-40.0, 35.0	-65.0, 35.0
LS Mean (SE)	-5.37 (9.658)	0.49 (3.487)	6.33 (4.466)	1.64 (4.595)
95% CI	(-24.38, 13.64)	(-6.37, 7.35)	(-2.45, 15.12)	(-7.38, 10.67)
p-value	0.579	0.889	0.157	0.721

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	74.38 (27.182)	77.22 (20.017)	77.08 (21.155)	76.00 (23.090)
Median	80.00	75.00	72.50	72.50
Min, Max	30.0, 100.0	50.0, 100.0	40.0, 100.0	30.0, 100.0
Change from Baseline at				
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	3.13 (26.041)	5.00 (21.506)	7.08 (12.873)	5.50 (18.701)
Median	2.50	0.00	5.00	5.00
Min, Max	-40.0, 45.0	-30.0, 40.0	-10.0, 30.0	-40.0, 45.0
LS Mean (SE)	3.09 (8.383)	7.31 (3.630)	6.85 (3.268)	5.33 (3.998)
95% CI	(-13.41, 19.59)	(0.17, 14.45)	(0.42, 13.28)	(-2.52, 13.18)
p-value	0.713	0.045	0.037	0.183

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	73.75 (22.867)	61.25 (22.500)	75.00 (18.323)	74.58 (18.885)
Median	75.00	50.00	70.00	72.50
Min, Max	45.0, 100.0	50.0, 95.0	55.0, 100.0	45.0, 100.0
Change from Baseline at				
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	-2.50 (26.300)	-7.50 (17.078)	8.13 (12.229)	4.58 (17.640)
Median	5.00	-5.00	5.00	5.00
Min, Max	-40.0, 20.0	-30.0, 10.0	-10.0, 30.0	-40.0, 30.0
LS Mean (SE)	NA	NA	7.00 (3.227)	6.88 (4.280)
95% CI	(NA, NA)	(NA, NA)	(0.65, 13.36)	(-1.53, 15.28)
p-value	NA	NA	0.031	0.109

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	95.00	75.00	77.00 (21.966)	80.00 (20.976)
Median	95.00	75.00	85.00	87.50
Min, Max	95.0, 95.0	75.0, 75.0	45.0, 100.0	45.0, 100.0
Change from Baseline at				
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	40.00	25.00	8.00 (15.248)	13.33 (18.886)
Median	40.00	25.00	15.00	17.50
Min, Max	40.0, 40.0	25.0, 25.0	-15.0, 20.0	-15.0, 40.0
LS Mean (SE)	NA	NA	4.31 (5.743)	6.76 (6.055)
95% CI	(NA, NA)	(NA, NA)	(-6.99, 15.62)	(-5.13, 18.65)
p-value	NA	NA	0.453	0.264

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Emotional Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	75.00	75.00
Median	NA	NA	75.00	75.00
Min, Max	(NA, NA)	(NA, NA)	75.0, 75.0	75.0, 75.0
Change from Baseline at				
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	25.00	25.00
Median	NA	NA	25.00	25.00
Min, Max	(NA, NA)	(NA, NA)	25.0, 25.0	25.0, 25.0
LS Mean (SE)	NA	NA	NA	NA
95% CI	(NA, NA)	(NA, NA)	(NA, NA)	(NA, NA)
p-value	NA	NA	NA	NA

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
n (%)	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
Mean (SD)	80.90 (19.915)	72.64 (24.111)	80.27 (21.396)	80.57 (20.608)
Median	90.00	75.00	80.00	90.00
Min, Max	20.0, 100.0	5.0, 100.0	10.0, 100.0	10.0, 100.0

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	81.77 (21.475)	79.52 (20.006)	80.83 (20.088)	81.30 (20.689)
Median	87.50	80.00	85.00	85.00
Min, Max	15.0, 100.0	25.0, 100.0	25.0, 100.0	15.0, 100.0
Change from Baseline at				
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	1.25 (19.611)	6.73 (18.065)	3.33 (13.461)	2.29 (16.763)
Median	0.00	0.00	0.00	0.00
Min, Max	-80.0, 60.0	-20.0, 55.0	-40.0, 30.0	-80.0, 60.0
LS Mean (SE)	0.75 (2.645)	6.00 (2.050)	2.58 (1.922)	1.54 (1.621)
95% CI	(-4.45, 5.96)	(1.96, 10.03)	(-1.20, 6.36)	(-1.64, 4.73)
p-value	0.776	0.004	0.181	0.341

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	81.28 (19.010)	78.46 (20.497)	84.78 (17.825)	83.01 (18.418)
Median	85.00	80.00	90.00	90.00
Min, Max	10.0, 100.0	25.0, 100.0	15.0, 100.0	10.0, 100.0
Change from Baseline at				
CSD15				
n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Mean (SD)	-0.21 (17.784)	4.71 (16.845)	5.54 (13.631)	2.63 (16.043)
Median	0.00	0.00	0.00	0.00
Min, Max	-45.0, 50.0	-40.0, 45.0	-25.0, 45.0	-45.0, 50.0
LS Mean (SE)	-0.91 (2.762)	3.85 (2.070)	5.30 (1.969)	2.11 (1.683)
95% CI	(-6.35, 4.52)	(-0.22, 7.92)	(1.42, 9.17)	(-1.19, 5.42)
p-value	0.741	0.064	0.008	0.210

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	84.02 (21.337)	80.31 (20.380)	79.80 (18.076)	81.84 (19.712)
Median	90.00	87.50	80.63	90.00
Min, Max	0.0, 100.0	30.0, 100.0	25.0, 100.0	0.0, 100.0
Change from Baseline at				
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	2.20 (24.951)	4.38 (21.577)	0.60 (13.304)	1.37 (19.690)
Median	5.00	0.00	0.00	0.00
Min, Max	-100.0, 70.0	-60.0, 50.0	-35.0, 35.0	-100.0, 70.0
LS Mean (SE)	2.05 (3.356)	5.31 (2.715)	0.37 (1.876)	1.00 (1.880)
95% CI	(-4.55, 8.66)	(-0.04, 10.65)	(-3.32, 4.06)	(-2.69, 4.70)
p-value	0.541	0.052	0.844	0.594

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	82.92 (20.166)	79.04 (19.100)	83.64 (18.813)	83.28 (19.374)
Median	90.00	80.00	90.00	90.00
Min, Max	0.0, 100.0	35.0, 100.0	30.0, 100.0	0.0, 100.0
Change from Baseline at				
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	2.20 (28.489)	5.00 (22.674)	3.52 (15.234)	2.88 (22.569)
Median	0.00	0.00	0.00	0.00
Min, Max	-100.0, 80.0	-40.0, 60.0	-25.0, 35.0	-100.0, 80.0
LS Mean (SE)	1.66 (3.569)	5.07 (2.481)	3.49 (2.037)	2.38 (2.004)
95% CI	(-5.36, 8.69)	(0.19, 9.95)	(-0.52, 7.49)	(-1.56, 6.31)
p-value	0.642	0.042	0.088	0.236

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	82.66 (19.878)	81.98 (18.713)	82.65 (17.720)	82.66 (18.758)
Median	92.50	85.00	90.00	90.00
Min, Max	35.0, 100.0	50.0, 100.0	35.0, 100.0	35.0, 100.0
Change from Baseline at				
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	1.48 (24.436)	6.28 (19.275)	1.32 (15.438)	1.41 (20.542)
Median	0.00	0.00	0.00	0.00
Min, Max	-50.0, 80.0	-40.0, 50.0	-30.0, 45.0	-50.0, 80.0
LS Mean (SE)	1.27 (2.927)	7.09 (2.324)	1.65 (1.975)	1.37 (1.795)
95% CI	(-4.49, 7.03)	(2.52, 11.66)	(-2.24, 5.53)	(-2.15, 4.90)
p-value	0.665	0.002	0.405	0.444

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	81.62 (18.898)	82.78 (17.462)	83.13 (19.124)	82.35 (18.877)
Median	87.50	85.00	87.50	87.50
Min, Max	40.0, 100.0	35.0, 100.0	25.0, 100.0	25.0, 100.0
Change from Baseline at				
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	-1.47 (24.075)	5.83 (18.303)	1.09 (14.959)	-0.23 (20.066)
Median	0.00	0.00	0.00	0.00
Min, Max	-60.0, 70.0	-40.0, 55.0	-25.0, 45.0	-60.0, 70.0
LS Mean (SE)	-0.61 (2.811)	7.52 (2.226)	2.23 (1.996)	0.87 (1.746)
95% CI	(-6.15, 4.92)	(3.14, 11.90)	(-1.69, 6.16)	(-2.56, 4.30)
p-value	0.828	<0.001	0.264	0.617

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	79.38 (18.217)	79.03 (24.048)	83.75 (17.407)	81.42 (17.829)
Median	80.00	85.00	87.50	85.00
Min, Max	45.0, 100.0	0.0, 100.0	40.0, 100.0	40.0, 100.0
Change from Baseline at				
C21D15				
n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Mean (SD)	-4.84 (22.486)	0.83 (25.171)	1.43 (15.803)	-1.92 (19.746)
Median	0.00	0.00	0.00	0.00
Min, Max	-50.0, 80.0	-100.0, 50.0	-25.0, 45.0	-50.0, 80.0
LS Mean (SE)	-2.21 (2.830)	4.62 (3.506)	2.47 (2.025)	0.13 (1.749)
95% CI	(-7.78, 3.36)	(-2.28, 11.52)	(-1.51, 6.46)	(-3.30, 3.56)
p-value	0.436	0.188	0.223	0.941

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	76.38 (28.186)	79.24 (20.468)	84.64 (17.635)	80.44 (23.760)
Median	85.00	80.00	90.00	90.00
Min, Max	0.0, 100.0	40.0, 100.0	45.0, 100.0	0.0, 100.0
Change from Baseline at				
C24D21				
n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)	-8.62 (33.029)	1.82 (16.855)	3.39 (15.399)	-2.72 (26.391)
Median	0.00	0.00	0.00	0.00
Min, Max	-100.0, 80.0	-45.0, 45.0	-25.0, 45.0	-100.0, 80.0
LS Mean (SE)	-3.36 (4.024)	4.47 (2.401)	3.69 (2.202)	0.40 (2.383)
95% CI	(-11.28, 4.56)	(-0.25, 9.20)	(-0.64, 8.02)	(-4.28, 5.08)
p-value	0.404	0.063	0.095	0.866

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	77.00 (19.712)	78.24 (20.228)	83.89 (15.770)	80.76 (17.727)
Median	75.00	75.00	82.50	80.00
Min, Max	40.0, 100.0	45.0, 100.0	55.0, 100.0	40.0, 100.0
Change from Baseline at				
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	-6.33 (19.130)	6.18 (12.934)	1.94 (11.649)	-1.82 (15.802)
Median	0.00	0.00	2.50	0.00
Min, Max	-50.0, 20.0	-20.0, 40.0	-25.0, 30.0	-50.0, 30.0
LS Mean (SE)	-0.64 (3.471)	6.68 (2.479)	3.82 (2.377)	1.62 (2.071)
95% CI	(-7.47, 6.19)	(1.80, 11.55)	(-0.86, 8.50)	(-2.44, 5.69)
p-value	0.854	0.007	0.109	0.433

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	67.86 (23.427)	75.56 (25.055)	73.08 (28.762)	71.25 (26.501)
Median	65.00	65.00	70.00	70.00
Min, Max	40.0, 100.0	35.0, 100.0	0.0, 100.0	0.0, 100.0
Change from Baseline at				
C32D15				
n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Mean (SD)	-15.71 (25.728)	-3.89 (8.937)	-5.38 (24.019)	-9.00 (24.473)
Median	0.00	0.00	0.00	0.00
Min, Max	-60.0, 10.0	-20.0, 5.0	-75.0, 25.0	-75.0, 25.0
LS Mean (SE)	-5.23 (7.689)	3.43 (3.379)	-0.46 (8.689)	-2.38 (5.044)
95% CI	(-20.36, 9.91)	(-3.22, 10.07)	(-17.56, 16.64)	(-12.28, 7.53)
p-value	0.497	0.311	0.958	0.638

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	67.50 (21.876)	75.56 (22.001)	80.83 (22.036)	75.50 (22.414)
Median	65.00	75.00	87.50	80.00
Min, Max	40.0, 100.0	50.0, 100.0	40.0, 100.0	40.0, 100.0
Change from Baseline at				
C36D15				
n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Mean (SD)	-17.50 (24.785)	-3.89 (16.159)	2.50 (9.653)	-5.50 (19.527)
Median	-15.00	0.00	0.00	0.00
Min, Max	-60.0, 10.0	-30.0, 25.0	-10.0, 25.0	-60.0, 25.0
LS Mean (SE)	-12.79 (6.564)	3.96 (5.012)	2.93 (3.275)	-2.56 (3.584)
95% CI	(-25.71, 0.13)	(-5.90, 13.82)	(-3.52, 9.37)	(-9.60, 4.48)
p-value	0.052	0.430	0.372	0.475

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	56.25 (24.958)	53.75 (14.930)	71.88 (26.178)	66.67 (25.791)
Median	52.50	55.00	70.00	57.50
Min, Max	30.0, 90.0	35.0, 70.0	40.0, 100.0	30.0, 100.0
Change from Baseline at				
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	-33.75 (31.458)	-16.25 (12.500)	-1.88 (7.530)	-12.50 (23.500)
Median	-30.00	-17.50	0.00	-7.50
Min, Max	-70.0, -5.0	-30.0, 0.0	-10.0, 10.0	-70.0, 10.0
LS Mean (SE)	NA	NA	-2.16 (2.837)	-6.26 (3.873)
95% CI	(NA, NA)	(NA, NA)	(-7.74, 3.42)	(-13.87, 1.34)
p-value	NA	NA	0.447	0.106

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	85.00	65.00	84.00 (23.022)	84.17 (20.595)
Median	85.00	65.00	100.00	92.50
Min, Max	85.0, 85.0	65.0, 65.0	50.0, 100.0	50.0, 100.0
Change from Baseline at				
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Mean (SD)	5.00	-15.00	-5.00 (8.660)	-3.33 (8.756)
Median	5.00	-15.00	0.00	0.00
Min, Max	5.0, 5.0	-15.0, -15.0	-20.0, 0.0	-20.0, 5.0
LS Mean (SE)	NA	NA	-2.81 (4.043)	-9.38 (4.076)
95% CI	(NA, NA)	(NA, NA)	(-10.77, 5.14)	(-17.39, -1.38)
p-value	NA	NA	0.487	0.022

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Social Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	80.00	80.00
Median	NA	NA	80.00	80.00
Min, Max	(NA, NA)	(NA, NA)	80.0, 80.0	80.0, 80.0
Change from Baseline at				
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	-10.00	-10.00
Median	NA	NA	-10.00	-10.00
Min, Max	(NA, NA)	(NA, NA)	-10.0, -10.0	-10.0, -10.0
LS Mean (SE)	NA	NA	NA	NA
95% CI	(NA, NA)	(NA, NA)	(NA, NA)	(NA, NA)
p-value	NA	NA	NA	NA

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
n (%)	50 (100%)	54 (96.4%)	55 (94.8%)	105 (97.2%)
Mean (SD)	69.63 (24.811)	66.48 (26.142)	66.82 (23.714)	68.16 (24.167)
Median	67.50	65.00	70.00	70.00
Min, Max	15.0, 100.0	0.0, 100.0	15.0, 100.0	15.0, 100.0

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C3D15				
n (%)	48 (96.0%)	50 (89.3%)	48 (82.8%)	96 (88.9%)
Mean (SD)	67.81 (22.501)	67.97 (23.667)	69.17 (24.437)	68.49 (23.375)
Median	70.00	72.50	72.50	70.00
Min, Max	15.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0
Change from Baseline at				
C3D15				
n (%)	48 (96.0%)	50 (89.3%)	48 (82.8%)	96 (88.9%)
Mean (SD)	-2.74 (18.475)	0.97 (18.973)	4.48 (21.319)	0.87 (20.172)
Median	0.00	0.00	5.00	0.00
Min, Max	-65.0, 35.0	-50.0, 50.0	-50.0, 55.0	-65.0, 55.0
LS Mean (SE)	-3.22 (2.454)	-0.08 (2.324)	3.17 (2.859)	-0.22 (1.960)
95% CI	(-8.05, 1.61)	(-4.65, 4.49)	(-2.46, 8.80)	(-4.07, 3.63)
p-value	0.190	0.972	0.268	0.911

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
CSD15				
n (%)	47 (94.0%)	50 (89.3%)	45 (77.6%)	92 (85.2%)
Mean (SD)	69.68 (22.273)	66.23 (23.103)	73.33 (21.079)	71.47 (21.656)
Median	70.00	62.50	80.00	77.50
Min, Max	0.0, 100.0	25.0, 100.0	25.0, 100.0	0.0, 100.0
Change from Baseline at				
CSD15				
n (%)	47 (94.0%)	50 (89.3%)	45 (77.6%)	92 (85.2%)
Mean (SD)	-0.46 (24.328)	-1.37 (22.294)	5.22 (15.846)	2.32 (20.706)
Median	0.00	0.00	0.00	0.00
Min, Max	-90.0, 50.0	-65.0, 33.3	-35.0, 40.0	-90.0, 50.0
LS Mean (SE)	-1.19 (2.992)	-2.84 (2.695)	5.33 (2.349)	1.91 (1.982)
95% CI	(-7.08, 4.70)	(-8.15, 2.46)	(0.71, 9.96)	(-1.98, 5.81)
p-value	0.691	0.292	0.024	0.335

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C7D15				
n (%)	41 (82.0%)	47 (83.9%)	43 (74.1%)	84 (77.8%)
Mean (SD)	69.63 (24.223)	67.98 (23.015)	73.84 (19.421)	71.79 (21.865)
Median	75.00	70.00	75.00	75.00
Min, Max	0.0, 100.0	20.0, 100.0	30.0, 100.0	0.0, 100.0
Change from Baseline at				
C7D15				
n (%)	41 (82.0%)	47 (83.9%)	43 (74.1%)	84 (77.8%)
Mean (SD)	-3.58 (23.972)	-1.81 (17.953)	4.53 (16.103)	0.58 (20.611)
Median	-5.00	0.00	0.00	0.00
Min, Max	-90.0, 60.0	-50.0, 30.0	-35.0, 40.0	-90.0, 60.0
LS Mean (SE)	-2.07 (3.089)	-1.75 (2.428)	4.93 (2.077)	1.63 (1.869)
95% CI	(-8.15, 4.01)	(-6.53, 3.03)	(0.85, 9.02)	(-2.04, 5.30)
p-value	0.503	0.472	0.018	0.384

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
n (%)	42 (84.0%)	45 (80.4%)	44 (75.9%)	86 (79.6%)
Mean (SD)	73.93 (23.929)	68.26 (23.268)	74.66 (18.937)	74.30 (21.395)
Median	80.00	66.67	75.00	80.00
Min, Max	0.0, 100.0	15.0, 100.0	30.0, 100.0	0.0, 100.0
Change from Baseline at				
C9D15				
n (%)	42 (84.0%)	45 (80.4%)	44 (75.9%)	86 (79.6%)
Mean (SD)	2.10 (25.575)	0.70 (20.996)	7.05 (18.842)	4.63 (22.389)
Median	5.00	5.00	0.00	0.00
Min, Max	-90.0, 40.0	-60.0, 50.0	-25.0, 50.0	-90.0, 50.0
LS Mean (SE)	2.37 (3.094)	-0.10 (2.838)	6.15 (2.364)	4.37 (1.890)
95% CI	(-3.72, 8.46)	(-5.69, 5.48)	(1.50, 10.81)	(0.66, 8.09)
p-value	0.444	0.971	0.010	0.021

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C13D15				
n (%)	38 (76.0%)	42 (75.0%)	34 (58.6%)	72 (66.7%)
Mean (SD)	71.58 (24.635)	70.08 (23.596)	74.01 (20.211)	72.73 (22.531)
Median	75.00	75.00	75.00	75.00
Min, Max	0.0, 100.0	25.0, 100.0	31.3, 100.0	0.0, 100.0
Change from Baseline at				
C13D15				
n (%)	38 (76.0%)	42 (75.0%)	34 (58.6%)	72 (66.7%)
Mean (SD)	1.14 (28.353)	1.63 (21.119)	4.15 (14.683)	2.56 (22.835)
Median	0.00	0.00	0.00	0.00
Min, Max	-90.0, 50.0	-60.0, 55.0	-20.0, 50.0	-90.0, 50.0
LS Mean (SE)	-0.00 (3.338)	1.26 (2.944)	4.95 (2.064)	2.55 (2.030)
95% CI	(-6.57, 6.57)	(-4.53, 7.06)	(0.89, 9.01)	(-1.43, 6.54)
p-value	0.999	0.668	0.017	0.209

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	71.03 (22.319)	67.41 (19.613)	76.88 (18.741)	73.86 (20.714)
Median	70.00	70.00	80.00	77.50
Min, Max	20.0, 100.0	20.0, 100.0	35.0, 100.0	20.0, 100.0
Change from Baseline at				
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	0.83 (25.973)	-1.20 (24.481)	5.47 (16.331)	3.08 (21.798)
Median	1.67	2.50	2.50	1.67
Min, Max	-70.0, 60.0	-60.0, 50.0	-15.0, 65.0	-70.0, 65.0
LS Mean (SE)	-1.14 (3.051)	-1.99 (3.023)	6.78 (2.285)	2.85 (2.007)
95% CI	(-7.15, 4.86)	(-7.93, 3.96)	(2.28, 11.27)	(-1.09, 6.79)
p-value	0.709	0.512	0.003	0.156

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C21D15				
n (%)	32 (64.0%)	35 (62.5%)	28 (48.3%)	60 (55.6%)
Mean (SD)	71.09 (22.061)	72.67 (20.021)	74.46 (18.774)	72.67 (20.491)
Median	75.00	70.00	75.00	75.00
Min, Max	20.0, 100.0	40.0, 100.0	35.0, 100.0	20.0, 100.0
Change from Baseline at				
C21D15				
n (%)	32 (64.0%)	35 (62.5%)	28 (48.3%)	60 (55.6%)
Mean (SD)	-0.99 (25.445)	0.67 (20.204)	3.57 (20.943)	1.14 (23.371)
Median	0.00	0.00	0.00	0.00
Min, Max	-60.0, 50.0	-55.0, 40.0	-25.0, 55.0	-60.0, 55.0
LS Mean (SE)	-2.28 (3.365)	2.22 (2.708)	4.57 (2.841)	1.34 (2.333)
95% CI	(-8.91, 4.34)	(-3.11, 7.55)	(-1.02, 10.16)	(-3.24, 5.92)
p-value	0.498	0.413	0.109	0.567

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21				
n (%)	29 (58.0%)	32 (57.1%)	28 (48.3%)	57 (52.8%)
Mean (SD)	69.66 (26.690)	71.20 (23.041)	77.37 (20.442)	73.44 (23.933)
Median	75.00	75.00	78.13	75.00
Min, Max	10.0, 100.0	25.0, 100.0	40.0, 100.0	10.0, 100.0
Change from Baseline at				
C24D21				
n (%)	29 (58.0%)	32 (57.1%)	28 (48.3%)	57 (52.8%)
Mean (SD)	-2.07 (30.429)	-0.21 (23.619)	8.08 (18.483)	2.92 (25.571)
Median	0.00	0.00	2.50	0.00
Min, Max	-80.0, 60.0	-55.0, 55.0	-35.0, 55.0	-80.0, 60.0
LS Mean (SE)	-1.88 (4.031)	2.01 (3.416)	8.52 (2.893)	3.09 (2.772)
95% CI	(-9.82, 6.05)	(-4.71, 8.73)	(2.83, 14.22)	(-2.36, 8.53)
p-value	0.641	0.557	0.003	0.266

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C28D15				
n (%)	15 (30.0%)	16 (28.6%)	18 (31.0%)	33 (30.6%)
Mean (SD)	68.00 (23.361)	67.71 (19.397)	78.33 (19.251)	73.64 (21.516)
Median	60.00	62.50	80.00	80.00
Min, Max	25.0, 100.0	35.0, 100.0	40.0, 100.0	25.0, 100.0
Change from Baseline at				
C28D15				
n (%)	15 (30.0%)	16 (28.6%)	18 (31.0%)	33 (30.6%)
Mean (SD)	-4.00 (24.799)	-1.56 (20.794)	9.44 (19.621)	3.33 (22.799)
Median	0.00	0.00	7.50	0.00
Min, Max	-55.0, 40.0	-45.0, 45.0	-30.0, 60.0	-55.0, 60.0
LS Mean (SE)	-1.27 (4.425)	0.59 (3.425)	8.62 (2.995)	3.17 (2.603)
95% CI	(-9.98, 7.44)	(-6.15, 7.33)	(2.72, 14.51)	(-1.94, 8.29)
p-value	0.774	0.863	0.004	0.223

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C32D15				
n (%)	7 (14.0%)	8 (14.3%)	13 (22.4%)	20 (18.5%)
Mean (SD)	58.57 (22.678)	61.25 (21.002)	77.31 (20.168)	70.75 (22.436)
Median	50.00	55.00	80.00	70.00
Min, Max	40.0, 90.0	40.0, 90.0	45.0, 100.0	40.0, 100.0
Change from Baseline at				
C32D15				
n (%)	7 (14.0%)	8 (14.3%)	13 (22.4%)	20 (18.5%)
Mean (SD)	-8.57 (33.256)	-7.29 (19.618)	15.38 (19.628)	7.00 (27.019)
Median	10.00	-6.67	15.00	12.50
Min, Max	-60.0, 20.0	-45.0, 20.0	-15.0, 60.0	-60.0, 60.0
LS Mean (SE)	-5.44 (5.760)	-4.69 (3.139)	10.98 (3.046)	1.64 (3.197)
95% CI	(-16.77, 5.90)	(-10.87, 1.49)	(4.98, 16.97)	(-4.64, 7.91)
p-value	0.346	0.136	<0.001	0.609

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C36D15				
n (%)	7 (14.0%)	8 (14.3%)	12 (20.7%)	19 (17.6%)
Mean (SD)	61.25 (24.548)	71.04 (22.501)	77.08 (22.306)	71.25 (23.801)
Median	65.00	67.50	77.50	70.00
Min, Max	30.0, 100.0	45.0, 100.0	30.0, 100.0	30.0, 100.0
Change from Baseline at				
C36D15				
n (%)	7 (14.0%)	8 (14.3%)	12 (20.7%)	19 (17.6%)
Mean (SD)	-5.89 (36.334)	2.50 (31.960)	16.25 (21.860)	8.09 (29.198)
Median	0.00	2.50	10.00	10.00
Min, Max	-60.0, 33.8	-45.0, 60.0	-10.0, 60.0	-60.0, 60.0
LS Mean (SE)	-8.70 (6.686)	5.82 (6.690)	12.57 (4.334)	3.78 (3.982)
95% CI	(-21.86, 4.46)	(-7.34, 18.99)	(4.04, 21.10)	(-4.04, 11.60)
p-value	0.194	0.385	0.004	0.343

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	65.00 (21.985)	57.50 (13.229)	70.00 (23.146)	68.33 (21.881)
Median	65.00	55.00	70.00	70.00
Min, Max	40.0, 90.0	45.0, 75.0	35.0, 100.0	35.0, 100.0
Change from Baseline at				
C40D15				
n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Mean (SD)	-18.75 (37.053)	-18.75 (18.875)	14.38 (19.719)	3.33 (29.797)
Median	-27.50	-20.00	7.50	5.00
Min, Max	-50.0, 30.0	-40.0, 5.0	0.0, 60.0	-50.0, 60.0
LS Mean (SE)	NA	NA	9.65 (3.744)	1.76 (4.289)
95% CI	(NA, NA)	(NA, NA)	(2.28, 17.02)	(-6.66, 10.18)
p-value	NA	NA	0.010	0.682

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	4 (6.9%)	5 (4.6%)
Mean (SD)	45.00	40.00	85.00 (21.213)	77.00 (25.642)
Median	45.00	40.00	92.50	85.00
Min, Max	45.0, 45.0	40.0, 40.0	55.0, 100.0	45.0, 100.0
Change from Baseline at				
C44D15				
n (%)	1 (2.0%)	1 (1.8%)	4 (6.9%)	5 (4.6%)
Mean (SD)	10.00	15.00	11.25 (16.520)	11.00 (14.318)
Median	10.00	15.00	5.00	10.00
Min, Max	10.0, 10.0	15.0, 15.0	0.0, 35.0	0.0, 35.0
LS Mean (SE)	NA	NA	NA	4.74 (5.666)
95% CI	(NA, NA)	(NA, NA)	(NA, NA)	(-6.39, 15.87)
p-value	NA	NA	NA	0.403

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: School/Work Functioning

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	55.00	55.00
Median	NA	NA	55.00	55.00
Min, Max	(NA, NA)	(NA, NA)	55.0, 55.0	55.0, 55.0
Change from Baseline at				
C48D15				
n (%)	0	0	1 (1.7%)	1 (0.9%)
Mean (SD)	NA	NA	0.00	0.00
Median	NA	NA	0.00	0.00
Min, Max	(NA, NA)	(NA, NA)	0.0, 0.0	0.0, 0.0
LS Mean (SE)	NA	NA	NA	NA
95% CI	(NA, NA)	(NA, NA)	(NA, NA)	(NA, NA)
p-value	NA	NA	NA	NA

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
Baseline				
n (%)	50 (100%)	55 (98.2%)	55 (94.8%)	105 (97.2%)
Mean (SD)	75.97 (17.022)	71.94 (18.058)	66.90 (19.398)	71.22 (18.778)
Median	75.00	69.57	66.30	70.65
Min, Max	18.5, 100.0	22.8, 98.9	23.9, 100.0	18.5, 100.0

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADQL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	77.20 (17.986)	76.26 (16.914)	69.13 (20.325)	73.17 (19.515)
Median	77.17	76.63	74.46	76.63
Min, Max	23.9, 100.0	22.8, 100.0	18.5, 100.0	18.5, 100.0
Change from Baseline at				
C3D15				
n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Mean (SD)	1.01 (13.736)	4.14 (13.052)	4.37 (12.410)	2.69 (13.130)
Median	2.17	2.17	4.35	3.26
Min, Max	-43.5, 26.1	-32.6, 33.7	-26.1, 32.6	-43.5, 32.6
LS Mean (SE)	0.83 (1.886)	3.79 (1.592)	3.49 (1.910)	2.08 (1.385)
95% CI	(-2.89, 4.54)	(0.66, 6.92)	(-0.27, 7.25)	(-0.64, 4.80)
p-value	0.662	0.018	0.069	0.133

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
CSD15	n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
	Mean (SD)	77.82 (16.716)	75.86 (16.241)	72.43 (19.414)	75.15 (18.205)
	Median	81.52	75.54	75.54	77.17
	Min, Max	17.4, 100.0	37.0, 100.0	26.1, 100.0	17.4, 100.0
Change from Baseline at					
CSD15	n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
	Mean (SD)	0.98 (14.250)	3.05 (12.999)	5.94 (10.910)	3.43 (12.883)
	Median	5.43	4.89	4.89	5.43
	Min, Max	-50.0, 27.2	-37.0, 28.8	-18.5, 28.3	-50.0, 28.3
	LS Mean (SE)	0.90 (1.948)	2.29 (1.696)	5.37 (1.751)	3.06 (1.349)
	95% CI	(-2.94, 4.73)	(-1.05, 5.63)	(1.92, 8.81)	(0.41, 5.71)
p-value		0.646	0.178	0.002	0.024

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	78.98 (19.130)	77.04 (15.961)	70.16 (19.525)	74.41 (19.724)
Median	82.61	79.35	72.83	78.26
Min, Max	0.0, 100.0	47.8, 100.0	23.9, 100.0	0.0, 100.0
Change from Baseline at				
C7D15				
n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Mean (SD)	1.12 (17.953)	3.16 (13.436)	2.92 (11.743)	2.05 (14.996)
Median	2.17	3.27	1.09	1.09
Min, Max	-67.4, 43.5	-38.0, 28.3	-19.9, 29.3	-67.4, 43.5
LS Mean (SE)	1.92 (2.457)	3.21 (1.853)	2.64 (1.738)	2.25 (1.471)
95% CI	(-2.92, 6.76)	(-0.44, 6.85)	(-0.78, 6.06)	(-0.64, 5.14)
p-value	0.436	0.084	0.130	0.127

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	78.23 (18.991)	76.21 (15.583)	73.09 (18.031)	75.60 (18.578)
Median	83.15	73.91	75.00	77.72
Min, Max	0.0, 100.0	45.7, 100.0	32.6, 100.0	0.0, 100.0
Change from Baseline at				
C9D15				
n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Mean (SD)	1.28 (19.386)	3.10 (16.845)	5.20 (12.759)	3.29 (16.356)
Median	1.63	4.35	1.63	1.63
Min, Max	-67.4, 39.1	-41.3, 33.7	-19.6, 30.1	-67.4, 39.1
LS Mean (SE)	1.58 (2.480)	2.74 (2.045)	5.11 (1.749)	3.22 (1.516)
95% CI	(-3.30, 6.46)	(-1.28, 6.77)	(1.67, 8.55)	(0.25, 6.20)
p-value	0.525	0.181	0.004	0.034

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	80.17 (16.492)	78.74 (15.240)	73.95 (17.050)	77.23 (16.930)
Median	80.43	82.61	75.54	78.80
Min, Max	50.0, 100.0	48.9, 100.0	44.6, 100.0	44.6, 100.0
Change from Baseline at				
C13D15				
n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Mean (SD)	3.95 (17.395)	5.24 (15.471)	2.98 (11.669)	3.49 (14.873)
Median	1.09	3.26	-0.54	0.00
Min, Max	-32.6, 52.2	-43.5, 32.6	-18.5, 26.1	-32.6, 52.2
LS Mean (SE)	4.02 (2.271)	5.46 (1.972)	3.60 (1.620)	3.76 (1.415)
95% CI	(-0.45, 8.49)	(1.58, 9.34)	(0.42, 6.79)	(0.98, 6.53)
p-value	0.078	0.006	0.027	0.008

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	77.91 (17.277)	79.21 (15.266)	75.00 (18.572)	76.50 (17.838)
Median	78.26	82.07	75.54	77.17
Min, Max	34.8, 100.0	28.3, 98.9	39.1, 100.0	34.8, 100.0
Change from Baseline at				
C17D15				
n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Mean (SD)	0.94 (17.877)	4.38 (14.897)	2.58 (11.214)	1.74 (14.930)
Median	2.72	2.82	0.54	2.17
Min, Max	-52.2, 50.0	-44.6, 41.3	-14.1, 30.4	-52.2, 50.0
LS Mean (SE)	1.12 (2.259)	4.61 (2.026)	4.06 (1.768)	2.33 (1.520)
95% CI	(-3.33, 5.57)	(0.62, 8.59)	(0.58, 7.54)	(-0.65, 5.32)
p-value	0.621	0.024	0.022	0.125

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C21D15	n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
	Mean (SD)	77.99 (16.760)	78.25 (18.206)	74.92 (18.101)	76.55 (17.318)
	Median	78.80	83.70	73.91	77.72
	Min, Max	43.5, 100.0	35.9, 100.0	41.3, 100.0	41.3, 100.0
Change from Baseline at					
C21D15	n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
	Mean (SD)	0.52 (18.419)	1.81 (17.707)	2.05 (13.660)	1.24 (16.255)
	Median	1.09	3.26	4.35	3.16
	Min, Max	-40.2, 45.7	-62.0, 33.7	-32.6, 31.5	-40.2, 45.7
	LS Mean (SE)	1.00 (2.427)	4.22 (2.486)	3.16 (2.130)	1.91 (1.719)
	95% CI	(-3.78, 5.78)	(-0.67, 9.11)	(-1.04, 7.35)	(-1.46, 5.29)
p-value		0.681	0.091	0.139	0.266

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C24D21					
n (%)		29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)		75.15 (22.707)	78.44 (18.081)	75.69 (17.902)	75.41 (20.307)
Median		80.43	79.35	75.00	78.26
Min, Max		17.4, 100.0	33.7, 100.0	46.7, 100.0	17.4, 100.0
Change from Baseline at					
C24D21					
n (%)		29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Mean (SD)		-2.62 (22.094)	2.27 (13.420)	4.41 (12.649)	0.83 (18.271)
Median		-2.17	2.17	4.89	0.00
Min, Max		-53.3, 52.2	-35.9, 38.0	-15.2, 31.2	-53.3, 52.2
LS Mean (SE)		-0.55 (3.105)	4.50 (2.082)	4.86 (1.972)	1.70 (2.087)
95% CI		(-6.66, 5.57)	(0.40, 8.59)	(0.98, 8.75)	(-2.40, 5.80)
p-value		0.860	0.032	0.014	0.416

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

	Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	75.51 (16.319)	76.59 (18.694)	75.54 (17.017)	75.53 (16.442)
Median	73.91	70.65	72.28	73.91
Min, Max	40.2, 100.0	44.6, 100.0	47.8, 100.0	40.2, 100.0
Change from Baseline at				
C28D15				
n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Mean (SD)	-1.88 (13.560)	2.00 (11.494)	4.65 (9.806)	1.68 (11.935)
Median	0.00	0.00	3.26	2.17
Min, Max	-31.5, 13.0	-17.4, 34.8	-14.1, 20.7	-31.5, 20.7
LS Mean (SE)	1.05 (2.588)	3.26 (2.425)	5.98 (1.850)	2.83 (1.592)
95% CI	(-4.04, 6.15)	(-1.52, 8.03)	(2.34, 9.62)	(-0.30, 5.96)
p-value	0.685	0.180	0.001	0.076

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C32D15		7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
n (%)		66.93 (21.066)	74.39 (20.586)	71.02 (19.270)	69.58 (19.459)
Mean (SD)		61.96	67.39	69.57	65.22
Median		34.8, 97.8	43.5, 97.8	42.4, 100.0	34.8, 100.0
Min, Max					
Change from Baseline at					
C32D15		7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
n (%)		-11.34 (23.379)	-2.84 (10.474)	4.96 (13.077)	-0.74 (18.553)
Mean (SD)		-2.17	-1.09	4.35	2.17
Median		-58.7, 10.9	-23.9, 14.1	-22.8, 23.9	-58.7, 23.9
Min, Max		-3.07 (6.027)	0.56 (2.912)	5.39 (3.201)	-0.45 (3.156)
LS Mean (SE)		(-14.93, 8.79)	(-5.17, 6.29)	(-0.91, 11.69)	(-6.65, 5.74)
95% CI		0.611	0.848	0.093	0.885
p-value					

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C36D15	n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
	Mean (SD)	73.82 (18.688)	78.21 (19.162)	72.64 (21.510)	73.11 (19.922)
	Median	76.09	84.78	71.20	73.37
	Min, Max	41.3, 98.6	46.7, 97.6	39.1, 100.0	39.1, 100.0
Change from Baseline at					
C36D15	n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
	Mean (SD)	-5.94 (21.317)	0.98 (17.119)	6.61 (9.738)	1.59 (16.189)
	Median	-5.43	1.79	6.52	5.98
	Min, Max	-41.3, 23.5	-32.6, 27.2	-8.7, 20.7	-41.3, 23.5
	LS Mean (SE)	-3.54 (4.940)	6.28 (4.059)	6.58 (2.753)	1.43 (3.003)
	95% CI	(-13.27, 6.18)	(-1.71, 14.27)	(1.16, 12.00)	(-4.46, 7.33)
p-value		0.474	0.123	0.017	0.633

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C40D15	n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
	Mean (SD)	70.65 (16.769)	61.96 (17.255)	67.80 (22.614)	68.75 (20.102)
	Median	66.30	59.78	60.33	61.41
	Min, Max	56.5, 93.5	43.5, 84.8	45.7, 100.0	45.7, 100.0
Change from Baseline at					
C40D15	n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
	Mean (SD)	-14.13 (19.626)	-10.60 (11.134)	7.07 (10.458)	-0.00 (16.839)
	Median	-16.30	-10.87	7.61	3.26
	Min, Max	-33.7, 9.8	-23.9, 3.3	-12.0, 20.7	-33.7, 20.7
	LS Mean (SE)	NA	NA	5.83 (2.914)	1.60 (3.092)
	95% CI	(NA, NA)	(NA, NA)	(0.09, 11.56)	(-4.48, 7.67)
p-value		NA	NA	0.046	0.606

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C44D15	n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
	Mean (SD)	73.91	59.78	73.75 (28.947)	73.78 (25.891)
	Median	73.91	59.78	82.61	78.26
	Min, Max	73.9, 73.9	59.8, 59.8	32.9, 100.0	32.9, 100.0
Change from Baseline at					
C44D15	n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
	Mean (SD)	7.61	0.00	6.58 (9.505)	6.75 (8.512)
	Median	7.61	0.00	1.09	4.35
	Min, Max	7.6, 7.6	0.0, 0.0	-1.9, 18.5	-1.9, 18.5
	LS Mean (SE)	NA	NA	3.02 (4.614)	-0.45 (4.339)
	95% CI	(NA, NA)	(NA, NA)	(-6.06, 12.10)	(-8.98, 8.07)
p-value		NA	NA	0.513	0.917

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsq1.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 4: PedsQL Scores by Visit : Full Analysis Set

Domain: Total Score		Pediatric Self-Report (N=50)	Pediatric Parent Proxy (N=56)	Adult (N=58)	Total (N=108)
C48D15					
n (%)		0	0	1 (1.7%)	1 (0.9%)
Mean (SD)		NA	NA	59.78	59.78
Median		NA	NA	59.78	59.78
Min, Max		(NA, NA)	(NA, NA)	59.8, 59.8	59.8, 59.8
Change from Baseline at					
C48D15					
n (%)		0	0	1 (1.7%)	1 (0.9%)
Mean (SD)		NA	NA	5.43	5.43
Median		NA	NA	5.43	5.43
Min, Max		(NA, NA)	(NA, NA)	5.4, 5.4	5.4, 5.4
LS Mean (SE)		NA	NA	NA	NA
95% CI		(NA, NA)	(NA, NA)	(NA, NA)	(NA, NA)
p-value		NA	NA	NA	NA

SD: Standard deviation; Min: Minimum; Max: Maximum; PedsQL: Pediatric Quality of Life Inventory.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Baseline is defined as the most recent PedsQL score taken on or before treatment start date.
Total column is comprised of the Pediatric Self-Report and Adult cohorts.

Program Name: t_pedsql.sas Output Generated: 2025-05-13T11:27 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	5 (10.0%)	6 (10.7%)	6 (10.3%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	9 (16.1%)	3 (5.2%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	7 (12.5%)	7 (12.1%)	13 (12.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	10 (17.9%)	5 (8.6%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	4 (8.0%)	4 (7.1%)	4 (6.9%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsqll_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	4 (8.0%)	4 (7.1%)	6 (10.3%)	10 (9.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	4 (7.1%)	5 (8.6%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	5 (10.0%)	4 (7.1%)	6 (10.3%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	5 (8.9%)	1 (1.7%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	1 (1.8%)	2 (3.4%)	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	29 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	1 (1.8%)	2 (3.4%)	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.8%)	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.8%)	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	17 (34.0%)	18 (32.1%)	16 (27.6%)	33 (30.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	7 (12.5%)	6 (10.3%)	12 (11.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	7 (12.5%)	4 (6.9%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	7 (12.5%)	8 (13.8%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	9 (16.1%)	6 (10.3%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	3 (5.4%)	6 (10.3%)	13 (12.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	2 (3.6%)	5 (8.6%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsqll_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	7 (12.5%)	2 (3.4%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	7 (12.5%)	3 (5.2%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	2 (3.6%)	2 (3.4%)	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsqll_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	0	1 (1.7%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	29 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	1 (1.8%)	0	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	1 (2.0%)	1 (1.8%)	0	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	19 (38.0%)	21 (37.5%)	19 (32.8%)	38 (35.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	5 (10.0%)	8 (14.3%)	4 (6.9%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	4 (7.1%)	2 (3.4%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	5 (10.0%)	6 (10.7%)	4 (6.9%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	9 (16.1%)	5 (8.6%)	12 (11.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	8 (16.0%)	3 (5.4%)	3 (5.2%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	3 (5.4%)	6 (10.3%)	12 (11.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	8 (14.3%)	4 (6.9%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	6 (10.7%)	4 (6.9%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	1 (1.8%)	2 (3.4%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	2 (3.6%)	2 (3.4%)	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	29 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	4 (8.0%)	2 (3.6%)	0	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	3 (5.4%)	0	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	1 (1.8%)	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	21 (42.0%)	19 (33.9%)	16 (27.6%)	37 (34.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	50 (89.3%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	6 (10.7%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	8 (14.3%)	8 (13.8%)	18 (16.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	50 (89.3%)	45 (77.6%)	92 (85.2%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	6 (10.7%)	13 (22.4%)	16 (14.8%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	10 (20.0%)	10 (17.9%)	4 (6.9%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	47 (83.9%)	43 (74.1%)	84 (77.8%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	9 (16.1%)	15 (25.9%)	24 (22.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	11 (22.0%)	10 (17.9%)	2 (3.4%)	13 (12.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	45 (80.4%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	11 (19.6%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	8 (16.0%)	6 (10.7%)	5 (8.6%)	13 (12.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	42 (75.0%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	14 (25.0%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	8 (16.0%)	7 (12.5%)	3 (5.2%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsqll_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	10 (17.9%)	3 (5.2%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	35 (62.5%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	21 (37.5%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	9 (18.0%)	6 (10.7%)	7 (12.1%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	32 (57.1%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	24 (42.9%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	7 (12.5%)	2 (3.4%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsqll_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	16 (28.6%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	40 (71.4%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	4 (8.0%)	4 (7.1%)	2 (3.4%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	2 (3.6%)	1 (1.7%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBA

Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	12 (20.7%)	19 (17.6%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	3 (5.4%)	0	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	3 (5.4%)	0	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	4 (6.9%)	5 (4.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	54 (93.1%)	103 (95.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	53 (94.6%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	3 (5.4%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	22 (44.0%)	26 (46.4%)	16 (27.6%)	38 (35.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	3 (5.4%)	2 (3.4%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	5 (8.9%)	3 (5.2%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	2 (3.6%)	2 (3.4%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	8 (14.3%)	1 (1.7%)	7 (6.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	3 (5.4%)	1 (1.7%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	5 (10.0%)	2 (3.6%)	0	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	6 (12.0%)	4 (7.1%)	3 (5.2%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	7 (14.0%)	2 (3.6%)	1 (1.7%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	1 (1.8%)	0	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	1 (1.8%)	1 (1.7%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	3 (6.0%)	1 (1.8%)	0	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	2 (4.0%)	1 (1.8%)	0	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by >=15% (-15) : Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_11_pedsql_objresp_wrsn_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.11: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Worsening by $\geq 15\%$ (-15): Full Analysis Set: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	-15	-15	-15	-15
Participants with Clinically Meaningful Score Worsening, n (%)	17 (34.0%)	12 (21.4%)	8 (13.8%)	25 (23.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		
95% CI	(8.9, 32.6)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

Program Name: t_55_3_pedsql_objresp_anch_nr.sas

Output Generated: 2025-05-02T13:36

Source: ADSL, ADQS

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	14 (28.0%)		
95% CI	(17.3, 44.9)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(12.4, 40.3)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)		
95% CI	(13.9, 42.0)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(13.4, 43.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		
95% CI	(12.9, 44.4)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)		
95% CI	(18.6, 53.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)		
95% CI	(12.7, 47.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C28D15			
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.0%)		
95% CI	(7.8, 55.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C32D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 41.0)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C36D15			
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)		
95% CI	(3.2, 65.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C40D15			
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 60.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C44D15			
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 97.5)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C48D15			
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	NE		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	24 (48.0%)		
95% CI	(34.4, 63.7)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)		18 (31.0%)
95% CI	(15.3, 41.8)		(24.0, 52.6)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		19 (32.8%)
95% CI	(10.7, 35.7)		(27.0, 56.8)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		15 (25.9%)
95% CI	(10.6, 37.6)		(20.5, 49.9)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		16 (27.6%)
95% CI	(10.3, 36.8)		(22.4, 52.2)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)		10 (17.2%)
95% CI	(19.6, 51.4)		(15.1, 47.5)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)		10 (17.2%)
95% CI	(8.7, 37.9)		(16.1, 50.0)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		10 (17.2%)
95% CI	(13.7, 46.7)		(18.6, 55.9)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.0%)		11 (19.0%)
95% CI	(8.0, 39.7)		(21.5, 59.4)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C28D15			
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)		5 (8.6%)
95% CI	(1.7, 40.5)		(9.7, 53.5)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C32D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		6 (10.3%)
95% CI	(0.4, 57.9)		(19.2, 74.9)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C36D15			
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)		4 (6.9%)
95% CI	(3.2, 65.1)		(9.9, 65.1)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C40D15			
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		3 (5.2%)
95% CI	(0.6, 80.6)		(8.5, 75.5)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C44D15			
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		3 (5.2%)
95% CI	(2.5, 100.0)		(14.7, 94.7)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C48D15			
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	0		1 (1.7%)
95% CI	NE		(2.5, 100.0)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)
Threshold for Meaningful Score Difference	18.5	n/a	10
Participants with Clinically Meaningful Score Improvement, n (%)	22 (44.0%)		33 (56.9%)
95% CI	(30.7, 59.8)		(51.2, 78.8)

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C28D15			
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C32D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C36D15			
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C40D15			
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C44D15			
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C48D15			
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)
Threshold for Meaningful Score Difference	n/a	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)			
95% CI			

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	50 (89.3%)	48 (82.8%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	6 (10.7%)	10 (17.2%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.0%)		
95% CI	(2.3, 20.0)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	50 (89.3%)	45 (77.6%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	6 (10.7%)	13 (22.4%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(10.7, 35.7)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	47 (83.9%)	43 (74.1%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	9 (16.1%)	15 (25.9%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)		
95% CI	(7.2, 32.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	45 (80.4%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	11 (19.6%)	14 (24.1%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)		
95% CI	(17.6, 47.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	42 (75.0%)	34 (58.6%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	14 (25.0%)	24 (41.4%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(13.4, 43.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)		
95% CI	(10.7, 41.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	35 (62.5%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	21 (37.5%)	30 (51.7%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(16.1, 50.0)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	32 (57.1%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	24 (42.9%)	30 (51.7%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)		
95% CI	(10.3, 43.5)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C28D15			
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	16 (28.6%)	18 (31.0%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	40 (71.4%)	40 (69.0%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)		
95% CI	(4.3, 48.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C32D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	13 (22.4%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	45 (77.6%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		
95% CI	(0.4, 57.9)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C36D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	12 (20.7%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	46 (79.3%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)		
95% CI	(9.9, 81.6)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C40D15			
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		
95% CI	(0.6, 80.6)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C44D15			
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	4 (6.9%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	54 (93.1%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 97.5)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C48D15			
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	NE		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	53 (94.6%)	50 (86.2%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	3 (5.4%)	8 (13.8%)
Threshold for Meaningful Score Difference	20	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	22 (44.0%)		
95% CI	(30.7, 59.8)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C3D15			
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)		
95% CI	(6.1, 27.8)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C5D15			
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(10.7, 35.7)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C7D15			
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		
95% CI	(10.6, 37.6)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C9D15			
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)		
95% CI	(12.1, 39.5)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C13D15			
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		
95% CI	(11.4, 40.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C17D15			
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.0%)		
95% CI	(5.0, 31.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C21D15			
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)		
95% CI	(13.7, 46.7)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C24D21			
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.0%)		
95% CI	(5.8, 35.8)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort.

The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach.

A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.

PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.

PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).

These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C28D15			
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)		
95% CI	(0.2, 31.9)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C32D15			
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 41.0)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C36D15			
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)		
95% CI	(3.2, 65.1)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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GBA

Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C40D15			
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 60.2)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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GBA

Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C44D15			
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	(0.0, 97.5)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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GBA

Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Visit C48D15			
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	0		
95% CI	NE		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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GBA

Table 55.3: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation: Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)
Total			
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)
Threshold for Meaningful Score Difference	12.5	n/a	n/a
Participants with Clinically Meaningful Score Improvement, n (%)	20 (40.0%)		
95% CI	(27.0, 55.8)		

PedsQL: Pediatric Quality of Life Inventory; CI: Confidence Interval; QoL: Quality of Life.

N represents the number of participants in the corresponding cohort. The anchor-based derivation of within-participant clinically meaningful thresholds is described in the meaningful change threshold (MCT) analysis plan. 95% CIs are derived using the Clopper-Pearson approach. A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold. PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing. PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem). These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)	8 (14.3%)	13 (22.4%)	21 (19.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	11 (19.6%)	15 (25.9%)	24 (22.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)	12 (21.4%)	12 (20.7%)	19 (17.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	13 (23.2%)	12 (20.7%)	21 (19.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)	12 (21.4%)	8 (13.8%)	18 (16.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.0%)	11 (19.6%)	8 (13.8%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)	8 (14.3%)	7 (12.1%)	17 (15.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)	6 (10.7%)	7 (12.1%)	14 (13.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)	2 (3.6%)	4 (6.9%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	1 (1.8%)	2 (3.4%)	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objjresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	1 (1.8%)	2 (3.4%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	2 (3.4%)	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Physical Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	18 (36.0%)	25 (44.6%)	30 (51.7%)	48 (44.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	16 (32.0%)	17 (30.4%)	12 (20.7%)	28 (25.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	15 (30.0%)	16 (28.6%)	12 (20.7%)	27 (25.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)	12 (21.4%)	9 (15.5%)	22 (20.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)	16 (28.6%)	12 (20.7%)	25 (23.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	14 (28.0%)	16 (28.6%)	6 (10.3%)	20 (18.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)	12 (21.4%)	7 (12.1%)	17 (15.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)	15 (26.8%)	6 (10.3%)	17 (15.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)	13 (23.2%)	8 (13.8%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	7 (12.5%)	4 (6.9%)	7 (6.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	3 (5.4%)	3 (5.2%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	0	2 (3.4%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	1 (1.8%)	3 (5.2%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Emotional Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	27 (54.0%)	30 (53.6%)	28 (48.3%)	55 (50.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	14 (25.0%)	11 (19.0%)	20 (18.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)	14 (25.0%)	10 (17.2%)	21 (19.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	11 (19.6%)	7 (12.1%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	13 (26.0%)	15 (26.8%)	12 (20.7%)	25 (23.1%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	10 (20.0%)	12 (21.4%)	6 (10.3%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	6 (12.0%)	9 (16.1%)	5 (8.6%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	2 (4.0%)	9 (16.1%)	4 (6.9%)	6 (5.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	4 (8.0%)	6 (10.7%)	6 (10.3%)	10 (9.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	4 (7.1%)	2 (3.4%)	5 (4.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objjresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	2 (3.4%)	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	1 (1.8%)	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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SpringWorks Therapeutics

MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: Social Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	19 (38.0%)	29 (51.8%)	21 (36.2%)	40 (37.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	50 (89.3%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	6 (10.7%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)	11 (19.6%)	19 (32.8%)	27 (25.0%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	50 (89.3%)	45 (77.6%)	92 (85.2%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	6 (10.7%)	13 (22.4%)	16 (14.8%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	16 (32.0%)	12 (21.4%)	12 (20.7%)	28 (25.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	47 (83.9%)	43 (74.1%)	84 (77.8%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	9 (16.1%)	15 (25.9%)	24 (22.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	10 (17.9%)	12 (20.7%)	21 (19.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	45 (80.4%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	11 (19.6%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	16 (32.0%)	10 (17.9%)	15 (25.9%)	31 (28.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	42 (75.0%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	14 (25.0%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)	11 (19.6%)	5 (8.6%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)	9 (16.1%)	8 (13.8%)	19 (17.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	35 (62.5%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	21 (37.5%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	11 (22.0%)	7 (12.5%)	8 (13.8%)	19 (17.6%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	32 (57.1%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	24 (42.9%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	8 (14.3%)	9 (15.5%)	18 (16.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	16 (28.6%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	40 (71.4%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	3 (5.4%)	6 (10.3%)	9 (8.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	1 (1.8%)	7 (12.1%)	10 (9.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	8 (14.3%)	12 (20.7%)	19 (17.6%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	48 (85.7%)	46 (79.3%)	89 (82.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	2 (3.6%)	5 (8.6%)	8 (7.4%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	0	3 (5.2%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	4 (6.9%)	5 (4.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	54 (93.1%)	103 (95.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	1 (1.8%)	1 (1.7%)	1 (0.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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GBA

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: School/Work Functioning

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	53 (94.6%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	3 (5.4%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	27 (54.0%)	25 (44.6%)	29 (50.0%)	56 (51.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objjresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C3D15				
Number of Participants Completed the Assessment, n (%)	48 (96.0%)	52 (92.9%)	48 (82.8%)	96 (88.9%)
Number of Participants Missing the Assessment, n (%)	2 (4.0%)	4 (7.1%)	10 (17.2%)	12 (11.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.0%)	11 (19.6%)	10 (17.2%)	15 (13.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C5D15				
Number of Participants Completed the Assessment, n (%)	47 (94.0%)	52 (92.9%)	46 (79.3%)	93 (86.1%)
Number of Participants Missing the Assessment, n (%)	3 (6.0%)	4 (7.1%)	12 (20.7%)	15 (13.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)	8 (14.3%)	12 (20.7%)	20 (18.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C7D15				
Number of Participants Completed the Assessment, n (%)	41 (82.0%)	48 (85.7%)	44 (75.9%)	85 (78.7%)
Number of Participants Missing the Assessment, n (%)	9 (18.0%)	8 (14.3%)	14 (24.1%)	23 (21.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)	11 (19.6%)	8 (13.8%)	15 (13.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C9D15				
Number of Participants Completed the Assessment, n (%)	42 (84.0%)	47 (83.9%)	44 (75.9%)	86 (79.6%)
Number of Participants Missing the Assessment, n (%)	8 (16.0%)	9 (16.1%)	14 (24.1%)	22 (20.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	9 (18.0%)	11 (19.6%)	11 (19.0%)	20 (18.5%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C13D15				
Number of Participants Completed the Assessment, n (%)	38 (76.0%)	43 (76.8%)	34 (58.6%)	72 (66.7%)
Number of Participants Missing the Assessment, n (%)	12 (24.0%)	13 (23.2%)	24 (41.4%)	36 (33.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	8 (16.0%)	12 (21.4%)	8 (13.8%)	16 (14.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C17D15				
Number of Participants Completed the Assessment, n (%)	34 (68.0%)	36 (64.3%)	32 (55.2%)	66 (61.1%)
Number of Participants Missing the Assessment, n (%)	16 (32.0%)	20 (35.7%)	26 (44.8%)	42 (38.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	5 (10.0%)	10 (17.9%)	5 (8.6%)	10 (9.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBA

SpringWorks Therapeutics

Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: PedsQL Score				
Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C21D15				
Number of Participants Completed the Assessment, n (%)	32 (64.0%)	36 (64.3%)	28 (48.3%)	60 (55.6%)
Number of Participants Missing the Assessment, n (%)	18 (36.0%)	20 (35.7%)	30 (51.7%)	48 (44.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	7 (14.0%)	6 (10.7%)	3 (5.2%)	10 (9.3%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C24D21				
Number of Participants Completed the Assessment, n (%)	29 (58.0%)	33 (58.9%)	28 (48.3%)	57 (52.8%)
Number of Participants Missing the Assessment, n (%)	21 (42.0%)	23 (41.1%)	30 (51.7%)	51 (47.2%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	3 (6.0%)	5 (8.9%)	8 (13.8%)	11 (10.2%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self- Report (N=50)	Pediatric Parent- Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C28D15				
Number of Participants Completed the Assessment, n (%)	15 (30.0%)	17 (30.4%)	18 (31.0%)	33 (30.6%)
Number of Participants Missing the Assessment, n (%)	35 (70.0%)	39 (69.6%)	40 (69.0%)	75 (69.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	2 (3.6%)	3 (5.2%)	3 (2.8%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C32D15				
Number of Participants Completed the Assessment, n (%)	7 (14.0%)	9 (16.1%)	13 (22.4%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	43 (86.0%)	47 (83.9%)	45 (77.6%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	4 (6.9%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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Table 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by >=15% (15) : Full Analysis Set

Domain: PedsQL Score				
Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C36D15				
Number of Participants Completed the Assessment, n (%)	8 (16.0%)	9 (16.1%)	12 (20.7%)	20 (18.5%)
Number of Participants Missing the Assessment, n (%)	42 (84.0%)	47 (83.9%)	46 (79.3%)	88 (81.5%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	1 (2.0%)	2 (3.6%)	3 (5.2%)	4 (3.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
N represents the number of participants in the corresponding cohort.
A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if >50% of the individual questions are missing.
PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objjresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C40D15				
Number of Participants Completed the Assessment, n (%)	4 (8.0%)	4 (7.1%)	8 (13.8%)	12 (11.1%)
Number of Participants Missing the Assessment, n (%)	46 (92.0%)	52 (92.9%)	50 (86.2%)	96 (88.9%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	2 (3.4%)	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsq_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

SpringWorks Therapeutics

MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C44D15				
Number of Participants Completed the Assessment, n (%)	1 (2.0%)	1 (1.8%)	5 (8.6%)	6 (5.6%)
Number of Participants Missing the Assessment, n (%)	49 (98.0%)	55 (98.2%)	53 (91.4%)	102 (94.4%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	2 (3.4%)	2 (1.9%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsq_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Visit C48D15				
Number of Participants Completed the Assessment, n (%)	0	0	1 (1.7%)	1 (0.9%)
Number of Participants Missing the Assessment, n (%)	0	0	57 (98.3%)	107 (99.1%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	0	0	0	0

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 55.7: Anchor-Based Analysis of Meaningful PedsQL Score Difference - Non-Responder Imputation - Improvement by $\geq 15\%$ (15): Full Analysis Set

Domain: PedsQL Score

Visits	Pediatric Self-Report (N=50)	Pediatric Parent-Proxy (N=56)	Adult (N=58)	Total (N=108)
Total				
Number of Participants Completed the Assessment, n (%)	49 (98.0%)	54 (96.4%)	50 (86.2%)	99 (91.7%)
Number of Participants Missing the Assessment, n (%)	1 (2.0%)	2 (3.6%)	8 (13.8%)	9 (8.3%)
Threshold for Meaningful Score Difference	15	15	15	15
Participants with Clinically Meaningful Score Improvement, n (%)	17 (34.0%)	25 (44.6%)	27 (46.6%)	44 (40.7%)

PedsQL: Pediatric Quality of Life Inventory; QoL: Quality of Life.
 N represents the number of participants in the corresponding cohort.
 A participant is defined as having clinically meaningful improvement at a visit if their change from baseline in PedsQL score is greater than or equal to the corresponding threshold.
 PedsQL domain scores are calculated as the mean of the individual question scores from that domain. Domain scores are missing if $>50\%$ of the individual questions are missing.
 PedsQL items are answered on a Likert scale with responses ranging from 0 to 4 (where 0 means it is never a problem and 4 means it is almost always a problem).
 These items are then reverse scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0 with higher scores indicating better outcomes.
 Total column is the count of Pediatric Self-Report and Adult cohorts.

Program Name: t_55_7_pedsql_objresp_impr_nr.sas Output Generated: 2025-05-02T13:37 Source: ADSL, ADQS Data Cutoff Date: 2023-09-20

7 Sicherheit

Springworks Therapeutics	MEK-NF-201 GBA		
	Table 2: Number of Deaths: Full Analysis Set		
		Pediatric (N=56)	Adult (N=58)
	n (%)	0	1 (1.7%)
			Total (N=114)
			1 (0.9%)
There was no death in pediatric cohort. N represents the number of participants in the corresponding cohort.			
Program Name: t_dth_fas.sas Output Generated: 2025-05-02T13:31 Source: ADSL Data Cutoff Date: 2023-09-20			

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Table 37: Summary of Treatment-Emergent Adverse Events: Safety Analysis Set

	Pediatric (N=56) n (%)	Adult (N=58) n (%)	Total (N=114) n (%)
Participants with at Least One Adverse Event	56 (100%)	58 (100%)	114 (100%)
Overall Rate of Participants with at Least One:			
Grade 1 AE	56 (100%)	56 (96.6%)	112 (98.2%)
Grade 2 AE	47 (83.9%)	49 (84.5%)	96 (84.2%)
Grade 3 AE	21 (37.5%)	19 (32.8%)	40 (35.1%)
Grade 4 AE	2 (3.6%)	3 (5.2%)	5 (4.4%)
Grade 5 AE	0	1 (1.7%)	1 (0.9%)

Program Name: t_ae_grd.sas Output Generated: 2025-05-02T13:33 Source: ADL, ADAE Data Cutoff Date: 2023-09-20

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GBATable 38: Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Pediatric (N=56)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	49 (87.5%)
Dermatitis acneiform	24 (42.9%)
Rash	11 (19.6%)
Dry skin	10 (17.9%)
Gastrointestinal disorders	42 (75.0%)
Diarrhoea	31 (55.4%)
Vomiting	22 (39.3%)
Abdominal pain	15 (26.8%)
Nausea	15 (26.8%)
Infections and infestations	40 (71.4%)
Paronychia	18 (32.1%)
COVID-19	14 (25.0%)
Upper respiratory tract infection	13 (23.2%)
Investigations	36 (64.3%)
Ejection fraction decreased	15 (26.8%)
Blood creatine phosphokinase increased	12 (21.4%)
SARS-CoV-2 test positive	11 (19.6%)
General disorders and administration site conditions	26 (46.4%)
Pyrexia	11 (19.6%)
Musculoskeletal and connective tissue disorders	25 (44.6%)
Pain in extremity	11 (19.6%)
Nervous system disorders	25 (44.6%)
Headache	19 (33.9%)
Respiratory, thoracic and mediastinal disorders	21 (37.5%)
Cough	12 (21.4%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events.

Program Name: t_ae_10p_updated.sas Output Generated: 2025-08-19T13:16 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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GBATable 38: Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Adult (N=58)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	54 (93.1%)
Dermatitis acneiform	45 (77.6%)
Gastrointestinal disorders	49 (84.5%)
Diarrhoea	34 (58.6%)
Nausea	30 (51.7%)
Vomiting	22 (37.9%)
Abdominal pain	10 (17.2%)
Infections and infestations	30 (51.7%)
COVID-19	13 (22.4%)
Investigations	29 (50.0%)
SARS-CoV-2 test positive	12 (20.7%)
General disorders and administration site conditions	28 (48.3%)
Fatigue	17 (29.3%)
Nervous system disorders	24 (41.4%)
Dizziness	10 (17.2%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events.

Program Name: t_ae_10p_updated.sas Output Generated: 2025-08-19T13:16 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 38: Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Total (N=114)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	103 (90.4%)
Dermatitis acneiform	69 (60.5%)
Dry skin	19 (16.7%)
Alopecia	15 (13.2%)
Rash	15 (13.2%)
Pruritus	14 (12.3%)
Eczema	10 (8.8%)
Gastrointestinal disorders	91 (79.8%)
Diarrhoea	65 (57.0%)
Nausea	45 (39.5%)
Vomiting	44 (38.6%)
Abdominal pain	25 (21.9%)
Constipation	15 (13.2%)
Abdominal pain upper	12 (10.5%)
Stomatitis	10 (8.8%)
Infections and infestations	70 (61.4%)
COVID-19	27 (23.7%)
Paronychia	19 (16.7%)
Upper respiratory tract infection	13 (11.4%)
Investigations	65 (57.0%)
Ejection fraction decreased	24 (21.1%)
SARS-CoV-2 test positive	23 (20.2%)
Blood creatine phosphokinase increased	20 (17.5%)
Weight increased	13 (11.4%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events.

Program Name: t_ae_10p_updated.sas Output Generated: 2025-08-19T13:16 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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GBATable 38: Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Total (N=114)

System Organ Class Preferred Term	n (%)
General disorders and administration site conditions	54 (47.4%)
Fatigue	24 (21.1%)
Pyrexia	15 (13.2%)
Musculoskeletal and connective tissue disorders	49 (43.0%)
Pain in extremity	20 (17.5%)
Arthralgia	18 (15.8%)
Back pain	14 (12.3%)
Nervous system disorders	49 (43.0%)
Headache	25 (21.9%)
Dizziness	15 (13.2%)
Respiratory, thoracic and mediastinal disorders	33 (28.9%)
Cough	17 (14.9%)
Nasal congestion	10 (8.8%)
Eye disorders	29 (25.4%)
Vision blurred	11 (9.6%)
Vascular disorders	14 (12.3%)
Hypertension	10 (8.8%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events.

Program Name: t_ae_10p_updated.sas Output Generated: 2025-08-19T13:16 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 39: Grade 1 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Pediatric (N=56)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	47 (83.9%)
Dermatitis acneiform	20 (35.7%)
Rash	11 (19.6%)
Dry skin	10 (17.9%)
Gastrointestinal disorders	39 (69.6%)
Diarrhoea	27 (48.2%)
Vomiting	20 (35.7%)
Abdominal pain	12 (21.4%)
Nausea	12 (21.4%)
Infections and infestations	32 (57.1%)
COVID-19	11 (19.6%)
Paronychia	11 (19.6%)
Investigations	29 (51.8%)
Blood creatine phosphokinase increased	11 (19.6%)
General disorders and administration site conditions	21 (37.5%)
Pyrexia	10 (17.9%)
Respiratory, thoracic and mediastinal disorders	21 (37.5%)
Cough	12 (21.4%)
Nervous system disorders	20 (35.7%)
Headache	17 (30.4%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 1.

Program Name: t_ae_10p_grd1_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 39: Grade 1 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and >=1% in the Population: Safety Analysis Set

Cohort: Adult (N=58)

System Organ Class Preferred Term	n (%)
Gastrointestinal disorders	48 (82.8%)
Diarrhoea	31 (53.4%)
Nausea	27 (46.6%)
Vomiting	21 (36.2%)
Skin and subcutaneous tissue disorders	48 (82.8%)
Dermatitis acneiform	38 (65.5%)
General disorders and administration site conditions	22 (37.9%)
Fatigue	12 (20.7%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 1.

Program Name: t_ae_10p_grd1_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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GBATable 39: Grade 1 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and $\geq 1\%$ in the Population: Safety Analysis Set

Cohort: Total (N=114)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	95 (83.3%)
Dermatitis acneiform	58 (50.9%)
Dry skin	16 (14.0%)
Alopecia	15 (13.2%)
Rash	15 (13.2%)
Pruritus	13 (11.4%)
Gastrointestinal disorders	87 (76.3%)
Diarrhoea	58 (50.9%)
Vomiting	41 (36.0%)
Nausea	39 (34.2%)
Abdominal pain	21 (18.4%)
Abdominal pain upper	10 (8.8%)
Constipation	10 (8.8%)
Infections and infestations	48 (42.1%)
COVID-19	17 (14.9%)
Paronychia	12 (10.5%)
Investigations	48 (42.1%)
Blood creatine phosphokinase increased	18 (15.8%)
SARS-CoV-2 test positive	16 (14.0%)
General disorders and administration site conditions	43 (37.7%)
Fatigue	19 (16.7%)
Pyrexia	13 (11.4%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 1.

Program Name: t_ae_10p_grd1_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 39: Grade 1 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and >=1% in the Population: Safety Analysis Set

Cohort: Total (N=114)

System Organ Class Preferred Term	n (%)
Musculoskeletal and connective tissue disorders	41 (36.0%)
Arthralgia	17 (14.9%)
Pain in extremity	15 (13.2%)
Nervous system disorders	41 (36.0%)
Headache	20 (17.5%)
Dizziness	12 (10.5%)
Respiratory, thoracic and mediastinal disorders	32 (28.1%)
Cough	17 (14.9%)
Nasal congestion	10 (8.8%)
Eye disorders	28 (24.6%)
Vision blurred	10 (8.8%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 1.

Program Name: t_ae_10p_grd1_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 40: Grade 2 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and >=1% in the Population: Safety Analysis Set

Cohort: Pediatric (N=56)

System Organ Class Preferred Term	n (%)
Infections and infestations	29 (51.8%)
Paronychia	12 (21.4%)
Investigations	22 (39.3%)
Ejection fraction decreased	14 (25.0%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 2.

Program Name: t_ae_10p_grd2_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 40: Grade 2 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and >=1% in the Population: Safety Analysis Set

Cohort: Adult (N=58)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders Dermatitis acneiform	27 (46.6%) 15 (25.9%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 2.

Program Name: t_ae_10p_grd2_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 40: Grade 2 Treatment-Emergent Adverse Events Occurring in at Least 10 Participants and >=1% in the Population: Safety Analysis Set

Cohort: Total (N=114)

System Organ Class Preferred Term	n (%)
Infections and infestations	49 (43.0%)
Paronychia	12 (10.5%)
COVID-19	10 (8.8%)
Skin and subcutaneous tissue disorders	43 (37.7%)
Dermatitis acneiform	23 (20.2%)
Investigations	39 (34.2%)
Ejection fraction decreased	23 (20.2%)
Weight increased	10 (8.8%)
Gastrointestinal disorders	36 (31.6%)
Diarrhoea	13 (11.4%)
Nausea	13 (11.4%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 2.

Program Name: t_ae_10p_grd2_updated.sas Output Generated: 2025-08-19T13:17 Source: ADL, ADAE Data Cutoff Date: 2023-09-20

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Table 41: Grade >=3 Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set	
Cohort: Pediatric (N=56)	
System Organ Class	n (%)
Investigations	11 (19.6%)
Neutrophil count decreased	5 (8.9%)
Blood creatine phosphokinase increased	4 (7.1%)
Gastrointestinal disorders	4 (7.1%)
Diarrhoea	3 (5.4%)
Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 3 and higher.	
Program Name: t_ae_10p_5pct_grd3_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20	

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Table 41: Grade >=3 Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set

Cohort: Adult (N=58)

System Organ Class Preferred Term	n (%)
Skin and subcutaneous tissue disorders	8 (13.8%)
Dermatitis acneiform	5 (8.6%)
Infections and infestations	4 (6.9%)
COVID-19	3 (5.2%)

Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 3 and higher.

Program Name: t_ae_10p_5pct_grd3_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 41: Grade >=3 Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set	
Cohort: Total (N=114)	
System Organ Class	n (%)
Preferred Term	
Skin and subcutaneous tissue disorders	10 (8.8%)
Dermatitis acneiform	6 (5.3%)
Thresholds are applied at Preferred Term level only. System Organ class represent all subjects who had treatment emergent adverse events with grade 3 and higher.	
Program Name: t_ae_10p_5pct_grd3_updated.sas Output Generated: 2025-08-19T13:17 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20	

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Table 42: Summary of Serious Treatment-Emergent Adverse Events: Safety Population

	Pediatric (N=56) n (%)	Adult (N=58) n (%)	Total (N=114) n (%)
Participants with at Least One SAE	8 (14.3%)	10 (17.2%)	18 (15.8%)

Program Name: t_sae.sas Output Generated: 2025-05-02T13:34 Source: ADL, ADAE Data Cutoff Date: 2023-09-20

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Table 43: Serious Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set

Cohort: Pediatric (N=56)

System Organ Class Preferred Term	n (%)
No Participant meets the reporting criteria	

Program Name: t_sae_10p_5pct_updated.sas Output Generated: 2025-08-19T13:08 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 43: Serious Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set

Cohort: Adult (N=58)

System Organ Class Preferred Term	n (%)
No Participant meets the reporting criteria	

Program Name: t_sae_10p_5pct_updated.sas Output Generated: 2025-08-19T13:08 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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Table 43: Serious Treatment-Emergent Adverse Events Occurring in >=5% in the Population: Safety Analysis Set	
Cohort: Total (N=114)	
System Organ Class Preferred Term	n (%)
No Participant meets the reporting criteria	
Program Name: t_sae_10p_5pct_updated.sas Output Generated: 2025-08-19T13:08 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20	

Table 44: Summary of Treatment-Emergent Adverse Events of Special Interest: Safety Analysis Set

	Pediatric (N=56) n (%)	Adult (N=58) n (%)	Total (N=114) n (%)
Participants with at Least One AESI	19 (33.9%)	18 (31.0%)	37 (32.5%)
Overall Rate of Participants with at Least One:			
Grade 2 AESI	14 (25.0%)	11 (19.0%)	25 (21.9%)
Grade >=3 AESI	7 (12.5%)	7 (12.1%)	14 (12.3%)
Serious AESI	0	1 (1.7%)	1 (0.9%)

Program Name: t_ae_grd_si.sas Output Generated: 2025-05-02T13:34 Source: ADL,ADAE Data Cutoff Date: 2023-09-20

Table 45: Number of Participants with Grade 2 Treatment-Emergent AESI by SOC and PT: Safety Analysis Set

System Organ Class Preferred Term	Pediatric (N=56) n (%)		Adult (N=58) n (%)		Total (N=114) n (%)	
Investigations		14 (25.0%)	9 (15.5%)	23 (20.2%)		
Ejection fraction decreased		14 (25.0%)	9 (15.5%)	23 (20.2%)		
Skin and subcutaneous tissue disorders ^a		0	2 (3.4%)	2 (1.8%)		
Dermatitis acneiform		0	1 (1.7%)	1 (0.9%)		
Rash ^b		0	1 (1.7%)	1 (0.9%)		

a. Rash and Acneiform rash were considered an AESI for Grade >=2 in earlier versions of the protocol. Due to this, there may be some Grade 2 rashes marked as AESIs by the investigators, which are reported as such.

b. Rash is a composite term of the PTs listed in SAP Appendix 2.

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Table 46: Number of Participants with Grade ≥3 Treatment-Emergent AESI by SOC and PT: Safety Analysis Set

System Organ Class Preferred Term	Pediatric (N = 56) n (%)	Adult (N = 58) n (%)	Total (N = 114) n (%)
Eye disorders	0	1 (1.7%)	1 (0.9%)
Retinal vein occlusion	0	1 (1.7%)	1 (0.9%)
Gastrointestinal disorders	3 (5.4%)	0	3 (2.6%)
Diarrhoea	3 (5.4%)	0	3 (2.6%)
Infections and infestations	1 (1.8%)	0	1 (0.9%)
Viral rash	1 (1.8%)	0	1 (0.9%)
Investigations	1 (1.8%)	0	1 (0.9%)
Ejection fraction decreased	1 (1.8%)	0	1 (0.9%)
Skin and subcutaneous tissue disorders	2 (3.6%)	6 (10.3%)	8 (7.0%)
Dermatitis acneiform	1 (1.8%)	5 (8.6%)	6 (5.3%)
Rash erythematous	0	1 (1.7%)	1 (0.9%)
Rash ^a	1 (1.8%)	0	1 (0.9%)

a. Rash is a composite term of the PTs listed in SAP Appendix 2.

Program Name: t_aesi_grd3.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

Table 47: Number of Participants with Serious Treatment-Emergent AESI by SOC and PT: Safety Analysis Set

System Organ Class Preferred Term	Pediatric (N = 56) n (%)	Adult (N = 58) n (%)	Total (N = 114) n (%)
Eye disorders		1 (1.7%)	1 (0.9%)
Retinal vein occlusion	0	1 (1.7%)	1 (0.9%)

Program Name: t_aesi_ser.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

Table 48: Summary of Study Treatment Discontinuations Due to Treatment-Emergent Adverse Events: Safety Analysis Set

	Pediatric (N = 56) n (%)	Adult (N = 58) n (%)	Total (N = 114) n (%)
Number of Participants who Discontinued Study Treatment due to AE	5 (8.9)	13 (22.4)	18 (15.8)

Program Name: t_ae_trt_disc_sum.sas Output Generated: 2025-05-02T13:34 Source: ADL, ADAE Data Cutoff Date: 2023-09-20

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GBATable 49: Number of Participants with Treatment-Emergent Adverse Events that Led to Study Treatment Discontinuations by SOC and PT:
Safety Analysis Set

System Organ Class Preferred Term	Pediatric (N=56)		Adult (N=58)		Total (N=114)	
	n (%)		n (%)		n (%)	
Skin and subcutaneous tissue disorders						
Dermatitis acneiform	4 (7.1%)		8 (13.8%)		12 (10.5%)	
Rash	1 (1.8%)		4 (6.9%)		5 (4.4%)	
Urticaria	1 (1.8%)		1 (1.7%)		2 (1.8%)	
Alopecia	2 (3.6%)		0		2 (1.8%)	
Dry skin	0		1 (1.7%)		1 (0.9%)	
Rash erythematous	0		1 (1.7%)		1 (0.9%)	
Gastrointestinal disorders						
Diarrhoea	1 (1.8%)		5 (8.6%)		6 (5.3%)	
Nausea	1 (1.8%)		4 (6.9%)		5 (4.4%)	
Abdominal pain	0		4 (6.9%)		4 (3.5%)	
Constipation	1 (1.8%)		1 (1.7%)		2 (1.8%)	
Vomiting	1 (1.8%)		0		1 (0.9%)	
Eye disorders	0		1 (1.7%)		1 (0.9%)	
Retinal vein occlusion	0		1 (1.7%)		1 (0.9%)	
General disorders and administration site conditions						
Peripheral swelling	0		1 (1.7%)		1 (0.9%)	
Infections and infestations						
COVID-19	0		1 (1.7%)		1 (0.9%)	
Investigations	0		1 (1.7%)		1 (0.9%)	

Program Name: t_ae_num_trt_disc.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20

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MEK-NF-201
GBATable 49: Number of Participants with Treatment-Emergent Adverse Events that Led to Study Treatment Discontinuations by SOC and PT:
Safety Analysis Set

System Organ Class Preferred Term	Pediatric (N=56) n(%)	Adult (N=58) n(%)	Total (N=114) n(%)
Ejection fraction decreased	0	1 (1.7%)	1 (0.9%)
Nervous system disorders	0	1 (1.7%)	1 (0.9%)
Dizziness	0	1 (1.7%)	1 (0.9%)
Respiratory, thoracic and mediastinal disorders	0	1 (1.7%)	1 (0.9%)
Cough	0	1 (1.7%)	1 (0.9%)
Wheezing	0	1 (1.7%)	1 (0.9%)

Program Name: t_ae_num_trt_disc.sas Output Generated: 2025-05-02T13:34 Source: ADSL, ADAE Data Cutoff Date: 2023-09-20