Dimethylfumarat (Tecfidera™)

Biogen GmbH

Anhang 4-G zu Modul 4A

Behandlung von Kindern und Jugendlichen ab 13 Jahren mit schubförmig remittierender Multipler Sklerose (RRMS)

Stand: 10.06.2022

Content

Baseline Characteristics

109MS306_table9_BL_CHARACTERISTICS_DESCRIBE

Table 9: Demography - ITT Population, Aged 13 years and older (n=135)
ANALYSIS not USING SUBGROUPS

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Age category (years)			
10-12	0	0	0
13-14	18 (25)	14 (22)	32 (24)
15-17	53 (75)	50 (78)	103 (76)
Age (years)			
n	71	64	135
Mean (SD)	15.2 (1.25)	15.4 (1.06)	15.3 (1.16)
Mean (SE)	15.2 (0.15)	15.4 (0.13)	15.3 (0.10)
Median	15.0	16.0	15.0
Q1,Q3	14.0, 16.0	15.0, 16.0	15.0, 16.0
Min, Max	13, 17	13, 17	13, 17
Sex			
Male	21 (30)	18 (28)	39 (29)
Female	50 (70)	46 (72)	96 (71)

NOTE1: Numbers in parentheses are percentages.
NOTE2: One subject does not have height data.
NOTE3: Most patients have unknown race and that is due to country confidentiality regulations or to patients being given the option of not answering the race question.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table9_t-demog_n=135_ban012722.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Race			
White	9 (13)	13 (20)	22 (16)
Black or African American	0	0	0
Asian	1 (1)	1 (2)	2 (1)
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific-Islander	0	0	0
Not Reported due to Confidentiality Regulations	25 (35)	24 (38)	49 (36)
Other	3 (4)	0	3 (2)
Unknown/Missing	33 (46)	26 (41)	59 (44)
Weight (kg)			
n	71	64	135
Mean (SD)	65.6 (14.82)	65.4 (12.89)	65.5 (13.89)
Mean (SE)	65.6 (1.76)	65.4 (1.61)	65.5 (1.20)
Median	63.5	65.7	64.0
Q1,Q3	54.5, 74.1	54.2, 71.2	54.4, 72.4
Min, Max	40, 112	42, 101	40, 112
Height (cm)			
n	70	64	134
Mean (SD)	165.2 (7.63)	166.8 (7.98)	165.9 (7.81)
Mean (SE)	165.2 (0.91)	166.8 (1.00)	165.9 (0.67)
Median	164.8	165.1	165.0
Q1,Q3	160.0, 170.0	161.8, 172.0	161.0, 172.0
Min, Max	143, 180	150, 185	143, 185

NOTE1: Numbers in parentheses are percentages.
NOTE2: One subject does not have height data.
NOTE3: Most patients have unknown race and that is due to country confidentiality regulations or to patients being given the option of not answering the race question.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table9_t-demog_n=135_ban012722.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
BMI (kg/m^2)			
n	70	64	134
Mean (SD)	24.0 (4.76)	23.5 (3.95)	23.7 (4.38)
Mean (SE)	24.0 (0.57)	23.5 (0.49)	23.7 (0.38)
Median	23.2	22.9	23.1
Q1,Q3	20.2, 25.7	20.2, 26.1	20.2, 26.0
Min, Max	16, 35	17, 39	16, 39
Geographic region			
Europe	59 (83)	61 (95)	120 (89)
Non-Europe	12 (17)	3 (5)	15 (11)

NOTE1: Numbers in parentheses are percentages.
NOTE2: One subject does not have height data.
NOTE3: Most patients have unknown race and that is due to country confidentiality regulations or to patients being given the option of not answering the race question.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table9_t-demog_n=135_ban012722.sas date: 28JAN2022

109MS306_Table10_BL_CHARACTERISTICS_DESCRIBE

TABLE 10: HISTORY OF MS - ITT Population, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects in ITT population	71 (100)	64 (100)	135 (100)
Time since first MS symptoms (years)			
n	70	64	134
Mean (SD)	1.6 (1.55)	1.2 (1.32)	1.4 (1.45)
Mean (SE)	1.6 (0.18)	1.2 (0.16)	1.4 (0.13)
Median	1.0	1.0	1.0
Q1,Q3	1.0, 2.0	0.0, 1.0	1.0, 2.0
Min, Max	0, 8	0, 6	0, 8
Time since diagnosis of MS (years)			
n	70	64	134
Mean (SD)	0.8 (1.23)	0.5 (0.69)	0.7 (1.02)
Mean (SE)	0.8 (0.15)	0.5 (0.09)	0.7 (0.09)
Median	0.5	0.0	0.0
Q1,Q3	0.0, 1.0	0.0, 1.0	0.0, 1.0
Min, Max	0, 7	0, 4	0, 7

NOTE 1: Numbers in parentheses are percentages
NOTE 2: EDSS ranges from 0 to 10 (no score of 0.5)
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table10_t-bl-mshist_n=135_ban012822.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of relapses within the past 12 months			
0	0	2 (3)	2 (1)
1	40 (56)	33 (52)	73 (54)
2	17 (24)	23 (36)	40 (30)
3	10 (14)	6 (9)	16 (12)
>=4	3 (4)	0	3 (2)
n	70	64	134
Mean (SD)	1.7 (0.97)	1.5 (0.71)	1.6 (0.86)
Mean (SE)	1.7 (0.12)	1.5 (0.09)	1.6 (0.07)
Median	1.0	1.0	1.0
Q1,Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0
Min, Max	1, 5	0, 3	0, 5
Number of relapses within the past 2 years			
0	0	2 (3)	2 (1)
1	24 (34)	21 (33)	45 (33)
2	32 (45)	31 (48)	63 (47)
3	10 (14)	8 (13)	18 (13)
>=4	4 (6)	2 (3)	6 (4)
n	70	64	134
Mean (SD)	2.0 (1.19)	1.8 (0.94)	1.9 (1.07)
Mean (SE)	2.0 (0.14)	1.8 (0.12)	1.9 (0.09)
Median	2.0	2.0	2.0
Q1,Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0
Min, Max	1, 7	0, 6	0, 7

NOTE 1: Numbers in parentheses are percentages. NOTE 2: EDSS ranges from 0 to 10 (no score of 0.5). Source: /bdh-gxp/tec/German

Reimbursement/109MS306/stats/bn/programs/109MS306_table10_t-bl-mshist_n=135_ban012822.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of relapses within the past 3 years			
0	0	2 (3)	2 (1)
1	21 (30)	18 (28)	39 (29)
2	33 (46)	34 (53)	67 (50)
3	11 (15)	6 (9)	17 (13)
>=4	5 (7)	4 (6)	9 (7)
n	70	64	134
Mean (SD)	2.1 (1.22)	1.9 (1.01)	2.0 (1.13)
Mean (SE)	2.1 (0.15)	1.9 (0.13)	2.0 (0.10)
Median	2.0	2.0	2.0
Q1,Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0
Min, Max	1, 7	0, 6	0, 7
Time since most recent pre-study relapse in months			
n	70	63	133
Mean (SD)	4.9 (2.84)	4.7 (2.87)	4.8 (2.85)
Mean (SE)	4.9 (0.34)	4.7 (0.36)	4.8 (0.25)
Median	4.0	4.0	4.0
Q1,Q3	2.0, 6.0	3.0, 6.0	3.0, 6.0
Min, Max	2, 13	1, 13	1, 13

NOTE 1: Numbers in parentheses are percentages
NOTE 2: EDSS ranges from 0 to 10 (no score of 0.5)
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table10_t-bl-mshist_n=135_ban012822.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Baseline EDSS score			
0	21 (30)	19 (30)	40 (30)
1.0	24 (34)	15 (23)	39 (29)
1.5	6 (8)	15 (23)	21 (16)
2.0	13 (18)	9 (14)	22 (16)
2.5	4 (6)	3 (5)	7 (5)
3.0	1 (1)	1 (2)	2 (1)
3.5	0	0	0
4.0	0	2 (3)	2 (1)
4.5	0	0	0
5.0	2 (3)	0	2 (1)
>5.0	0	0	0
<=2.0	64 (90)	58 (91)	122 (90)
>2.0	7 (10)	6 (9)	13 (10)
n	71	64	135
Mean (SD)	1.2 (1.06)	1.2 (0.97)	1.2 (1.01)
Mean (SE)	1.2 (0.13)	1.2 (0.12)	1.2 (0.09)
Median	1.0	1.0	1.0
Q1,Q3	0.0, 2.0	0.0, 1.5	0.0, 2.0
Min, Max	0, 5	0, 4	0, 5
Dominant hand			
Left	5 (7)	8 (13)	13 (10)
Right	64 (90)	56 (88)	120 (89)
Missing	2 (3)	0	2 (1)

NOTE 1: Numbers in parentheses are percentages
NOTE 2: EDSS ranges from 0 to 10 (no score of 0.5)
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table10_t-bl-mshist_n=135_ban012822.sas date: 28JAN2022

109MS306_Table21_BL_CHARACTERISTICS_DESCRIBE

TABLE 21: MS TREATMENT HISTORY - ITT Population, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects who took any prior MS medication	19 (27)	22 (34)	41 (30)
Number of subjects who have taken the following medication prior to study entry	12 (17)	7 (11)	19 (14)
INTERFERON BETA-1A	8 (11)	3 (5)	11 (8)
GLATIRAMER ACETATE	3 (4)	3 (5)	6 (4)
INTERFERON BETA-1B	3 (4)	2 (3)	5 (4)
NATALIZUMAB	2 (3)	0	2 (1)
Other	9 (13)	16 (25)	25 (19)
METHYLPREDNISOLONE SODIUM SUCCINATE	5 (7)	5 (8)	10 (7)
CORTICOSTEROID NOS	2 (3)	6 (9)	8 (6)
PREDNISONE	4 (6)	1 (2)	5 (4)
METHYLPREDNISOLONE	1 (1)	2 (3)	3 (2)
DEXAMETHASONE	0	1 (2)	1 (<1)
PLASMAPHERESIS	0	1 (2)	1 (<1)
PREDNISOLONE	0	1 (2)	1 (<1)
STEROIDS	1 (1)	0	1 (<1)

NOTE 1: Numbers in parentheses are percentages.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table21_t-bl-prior-mshist_n=135_ban012822.sas date: 28JAN2022

Efficacy

Relapse

109MS306_Table38_TTE_DESCRIBE

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135)

Analysis NOT using subgroups

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects who relapsed	20 (28)	29 (45)	49 (36)
Number of relapse-free subjects (a)	51 (72)	35 (55)	86 (64)
Time to first relapse (weeks) (b)			
10th percentile	23.3	6.7	10.9
25th percentile	52.9	23.7	45.4
50th percentile (95% CI)	NA	94.4 (61.0, NA)	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	7 (10.2)	16 (26.2)	23 (17.7)
24 weeks, 95% CI	(5.0, 20.2)	(16.9, 39.2)	(12.1, 25.4)
48 weeks, n (%)	14 (20.5)	19 (31.4)	33 (25.6)
48 weeks, 95% CI	(12.7, 32.2)	(21.3, 44.8)	(19.0, 34.1)
72 weeks, n (%)	18 (26.7)	22 (37.1)	40 (31.6)
72 weeks, 95% CI	(17.7, 39.1)	(26.1, 50.8)	(24.2, 40.5)
96 weeks, n (%)	20 (29.9)	29 (51.6)	49 (39.7)
96 weeks, 95% CI	(20.4, 42.5)	(39.1, 65.5)	(31.6, 49.0)

NOTE 1: Numbers in parentheses are percentages
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_ban020222.sas date: 02FEB2022

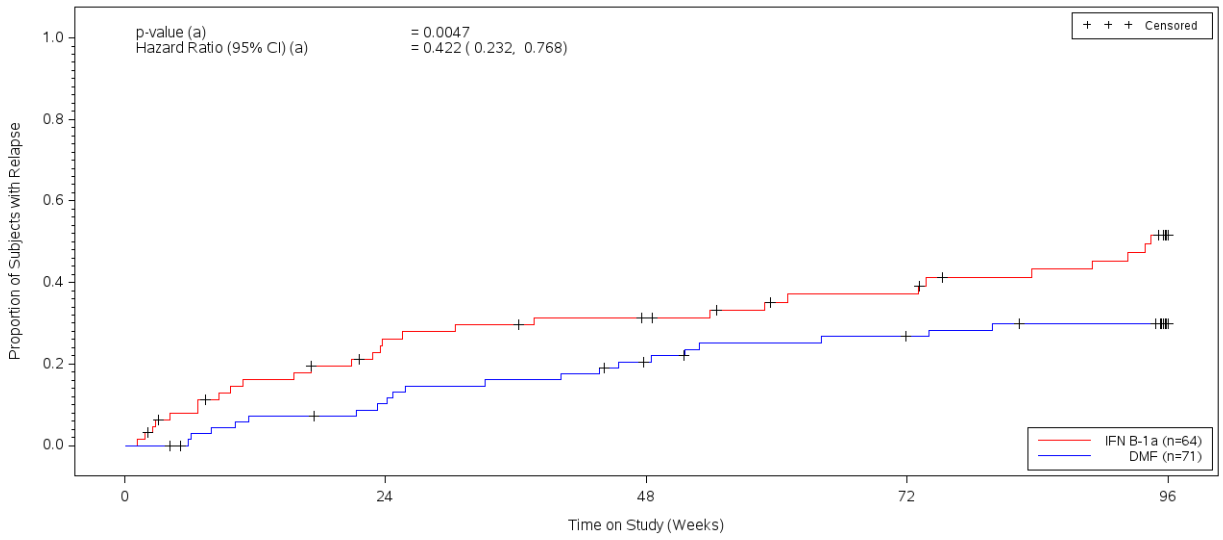
	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	61 (89.8)	43 (73.8)	104 (82.3)
24 weeks, 95% CI	(79.8, 95.0)	(60.8, 83.1)	(74.6, 87.9)
48 weeks, n (%)	52 (79.5)	38 (68.6)	90 (74.4)
48 weeks, 95% CI	(67.8, 87.3)	(55.2, 78.7)	(65.9, 81.0)
72 weeks, n (%)	46 (73.3)	32 (62.9)	78 (68.4)
72 weeks, 95% CI	(60.9, 82.3)	(49.2, 73.9)	(59.5, 75.8)
96 weeks, n (%)	30 (70.1)	15 (48.4)	45 (60.3)
96 weeks, 95% CI	(57.5, 79.6)	(34.5, 60.9)	(51.0, 68.4)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.422		
95% CI (c)(d)	(0.232, 0.768)		
p-value (c)(d)	0.0047		

NOTE 1: Numbers in parentheses are percentages
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_ban020222.sas date: 02FEB2022

109MS306_Table38_TTE_KMPLOT

Time to the first relapse based on protocol - defined relapses - ITT population, Aged 13 years or older

Analyis NOT using subgroups



Number of Subjects at Risk

IFN B-1a	64	43	38	32	15
DMF	71	61	52	46	30

NOTE 1: Plot uses Kaplan-Meier product-limit method.
NOTE 2: One subject in the DMF group was excluded due to missing number of relapses prior to the study
(a) Based on a Cox proportional hazards model,
adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_TABLE38_t-eff-relapse_kmplot_n=135_ban012922.sas DATE: 29JAN2022

109MS306_Table39_TTE_DESCRIBE

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135)

Analysis not using subgroups

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Week 0-48			
Number of subjects with relapse	14 (20)	19 (30)	33 (24)
Number of subjects with relapses of			
0	57 (80)	45 (70)	102 (76)
1	11 (15)	13 (20)	24 (18)
2	3 (4)	4 (6)	7 (5)
3	0	1 (2)	1 (<1)
>= 4	0	1 (2)	1 (<1)
Total number of relapses	17	29	46
Total number of subject-years followed	61.92	52.42	114.34
Unadjusted annualized relapse rate (a)	0.275	0.553	0.402
Adjusted annualized relapse rate (b) (c)	0.259	0.578	
(95% CI) (b) (c)	(0.142, 0.474)	(0.354, 0.942)	
p-value (b) (c)	<0.0001	0.0279	
Rate ratio (compared to IFN B-1a) (b) (c)	0.448		
(95% CI) (b) (c)	(0.220, 0.914)		
p-value (b) (c)	0.0284		
Subject relapse rate (d)			
n	71	64	135

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Mean (SD)	0.366 (1.0533)	0.668 (1.3759)	0.509 (1.2216)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.084	0.000, 0.000
Min, Max	0.00, 7.61	0.00, 7.45	0.00, 7.61

NOTE 1: Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for teh baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_ban012822.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Week 48-96			
Number of subjects with relapse	11 (15)	18 (28)	29 (21)
Number of subjects with relapses of			
0	53 (75)	31 (48)	84 (62)
1	8 (11)	14 (22)	22 (16)
2	2 (3)	3 (5)	5 (4)
3	1 (1)	1 (2)	2 (1)
>= 4	0	0	0
Total number of relapses	15	23	38
Total number of subject-years followed	54.17	38.62	92.79
Unadjusted annualized relapse rate (a)	0.277	0.596	0.410
Adjusted annualized relapse rate (b) (c)	0.165	0.553	
(95% CI) (b) (c)	(0.077, 0.353)	(0.298, 1.024)	
p-value (b) (c)	<0.0001	0.0596	
Rate ratio (compared to IFN B-1a) (b) (c)	0.299		
(95% CI) (b) (c)	(0.127, 0.706)		
p-value (b) (c)	0.0034		
Subject relapse rate (d)			
n	64	49	113
Mean (SD)	0.355 (0.9111)	1.392 (4.2327)	0.805 (2.9004)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.087	0.000, 1.087

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Min, Max	0.00, 4.84	0.00, 24.35	0.00, 24.35

NOTE 1: Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for teh baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_ban012822.sas date: 28JAN2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Week 0-96			
Number of subjects with relapse	20 (28)	29 (45)	49 (36)
Number of subjects with relapses of			
0	51 (72)	35 (55)	86 (64)
1	12 (17)	16 (25)	28 (21)
2	5 (7)	8 (13)	13 (10)
3	2 (3)	3 (5)	5 (4)
>= 4	1 (1)	2 (3)	3 (2)
Total number of relapses	32	52	84
Total number of subject-years followed	116.09	91.04	207.13
Unadjusted annualized relapse rate (a)	0.276	0.571	0.406
Adjusted annualized relapse rate (b) (c)	0.220	0.596	
(95% CI) (b) (c)	(0.130, 0.371)	(0.387, 0.917)	
p-value (b) (c)	<0.0001	0.0186	
Rate ratio (compared to IFN B-1a) (b) (c)	0.369		
(95% CI) (b) (c)	(0.200, 0.681)		
p-value (b) (c)	0.0016		
Subject relapse rate (d)			
n	71	64	135
Mean (SD)	0.401 (1.0481)	0.767 (1.3236)	0.574 (1.1963)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.543	0.000, 1.173	0.000, 0.547
Min, Max	0.00, 7.61	0.00, 7.45	0.00, 7.61

NOTE 1: Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for teh baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_ban012822.sas date: 28JAN2022

Sub groups

109MS306_Table38_TTE_DESCRIBE_age13to14

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

	DMF (N=18)	IFN B-1A (N=14)	Total (N=32)
Number of subjects who relapsed	0	8 (57)	8 (25)
Number of relapse-free subjects (a)	18 (100)	6 (43)	24 (75)
Time to first relapse (weeks) (b)			
10th percentile	NA	2.9	10.9
25th percentile	NA	10.9	92.3
50th percentile (95% CI)	NA	73.7 (6.7, NA)	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	NA	5 (36.5)	5 (16.2)
24 weeks, 95% CI	NA	(17.0, 66.9)	(7.1, 34.7)
48 weeks, n (%)	NA	5 (36.5)	5 (16.2)
48 weeks, 95% CI	NA	(17.0, 66.9)	(7.1, 34.7)
72 weeks, n (%)	NA	5 (36.5)	5 (16.2)
72 weeks, 95% CI	NA	(17.0, 66.9)	(7.1, 34.7)
96 weeks, n (%)	NA	8 (66.0)	8 (27.3)
96 weeks, 95% CI	NA	(39.1, 90.4)	(14.6, 47.5)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages

NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

	DMF (N=18)	IFN B-1A (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	NA	8 (63.5)	24 (83.8)
24 weeks, 95% CI	NA	(33.1, 83.0)	(65.3, 92.9)
48 weeks, n (%)	NA	8 (63.5)	24 (83.8)
48 weeks, 95% CI	NA	(33.1, 83.0)	(65.3, 92.9)
72 weeks, n (%)	NA	8 (63.5)	24 (83.8)
72 weeks, 95% CI	NA	(33.1, 83.0)	(65.3, 92.9)
96 weeks, n (%)	NA	1 (34.0)	13 (72.7)
96 weeks, 95% CI	NA	(9.6, 60.9)	(52.5, 85.4)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.000		
95% CI (c)(d)	(0.000, NA)		
p-value (c)(d)	0.9953		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

109MS306_Table38_TTE_DESCRIBE_age15to17

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF (N=53)	IFN B-1A (N=50)	Total (N=103)
Number of subjects who relapsed	20 (38)	21 (42)	41 (40)
Number of relapse-free subjects (a)	33 (62)	29 (58)	62 (60)
Time to first relapse (weeks) (b)			
10th percentile	21.3	8.7	11.4
25th percentile	43.7	25.6	37.7
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	7 (13.5)	11 (23.2)	18 (18.1)
24 weeks, 95% CI	(6.7, 26.2)	(13.6, 38.1)	(11.8, 27.2)
48 weeks, n (%)	14 (27.0)	14 (29.9)	28 (28.4)
48 weeks, 95% CI	(17.0, 41.3)	(18.9, 45.2)	(20.6, 38.4)
72 weeks, n (%)	18 (35.3)	17 (37.2)	35 (36.2)
72 weeks, 95% CI	(23.9, 50.0)	(24.9, 53.0)	(27.5, 46.7)
96 weeks, n (%)	20 (39.6)	21 (47.6)	41 (43.4)
96 weeks, 95% CI	(27.6, 54.5)	(34.0, 63.5)	(34.0, 54.1)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

	DMF (N=53)	IFN B-1A (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	45 (86.5)	35 (76.8)	80 (81.9)
24 weeks, 95% CI	(73.8, 93.3)	(61.9, 86.4)	(72.8, 88.2)
48 weeks, n (%)	36 (73.0)	30 (70.1)	66 (71.6)
48 weeks, 95% CI	(58.7, 83.0)	(54.8, 81.1)	(61.6, 79.4)
72 weeks, n (%)	30 (64.7)	25 (62.8)	55 (63.8)
72 weeks, 95% CI	(50.0, 76.1)	(47.0, 75.1)	(53.3, 72.5)
96 weeks, n (%)	18 (60.4)	14 (52.4)	32 (56.6)
96 weeks, 95% CI	(45.5, 72.4)	(36.5, 66.0)	(45.9, 66.0)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.644		
95% CI (c)(d)	(0.339, 1.224)		
p-value (c)(d)	0.1791		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

109MS306_Table38_TTE_DESCRIBE_female

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1A (N=46)	Total (N=96)
Number of subjects who relapsed	15 (30)	22 (48)	37 (39)
Number of relapse-free subjects (a)	35 (70)	24 (52)	59 (61)
Time to first relapse (weeks) (b)			
10th percentile	11.4	6.7	9.7
25th percentile	48.4	22.9	25.9
50th percentile (95% CI)	NA	93.9 (37.7, NA)	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	6 (12.5)	13 (29.7)	19 (20.7)
24 weeks, 95% CI	(5.8, 25.8)	(18.4, 45.7)	(13.7, 30.5)
48 weeks, n (%)	11 (23.3)	15 (34.6)	26 (28.6)
48 weeks, 95% CI	(13.6, 38.1)	(22.4, 50.7)	(20.5, 39.2)
72 weeks, n (%)	14 (30.2)	16 (37.2)	30 (33.5)
72 weeks, 95% CI	(19.1, 45.7)	(24.6, 53.5)	(24.7, 44.4)
96 weeks, n (%)	15 (32.6)	22 (54.1)	37 (42.6)
96 weeks, 95% CI	(21.0, 48.2)	(39.5, 70.2)	(32.9, 53.8)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

	DMF (N=50)	IFN B-1A (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	41 (87.5)	29 (70.3)	70 (79.3)
24 weeks, 95% CI	(74.2, 94.2)	(54.3, 81.6)	(69.5, 86.3)
48 weeks, n (%)	34 (76.7)	26 (65.4)	60 (71.4)
48 weeks, 95% CI	(61.9, 86.4)	(49.3, 77.6)	(60.8, 79.5)
72 weeks, n (%)	29 (69.8)	23 (62.8)	52 (66.5)
72 weeks, 95% CI	(54.3, 80.9)	(46.5, 75.4)	(55.6, 75.3)
96 weeks, n (%)	18 (67.4)	10 (45.9)	28 (57.4)
96 weeks, 95% CI	(51.8, 79.0)	(29.8, 60.5)	(46.2, 67.1)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.438		
95% CI (c)(d)	(0.221, 0.868)		
p-value (c)(d)	0.0181		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

109MS306_Table38_TTE_DESCRIBE_male

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1A (N=18)	Total (N=39)
Number of subjects who relapsed	5 (24)	7 (39)	12 (31)
Number of relapse-free subjects (a)	16 (76)	11 (61)	27 (69)
Time to first relapse (weeks) (b)			
10th percentile	40.1	6.7	23.7
25th percentile	NA	53.9	61.0
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	1 (4.8)	3 (17.0)	4 (10.4)
24 weeks, 95% CI	(0.7, 29.3)	(5.8, 44.1)	(4.0, 25.4)
48 weeks, n (%)	3 (14.3)	4 (23.0)	7 (18.4)
48 weeks, 95% CI	(4.8, 38.0)	(9.3, 50.3)	(9.2, 34.8)
72 weeks, n (%)	4 (19.0)	6 (37.0)	10 (26.8)
72 weeks, 95% CI	(7.6, 43.1)	(18.4, 65.0)	(15.4, 44.2)
96 weeks, n (%)	5 (23.8)	7 (44.8)	12 (32.8)
96 weeks, 95% CI	(10.7, 48.1)	(24.0, 72.5)	(20.1, 50.6)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

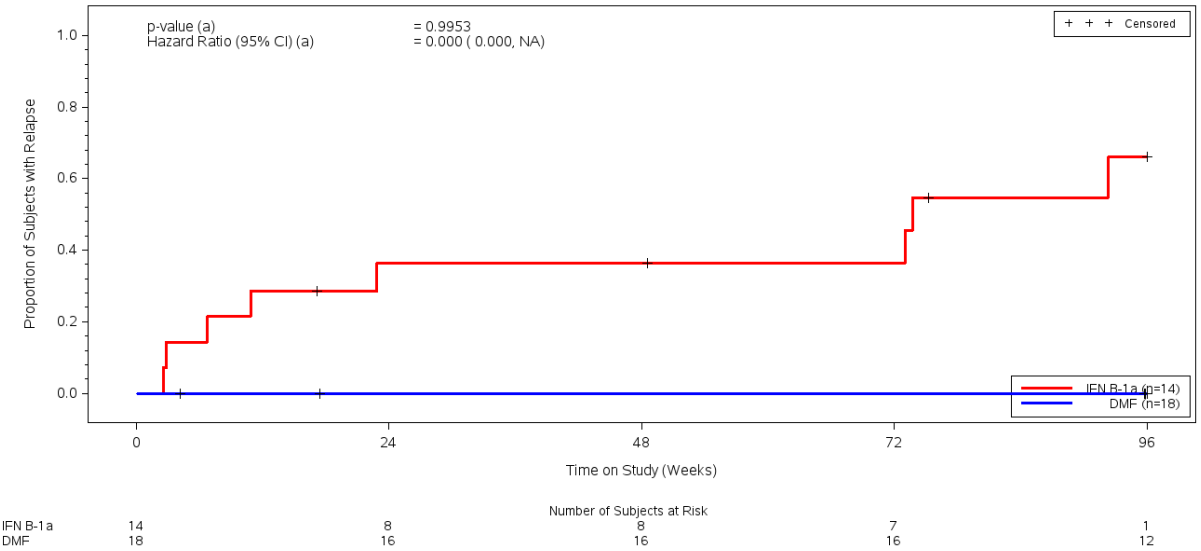
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

	DMF (N=21)	IFN B-1A (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	20 (95.2)	14 (83.0)	34 (89.6)
24 weeks, 95% CI	(70.7, 99.3)	(55.9, 94.2)	(74.6, 96.0)
48 weeks, n (%)	18 (85.7)	12 (77.0)	30 (81.6)
48 weeks, 95% CI	(62.0, 95.2)	(49.7, 90.7)	(65.2, 90.8)
72 weeks, n (%)	17 (81.0)	9 (63.0)	26 (73.2)
72 weeks, 95% CI	(56.9, 92.4)	(35.0, 81.6)	(55.8, 84.6)
96 weeks, n (%)	12 (76.2)	5 (55.2)	17 (67.2)
96 weeks, 95% CI	(51.9, 89.3)	(27.5, 76.0)	(49.4, 79.9)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.469		
95% CI (c)(d)	(0.132, 1.672)		
p-value (c)(d)	0.2433		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on a Cox proportional hazards model, adjusted for baseline relapse rate (the number of relapses in the 3 years prior to the study, divided by 3), age group and baseline EDSS
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban030322.sas date: 08MAR2022

109MS306_Table38_TTE_KMPLOT_age13to14

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for ages 13 to 14



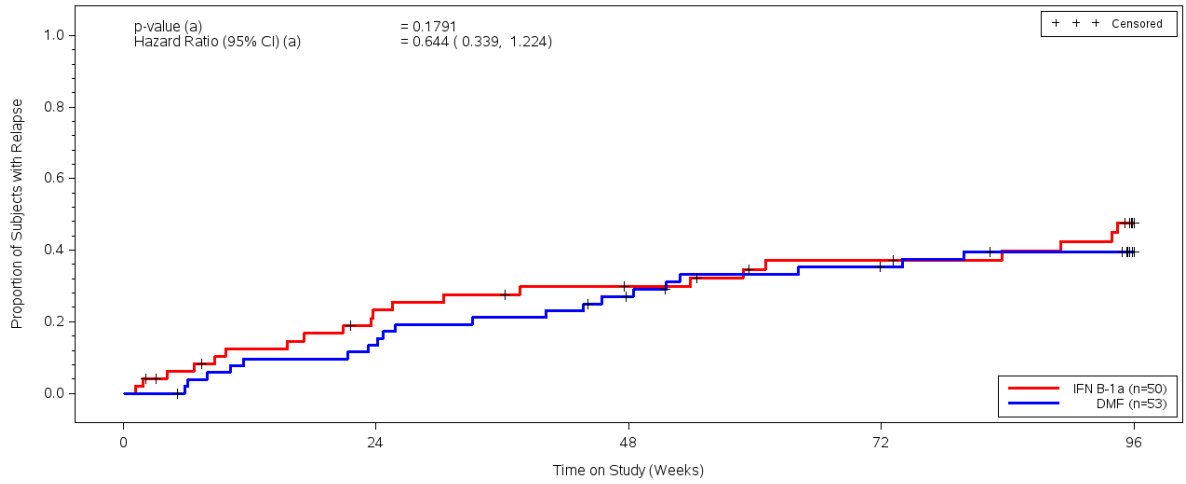
Number of Subjects at Risk

IFN B-1a	14	8	8	7	1
DMF	18	16	16	16	12

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
Note 2: Analysis from Kaplan-Meier product-limit method.
Note 3: One subject in the DMF group was excluded due to missing number of relapses prior to the study
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban030322.sas DATE: 08MAR2022

109MS306_Table38_TTE_KMPLOT_age15to17

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for Ages 15 to 17



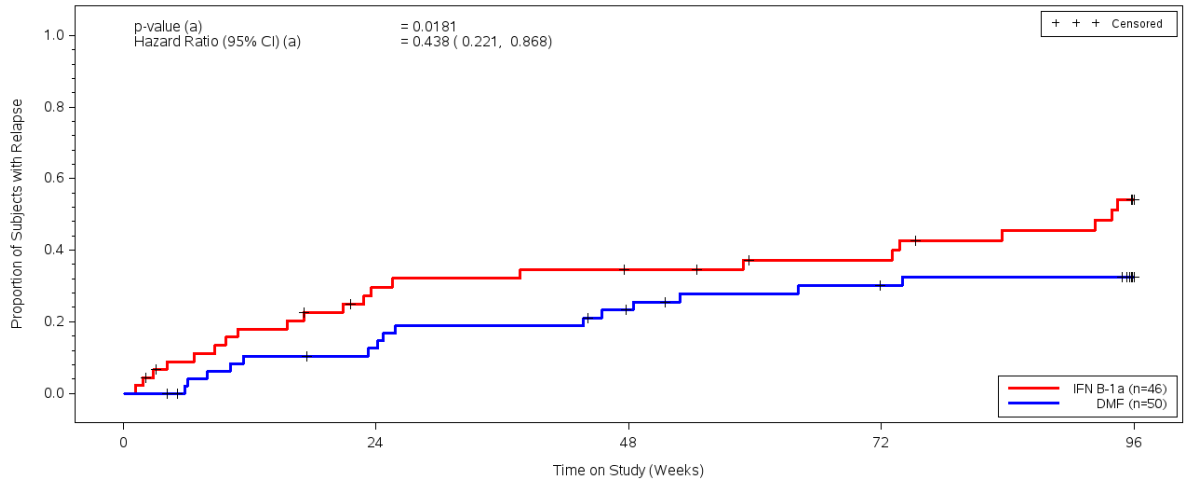
Number of Subjects at Risk

IFN B-1a	50	35	30	25	14
DMF	53	45	36	30	18

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
Note 2: Analysis from Kaplan-Meier product-limit method.
Note 3: One subject in the DMF group was excluded due to missing number of relapses prior to the study
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban030322.sas DATE: 08MAR2022

109MS306_Table38_TTE_KMPLOT_female

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for female sex



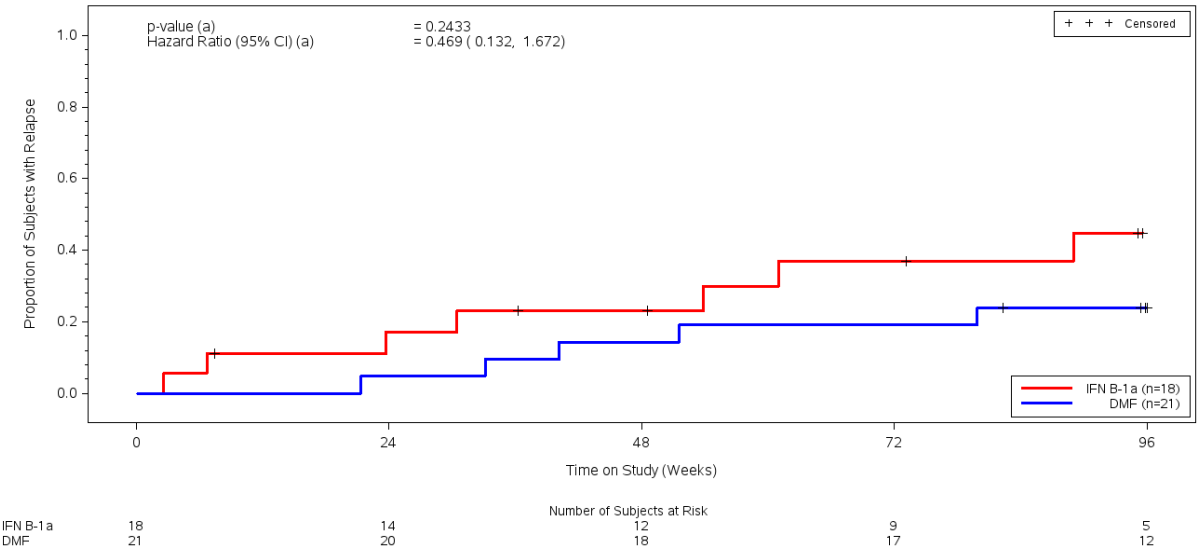
Number of Subjects at Risk

IFN B-1a	46	29	26	23	10
DMF	50	41	34	29	18

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
Note 2: Analysis from Kaplan-Meier product-limit method.
Note 3: One subject in the DMF group was excluded due to missing number of relapses prior to the study
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban030322.sas DATE: 08MAR2022

109MS306_Table38_TTE_KMPLOT_male

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for male sex



Number of Subjects at Risk

IFN B-1a	18	14	12	9	5
DMF	21	20	18	17	12

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
Note 2: Analysis from Kaplan-Meier product-limit method.
Note 3: One subject in the DMF group was excluded due to missing number of relapses prior to the study
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban030322.sas DATE: 08MAR2022

109MS306_Table39_TTE_DESCRIBE_age13to14

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for Ages 13 to 14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Week 0-48			
Number of subjects with relapse	0	5 (36)	5 (16)
Number of subjects with relapses of			
0	18 (100)	9 (64)	27 (84)
1	0	3 (21)	3 (9)
2	0	0	0
3	0	1 (7)	1 (3)
>= 4	0	1 (7)	1 (3)
Total number of relapses	0	11	11
Total number of subject-years followed	15.18	10.56	25.73
Unadjusted annualized relapse rate (a)	0.000	1.042	0.427
Adjusted annualized relapse rate (b) (c)	<0.001	0.897	
(95% CI) (b) (c)	(<0.001, NA)	(0.281, 2.864)	
p-value (b) (c)	0.9999	0.8544	
Rate ratio (compared to IFN B-1a) (b) (c)	0.000		
(95% CI) (b) (c)	(0.000, NA)		
p-value (b) (c)	0.0020		
Subject relapse rate (d)			
n	18	14	32
Mean (SD)	0.000 (0.0000)	1.482 (2.4099)	0.649 (1.7302)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 2.468	0.000, 0.000

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Min, Max	0.00, 0.00	0.00, 7.45	0.00, 7.45

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Week 48-96			
Number of subjects with relapse	0	4 (29)	4 (13)
Number of subjects with relapses of			
0	16 (89)	6 (43)	22 (69)
1	0	3 (21)	3 (9)
2	0	1 (7)	1 (3)
3	0	0	0
>= 4	0	0	0
Total number of relapses	0	5	5
Total number of subject-years followed	14.70	7.31	22.00
Unadjusted annualized relapse rate (a)	0.000	0.684	0.227
Adjusted annualized relapse rate (b) (c)	<0.001	0.007	
(95% CI) (b) (c)	(<0.001, NA)	(<0.001, 239E79)	
p-value (b) (c)	0.9484	0.9595	
Rate ratio (compared to IFN B-1a) (b) (c)	0.000		
(95% CI) (b) (c)	(0.000, NA)		
p-value (b) (c)	0.0020		
Subject relapse rate (d)			
n	16	10	26
Mean (SD)	0.000 (0.0000)	0.781 (1.3876)	0.301 (0.9184)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.087	0.000, 0.000
Min, Max	0.00, 0.00	0.00, 4.43	0.00, 4.43

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Week 0-96			
Number of subjects with relapse	0	8 (57)	8 (25)
Number of subjects with relapses of			
0	18 (100)	6 (43)	24 (75)
1	0	6 (43)	6 (19)
2	0	0	0
3	0	1 (7)	1 (3)
>= 4	0	1 (7)	1 (3)
Total number of relapses	0	16	16
Total number of subject-years followed	29.87	17.86	47.74
Unadjusted annualized relapse rate (a)	0.000	0.896	0.335
Adjusted annualized relapse rate (b) (c)	<0.001	0.761	
(95% CI) (b) (c)	(<0.001, NA)	(0.340, 1.705)	
p-value (b) (c)	0.9999	0.5065	
Rate ratio (compared to IFN B-1a) (b) (c)	0.000		
(95% CI) (b) (c)	(0.000, NA)		
p-value (b) (c)	<0.0001		
Subject relapse rate (d)			
n	18	14	32
Mean (SD)	0.000 (0.0000)	1.462 (2.2520)	0.640 (1.6340)
Median	0.000	0.543	0.000
Q1, Q3	0.000, 0.000	0.000, 2.161	0.000, 0.271
Min, Max	0.00, 0.00	0.00, 7.45	0.00, 7.45

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

109MS306_Table39_TTE_DESCRIBE_age15to17

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for Ages 15 to 17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Week 0-48			
Number of subjects with relapse	14 (26)	14 (28)	28 (27)
Number of subjects with relapses of			
0	39 (74)	36 (72)	75 (73)
1	11 (21)	10 (20)	21 (20)
2	3 (6)	4 (8)	7 (7)
3	0	0	0
>= 4	0	0	0
Total number of relapses	17	18	35
Total number of subject-years followed	46.74	41.86	88.60
Unadjusted annualized relapse rate (a)	0.364	0.430	0.395
Adjusted annualized relapse rate (b) (c)	0.325	0.436	
(95% CI) (b) (c)	(0.195, 0.542)	(0.275, 0.693)	
p-value (b) (c)	<0.0001	0.0004	
Rate ratio (compared to IFN B-1a) (b) (c)	0.745		
(95% CI) (b) (c)	(0.377, 1.474)		
p-value (b) (c)	0.3981		
Subject relapse rate (d)			
n	53	50	103
Mean (SD)	0.491 (1.1963)	0.440 (0.8065)	0.466 (1.0211)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 1.084	0.000, 1.084	0.000, 1.084

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Min, Max	0.00, 7.61	0.00, 3.03	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Week 48-96			
Number of subjects with relapse	11 (21)	14 (28)	25 (24)
Number of subjects with relapses of			
0	37 (70)	25 (50)	62 (60)
1	8 (15)	11 (22)	19 (18)
2	2 (4)	2 (4)	4 (4)
3	1 (2)	1 (2)	2 (2)
>= 4	0	0	0
Total number of relapses	15	18	33
Total number of subject-years followed	39.47	31.32	70.79
Unadjusted annualized relapse rate (a)	0.380	0.575	0.466
Adjusted annualized relapse rate (b) (c)	0.269	0.613	
(95% CI) (b) (c)	(0.136, 0.531)	(0.344, 1.092)	
p-value (b) (c)	0.0002	0.0968	
Rate ratio (compared to IFN B-1a) (b) (c)	0.438		
(95% CI) (b) (c)	(0.180, 1.066)		
p-value (b) (c)	0.0602		
Subject relapse rate (d)			
n	48	39	87
Mean (SD)	0.473 (1.0274)	1.549 (4.6959)	0.955 (3.2573)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.087	0.000, 1.087
Min, Max	0.00, 4.84	0.00, 24.35	0.00, 24.35

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Week 0-96			
Number of subjects with relapse	20 (38)	21 (42)	41 (40)
Number of subjects with relapses of			
0	33 (62)	29 (58)	62 (60)
1	12 (23)	10 (20)	22 (21)
2	5 (9)	8 (16)	13 (13)
3	2 (4)	2 (4)	4 (4)
>= 4	1 (2)	1 (2)	2 (2)
Total number of relapses	32	36	68
Total number of subject-years followed	86.21	73.17	159.39
Unadjusted annualized relapse rate (a)	0.371	0.492	0.427
Adjusted annualized relapse rate (b) (c)	0.316	0.520	
(95% CI) (b) (c)	(0.200, 0.501)	(0.343, 0.787)	
p-value (b) (c)	<0.0001	0.0020	
Rate ratio (compared to IFN B-1a) (b) (c)	0.609		
(95% CI) (b) (c)	(0.329, 1.126)		
p-value (b) (c)	0.1161		
Subject relapse rate (d)			
n	53	50	103
Mean (SD)	0.537 (1.1850)	0.572 (0.8545)	0.554 (1.0330)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.546	0.000, 1.085	0.000, 0.608
Min, Max	0.00, 7.61	0.00, 3.03	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

109MS306_Table39_TTE_DESCRIBE_female

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for female sex

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Week 0-48			
Number of subjects with relapse	11 (22)	15 (33)	26 (27)
Number of subjects with relapses of			
0	39 (78)	31 (67)	70 (73)
1	8 (16)	10 (22)	18 (19)
2	3 (6)	4 (9)	7 (7)
3	0	0	0
>= 4	0	1 (2)	1 (1)
Total number of relapses	14	23	37
Total number of subject-years followed	43.00	37.00	80.00
Unadjusted annualized relapse rate (a)	0.326	0.622	0.462
Adjusted annualized relapse rate (b) (c)	0.311	0.622	
(95% CI) (b) (c)	(0.156, 0.620)	(0.354, 1.091)	
p-value (b) (c)	0.0009	0.0977	
Rate ratio (compared to IFN B-1a) (b) (c)	0.500		
(95% CI) (b) (c)	(0.226, 1.106)		
p-value (b) (c)	0.0889		
Subject relapse rate (d)			
n	50	46	96
Mean (SD)	0.434 (1.2021)	0.782 (1.5270)	0.601 (1.3712)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.084	0.000, 1.084

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Min, Max	0.00, 7.61	0.00, 7.45	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Week 48-96			
Number of subjects with relapse	9 (18)	13 (28)	22 (23)
Number of subjects with relapses of			
0	35 (70)	21 (46)	56 (58)
1	7 (14)	10 (22)	17 (18)
2	1 (2)	2 (4)	3 (3)
3	1 (2)	1 (2)	2 (2)
>= 4	0	0	0
Total number of relapses	12	17	29
Total number of subject-years followed	36.56	28.16	64.73
Unadjusted annualized relapse rate (a)	0.328	0.604	0.448
Adjusted annualized relapse rate (b) (c)	0.208	0.576	
(95% CI) (b) (c)	(0.093, 0.465)	(0.314, 1.058)	
p-value (b) (c)	0.0001	0.0752	
Rate ratio (compared to IFN B-1a) (b) (c)	0.361		
(95% CI) (b) (c)	(0.145, 0.898)		
p-value (b) (c)	0.0168		
Subject relapse rate (d)			
n	44	34	78
Mean (SD)	0.381 (0.8263)	0.671 (1.0957)	0.507 (0.9575)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.087	0.000, 1.087
Min, Max	0.00, 3.26	0.00, 4.43	0.00, 4.43

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Week 0-96			
Number of subjects with relapse	15 (30)	22 (48)	37 (39)
Number of subjects with relapses of			
0	35 (70)	24 (52)	59 (61)
1	8 (16)	13 (28)	21 (22)
2	4 (8)	5 (11)	9 (9)
3	2 (4)	2 (4)	4 (4)
>= 4	1 (2)	2 (4)	3 (3)
Total number of relapses	26	40	66
Total number of subject-years followed	79.56	65.16	144.73
Unadjusted annualized relapse rate (a)	0.327	0.614	0.456
Adjusted annualized relapse rate (b) (c)	0.271	0.647	
(95% CI) (b) (c)	(0.148, 0.496)	(0.394, 1.061)	
p-value (b) (c)	<0.0001	0.0842	
Rate ratio (compared to IFN B-1a) (b) (c)	0.419		
(95% CI) (b) (c)	(0.208, 0.845)		
p-value (b) (c)	0.0161		
Subject relapse rate (d)			
n	50	46	96
Mean (SD)	0.464 (1.1936)	0.864 (1.4829)	0.656 (1.3480)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.543	0.000, 1.090	0.000, 0.590
Min, Max	0.00, 7.61	0.00, 7.45	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

109MS306_Table39_TTE_DESCRIBE_male

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for male sex

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Week 0-48			
Number of subjects with relapse	3 (14)	4 (22)	7 (18)
Number of subjects with relapses of			
0	18 (86)	14 (78)	32 (82)
1	3 (14)	3 (17)	6 (15)
2	0	0	0
3	0	1 (6)	1 (3)
>= 4	0	0	0
Total number of relapses	3	6	9
Total number of subject-years followed	18.92	15.41	34.33
Unadjusted annualized relapse rate (a)	0.159	0.389	0.262
Adjusted annualized relapse rate (b) (c)	0.130	0.530	
(95% CI) (b) (c)	(0.033, 0.514)	(0.199, 1.417)	
p-value (b) (c)	0.0036	0.2058	
Rate ratio (compared to IFN B-1a) (b) (c)	0.246		
(95% CI) (b) (c)	(0.043, 1.409)		
p-value (b) (c)	0.1081		
Subject relapse rate (d)			
n	21	18	39
Mean (SD)	0.206 (0.5513)	0.376 (0.8476)	0.284 (0.6992)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 0.000	0.000, 0.000

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Min, Max	0.00, 2.15	0.00, 3.25	0.00, 3.25

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Week 48-96			
Number of subjects with relapse	2 (10)	5 (28)	7 (18)
Number of subjects with relapses of			
0	18 (86)	10 (56)	28 (72)
1	1 (5)	4 (22)	5 (13)
2	1 (5)	1 (6)	2 (5)
3	0	0	0
>= 4	0	0	0
Total number of relapses	3	6	9
Total number of subject-years followed	17.60	10.46	28.07
Unadjusted annualized relapse rate (a)	0.170	0.574	0.321
Adjusted annualized relapse rate (b) (c)	<0.001	<0.001	
(95% CI) (b) (c)	(<0.001, <0.001)	(<0.001, <0.001)	
p-value (b) (c)	<0.0001	<0.0001	
Rate ratio (compared to IFN B-1a) (b) (c)	0.124		
(95% CI) (b) (c)	(0.011, 1.437)		
p-value (b) (c)	0.0894		
Subject relapse rate (d)			
n	20	15	35
Mean (SD)	0.296 (1.0962)	3.028 (7.3800)	1.467 (4.9980)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.100	0.000, 0.000
Min, Max	0.00, 4.84	0.00, 24.35	0.00, 24.35

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Week 0-96			
Number of subjects with relapse	5 (24)	7 (39)	12 (31)
Number of subjects with relapses of			
0	16 (76)	11 (61)	27 (69)
1	4 (19)	3 (17)	7 (18)
2	1 (5)	3 (17)	4 (10)
3	0	1 (6)	1 (3)
>= 4	0	0	0
Total number of relapses	6	12	18
Total number of subject-years followed	36.52	25.88	62.40
Unadjusted annualized relapse rate (a)	0.164	0.464	0.288
Adjusted annualized relapse rate (b) (c)	0.131	0.455	
(95% CI) (b) (c)	(0.046, 0.376)	(0.185, 1.117)	
p-value (b) (c)	0.0002	0.0857	
Rate ratio (compared to IFN B-1a) (b) (c)	0.288		
(95% CI) (b) (c)	(0.081, 1.021)		
p-value (b) (c)	0.0550		
Subject relapse rate (d)			
n	21	18	39
Mean (SD)	0.251 (0.5664)	0.519 (0.7619)	0.375 (0.6684)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.255	0.000, 0.543
Min, Max	0.00, 2.15	0.00, 2.08	0.00, 2.15

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, baseline EDSS score and age group. Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban030822.sas date: 08MAR2022

Progression of disability

109MS306_table51_TTE_12_Week_progression_DESCRIBE

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks- mITT Population, Aged 13 years or older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with progression of disability (a)	6 (8)	4 (6)	10 (7)
Number of subjects without disability progression (a)	65 (92)	60 (94)	125 (93)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects with disability progression at (b)			
12 weeks, n (%)	2 (3.0)	1 (1.6)	3 (2.3)
12 weeks, 95% CI	(0.8, 11.4)	(0.2, 10.7)	(0.8, 7.1)
24 weeks, n (%)	4 (6.0)	1 (1.6)	5 (3.9)
24 weeks, 95% CI	(2.3, 15.1)	(0.2, 10.7)	(1.7, 9.2)
36 weeks, n (%)	4 (6.0)	3 (5.2)	7 (5.6)
36 weeks, 95% CI	(2.3, 15.1)	(1.7, 15.3)	(2.7, 11.4)
48 weeks, n (%)	5 (7.5)	3 (5.2)	8 (6.5)
48 weeks, 95% CI	(3.2, 17.2)	(1.7, 15.3)	(3.3, 12.6)
60 weeks, n (%)	5 (7.5)	3 (5.2)	8 (6.5)

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
60 weeks, 95% CI	(3.2, 17.2)	(1.7, 15.3)	(3.3, 12.6)
72 weeks, n (%)	5 (7.5)	3 (5.2)	8 (6.5)
72 weeks, 95% CI	(3.2, 17.2)	(1.7, 15.3)	(3.3, 12.6)
84 weeks, n (%)	6 (9.5)	4 (7.5)	10 (8.6)
84 weeks, 95% CI	(4.3, 20.0)	(2.9, 19.0)	(4.7, 15.5)
96 weeks, n (%)	6 (9.5)	4 (7.5)	10 (8.6)
96 weeks, 95% CI	(4.3, 20.0)	(2.9, 19.0)	(4.7, 15.5)

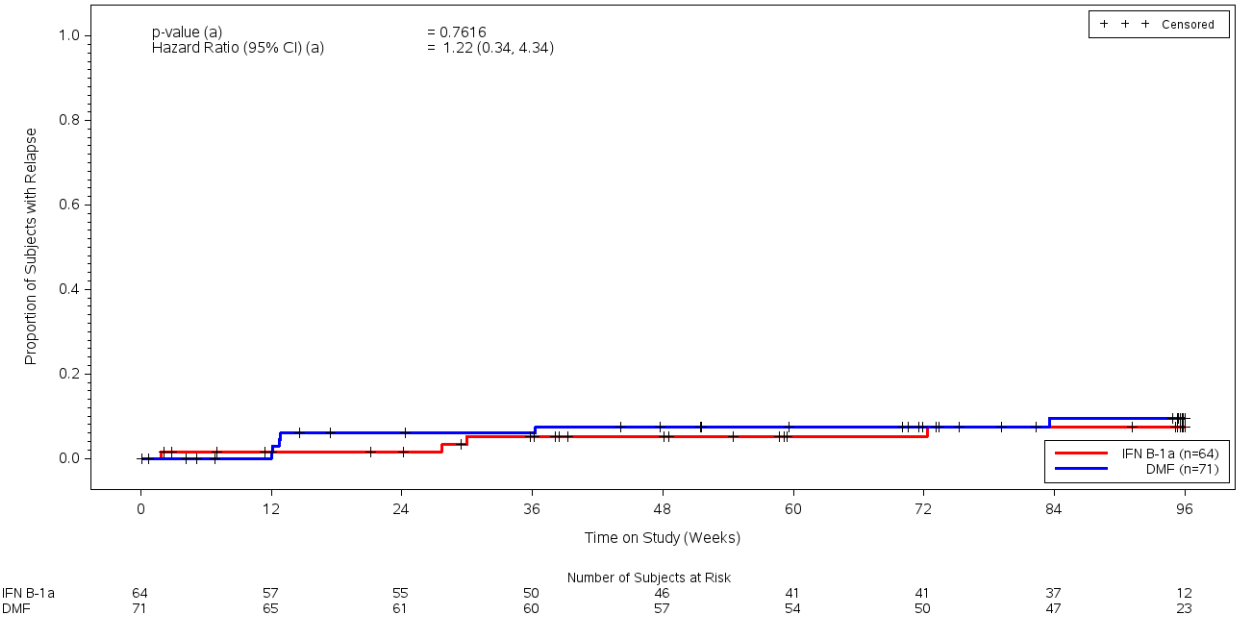
	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Estimated n (%), 95% CI of subjects without disability progressioin at (b)			
12 weeks, n (%)	65 (97.0)	57 (98.4)	122 (97.7)
12 weeks, 95% CI	(88.6, 99.2)	(89.3, 99.8)	(92.9, 99.2)
24 weeks, n (%)	61 (94.0)	57 (98.4)	116 (96.1)
24 weeks, 95% CI	(84.9, 97.7)	(89.3, 99.8)	(90.8, 98.3)
36 weeks, n (%)	61 (94.0)	50 (94.8)	110 (94.4)
36 weeks, 95% CI	(84.9, 97.7)	(84.7, 98.3)	(88.6, 97.3)
48 weeks, n (%)	57 (92.5)	50 (94.8)	103 (93.5)
48 weeks, 95% CI	(82.8, 96.8)	(84.7, 98.3)	(87.4, 96.7)
60 weeks, n (%)	57 (92.5)	50 (94.8)	103 (93.5)
60 weeks, 95% CI	(82.8, 96.8)	(84.7, 98.3)	(87.4, 96.7)
72 weeks, n (%)	57 (92.5)	50 (94.8)	103 (93.5)
72 weeks, 95% CI	(82.8, 96.8)	(84.7, 98.3)	(87.4, 96.7)
84 weeks, n (%)	47 (90.5)	37 (92.5)	84 (91.4)
84 weeks, 95% CI	(80.0, 95.7)	(81.0, 97.1)	(84.5, 95.3)
96 weeks, n (%)	47 (90.5)	37 (92.5)	84 (91.4)
96 weeks, 95% CI	(80.0, 95.7)	(81.0, 97.1)	(84.5, 95.3)
Hazard ratio (BG00012 vs IFN B-1a) (c)	1.218		
95% CI (c)	(0.341, 4.341)		
p-value (c)	0.7616		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_02022022_ban020222.sas date: 02FEB2022

109MS306_Table51_TTE_12_Week_progression_KMPLOT

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks, Aged 13 years or older



Number of Subjects at Risk

IFN B-1a	64	57	55	50	46	41	41	37	12
DMF	71	65	61	60	57	54	50	47	23

NOTE 1: Plot uses Kaplan-Meier product-limit method.
(a) Based on a Cox proportional hazards model.
Note 1: Analysis from Kaplan-Meier product-limit method.

109MS306_table51_TTE_24_Week_progression_DESCRIBE

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks - mITT Population

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with progression of disability (a)	3 (4)	4 (6)	7 (5)
Number of subjects without disability progression (a)	68 (96)	60 (94)	128 (95)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated proportion of subjects with disability progression at (b)			
12 weeks, n (%)	2 (3.0)	0 (0.0)	2 (1.6)
12 weeks, 95% CI	(0.8, 11.4)	NA	(0.4, 6.2)
24 weeks, n (%)	3 (4.5)	1 (1.7)	4 (3.2)
24 weeks, 95% CI	(1.5, 13.2)	(0.2, 11.6)	(1.2, 8.3)
36 weeks, n (%)	3 (4.5)	3 (5.3)	6 (4.9)
36 weeks, 95% CI	(1.5, 13.2)	(1.7, 15.5)	(2.2, 10.5)
48 weeks, n (%)	3 (4.5)	3 (5.3)	6 (4.9)
48 weeks, 95% CI	(1.5, 13.2)	(1.7, 15.5)	(2.2, 10.5)
60 weeks, n (%)	3 (4.5)	3 (5.3)	6 (4.9)
60 weeks, 95% CI	(1.5, 13.2)	(1.7, 15.5)	(2.2, 10.5)
72 weeks, n (%)	3 (4.5)	3 (5.3)	6 (4.9)
72 weeks, 95% CI	(1.5, 13.2)	(1.7, 15.5)	(2.2, 10.5)

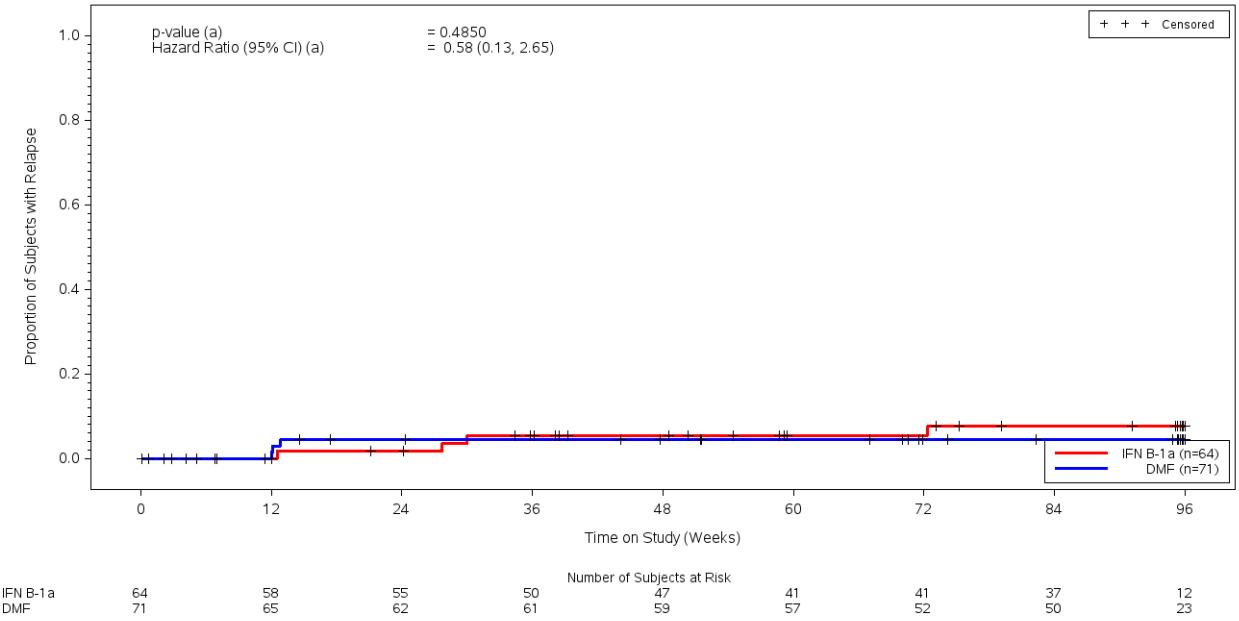
	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
84 weeks, n (%)	3 (4.5)	4 (7.6)	7 (5.9)
84 weeks, 95% CI	(1.5, 13.2)	(2.9, 19.2)	(2.8, 12.0)
96 weeks, n (%)	3 (4.5)	4 (7.6)	7 (5.9)
96 weeks, 95% CI	(1.5, 13.2)	(2.9, 19.2)	(2.8, 12.0)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Estimated proportion of subjects without disability progression at (b)			
12 weeks, n (%)	65 (97.0)	NA	123 (98.4)
12 weeks, 95% CI	(88.6, 99.2)	NA	(93.8, 99.6)
24 weeks, n (%)	62 (95.5)	55 (98.3)	117 (96.8)
24 weeks, 95% CI	(86.8, 98.5)	(88.4, 99.8)	(91.7, 98.8)
36 weeks, n (%)	62 (95.5)	50 (94.7)	111 (95.1)
36 weeks, 95% CI	(86.8, 98.5)	(84.5, 98.3)	(89.5, 97.8)
48 weeks, n (%)	62 (95.5)	50 (94.7)	111 (95.1)
48 weeks, 95% CI	(86.8, 98.5)	(84.5, 98.3)	(89.5, 97.8)
60 weeks, n (%)	62 (95.5)	50 (94.7)	111 (95.1)
60 weeks, 95% CI	(86.8, 98.5)	(84.5, 98.3)	(89.5, 97.8)
72 weeks, n (%)	62 (95.5)	50 (94.7)	111 (95.1)
72 weeks, 95% CI	(86.8, 98.5)	(84.5, 98.3)	(89.5, 97.8)
84 weeks, n (%)	62 (95.5)	37 (92.4)	87 (94.1)
84 weeks, 95% CI	(86.8, 98.5)	(80.8, 97.1)	(88.0, 97.2)
96 weeks, n (%)	62 (95.5)	37 (92.4)	87 (94.1)
96 weeks, 95% CI	(86.8, 98.5)	(80.8, 97.1)	(88.0, 97.2)
Hazard ratio (BG00012 vs IFN B-1a) (c)	0.583		
95% CI (c)	(0.128, 2.650)		
p-value (c)	0.4850		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE.sas date: 07FEB2022

109MS306_Table51_TTE_24_Week_progression_KMPLOT

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks, Aged 13 years or older



Number of Subjects at Risk

IFN B-1a	64	58	55	50	47	41	41	37	12
DMF	71	65	62	61	59	57	52	50	23

NOTE 1: Plot uses Kaplan-Meier product-limit method.
(a) Based on a Cox proportional hazards model,
Note 1: Analysis from Kaplan-Meier product-limit method.

109MS306_Table51_TTE_improvement_DESCRIBE

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	18 (25)	7 (11)	25 (19)
Number of subjects without confirmed improvement of disability (a)	53 (75)	57 (89)	110 (81)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	24.1	73.7	36.0
25th percentile	72.1	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	5 (7.5)	0 (0.0)	5 (4.0)
12 weeks, 95% CI	(3.2, 17.0)	NA	(1.7, 9.3)
24 weeks, n (%)	7 (10.5)	3 (5.3)	10 (8.1)
24 weeks, 95% CI	(5.2, 20.9)	(1.7, 15.5)	(4.4, 14.5)
36 weeks, n (%)	10 (15.3)	4 (7.1)	14 (11.5)
36 weeks, 95% CI	(8.5, 26.5)	(2.7, 17.8)	(6.9, 18.6)
48 weeks, n (%)	16 (24.9)	5 (9.1)	21 (17.7)
48 weeks, 95% CI	(16.0, 37.4)	(3.9, 20.5)	(11.9, 25.9)
60 weeks, n (%)	16 (24.9)	5 (9.1)	21 (17.7)
60 weeks, 95% CI	(16.0, 37.4)	(3.9, 20.5)	(11.9, 25.9)
72 weeks, n (%)	17 (26.7)	5 (9.1)	22 (18.7)
72 weeks, 95% CI	(17.5, 39.5)	(3.9, 20.5)	(12.7, 27.1)
84 weeks, n (%)	17 (26.7)	7 (14.0)	24 (20.9)
84 weeks, 95% CI	(17.5, 39.5)	(6.9, 27.5)	(14.4, 29.6)
96 weeks, n (%)	18 (28.6)	7 (14.0)	25 (22.0)
96 weeks, 95% CI	(19.0, 41.6)	(6.9, 27.5)	(15.3, 30.9)

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	62 (92.5)	58 (NA)	120 (96.0)
12 weeks, 95% CI	(83.0, 96.8)	NA	(90.7, 98.3)
24 weeks, n (%)	58 (89.5)	53 (94.7)	111 (91.9)
24 weeks, 95% CI	(79.1, 94.8)	(84.5, 98.3)	(85.5, 95.6)
36 weeks, n (%)	54 (84.7)	49 (92.9)	103 (88.5)
36 weeks, 95% CI	(73.5, 91.5)	(82.2, 97.3)	(81.4, 93.1)
48 weeks, n (%)	46 (75.1)	45 (90.9)	91 (82.3)
48 weeks, 95% CI	(62.6, 84.0)	(79.5, 96.1)	(74.1, 88.1)
60 weeks, n (%)	44 (75.1)	39 (90.9)	83 (82.3)
60 weeks, 95% CI	(62.6, 84.0)	(79.5, 96.1)	(74.1, 88.1)
72 weeks, n (%)	40 (73.3)	39 (90.9)	79 (81.3)
72 weeks, 95% CI	(60.5, 82.5)	(79.5, 96.1)	(72.9, 87.3)
84 weeks, n (%)	38 (73.3)	34 (86.0)	72 (79.1)
84 weeks, 95% CI	(60.5, 82.5)	(72.5, 93.1)	(70.4, 85.6)
96 weeks, n (%)	14 (71.4)	9 (86.0)	23 (78.0)
96 weeks, 95% CI	(58.4, 81.0)	(72.5, 93.1)	(69.1, 84.7)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Hazard ratio (DMF vs IFN B-1a) (c)	2.291		
95% CI (c)	(0.951, 5.522)		
p-value (c)	0.0647		

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	14 (20)	2 (3)	16 (12)
Number of subjects without confirmed improvement of disability (a)	57 (80)	62 (97)	119 (88)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	36.1	NA	47.6
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	3 (4.5)	0 (0.0)	3 (2.4)
12 weeks, 95% CI	(1.5, 13.2)	NA	(0.8, 7.2)
24 weeks, n (%)	4 (6.0)	1 (1.7)	5 (4.0)
24 weeks, 95% CI	(2.3, 15.2)	(0.2, 11.6)	(1.7, 9.4)
36 weeks, n (%)	7 (10.7)	1 (1.7)	8 (6.5)
36 weeks, 95% CI	(5.3, 21.2)	(0.2, 11.6)	(3.3, 12.7)
48 weeks, n (%)	13 (20.3)	2 (3.8)	15 (12.8)
48 weeks, 95% CI	(12.3, 32.4)	(1.0, 14.3)	(7.9, 20.3)
60 weeks, n (%)	13 (20.3)	2 (3.8)	15 (12.8)
60 weeks, 95% CI	(12.3, 32.4)	(1.0, 14.3)	(7.9, 20.3)
72 weeks, n (%)	14 (22.1)	2 (3.8)	16 (13.8)
72 weeks, 95% CI	(13.7, 34.6)	(1.0, 14.3)	(8.7, 21.6)
84 weeks, n (%)	14 (22.1)	2 (3.8)	16 (13.8)
84 weeks, 95% CI	(13.7, 34.6)	(1.0, 14.3)	(8.7, 21.6)
96 weeks, n (%)	14 (22.1)	2 (3.8)	16 (13.8)
96 weeks, 95% CI	(13.7, 34.6)	(1.0, 14.3)	(8.7, 21.6)

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

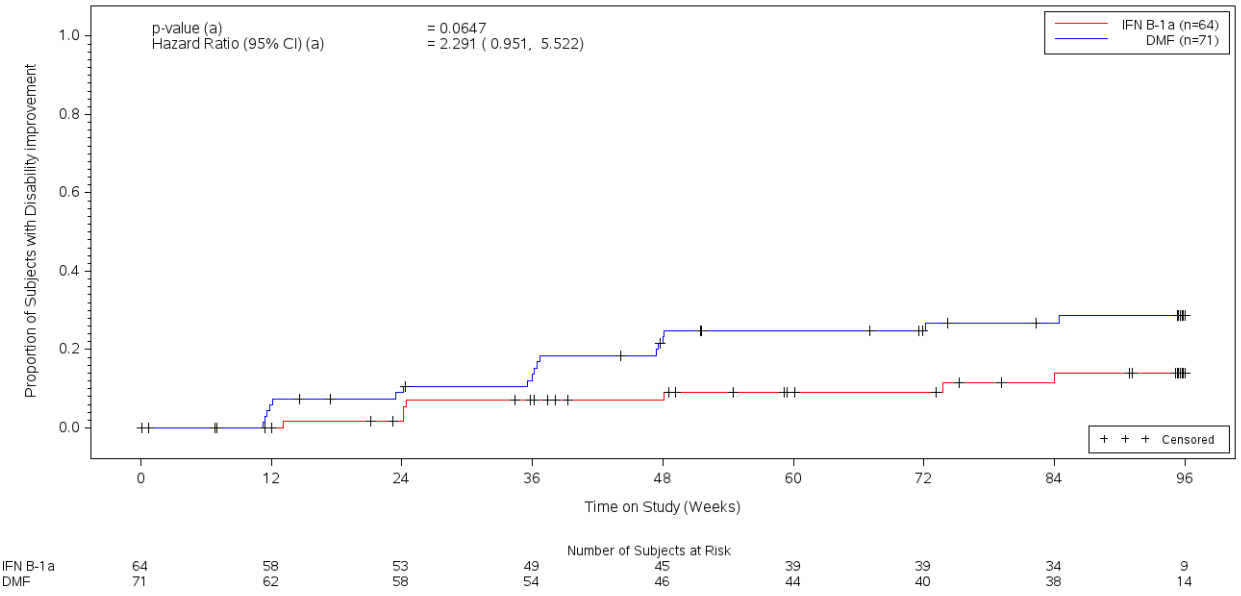
	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	64 (95.5)	58 (NA)	122 (97.6)
12 weeks, 95% CI	(86.8, 98.5)	NA	(92.8, 99.2)
24 weeks, n (%)	61 (94.0)	55 (98.3)	116 (96.0)
24 weeks, 95% CI	(84.8, 97.7)	(88.4, 99.8)	(90.6, 98.3)
36 weeks, n (%)	57 (89.3)	52 (98.3)	109 (93.5)
36 weeks, 95% CI	(78.8, 94.7)	(88.4, 99.8)	(87.3, 96.7)
48 weeks, n (%)	49 (79.7)	47 (96.2)	96 (87.2)
48 weeks, 95% CI	(67.6, 87.7)	(85.7, 99.0)	(79.7, 92.1)
60 weeks, n (%)	47 (79.7)	40 (96.2)	87 (87.2)
60 weeks, 95% CI	(67.6, 87.7)	(85.7, 99.0)	(79.7, 92.1)
72 weeks, n (%)	42 (77.9)	40 (96.2)	82 (86.2)
72 weeks, 95% CI	(65.4, 86.3)	(85.7, 99.0)	(78.4, 91.3)
84 weeks, n (%)	40 (77.9)	37 (96.2)	77 (86.2)
84 weeks, 95% CI	(65.4, 86.3)	(85.7, 99.0)	(78.4, 91.3)
96 weeks, n (%)	16 (77.9)	10 (96.2)	26 (86.2)
96 weeks, 95% CI	(65.4, 86.3)	(85.7, 99.0)	(78.4, 91.3)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Hazard ratio (DMF vs IFN B-1a) (c)	6.416		
95% CI (c)	(1.450, 28.38)		
p-value (c)	0.0143		

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_ban020422.sas date: 04FEB2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks
ITT population, Aged 13 years and older (n=135)
Analysis NOT using subgroups



Number of Subjects at Risk

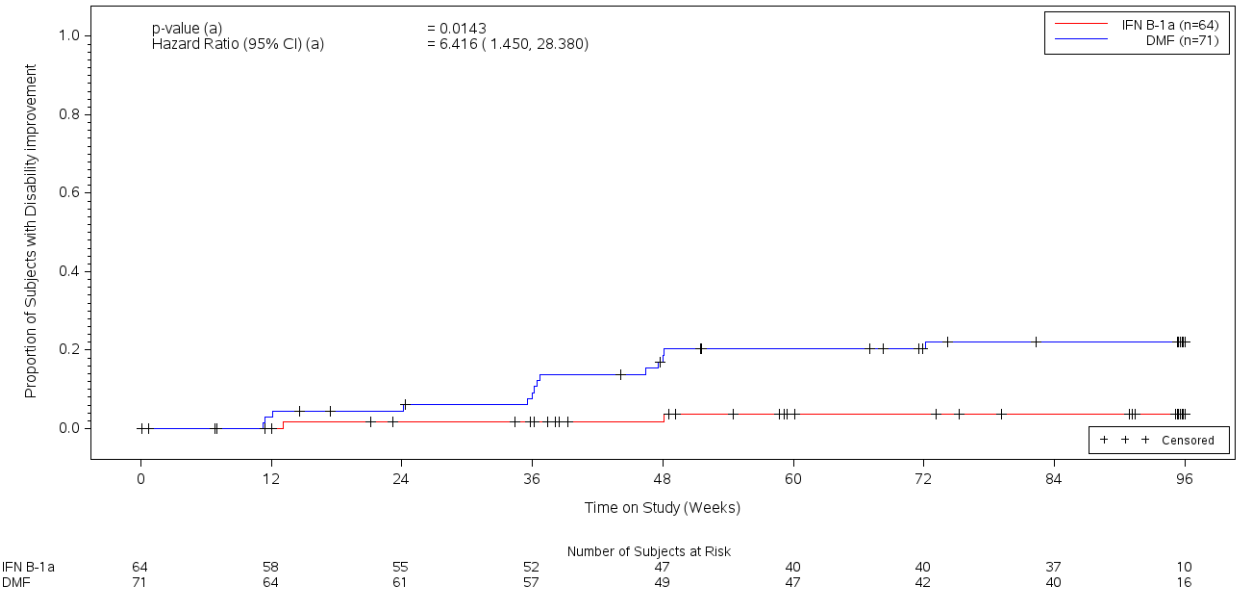
IFN B-1a	64	58	53	49	45	39	39	34	9
DMF	71	62	58	54	46	44	40	38	14

NOTE 1: Plot uses Kaplan-Meier product-limit method.
(a) Based on a Cox proportional hazards model adjusted for age group and baseline EDSS

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_ban020422.sas DATE: 04FEB2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks
ITT population, Aged 13 years and older (n=135)
Analysis NOT using subgroups



Number of Subjects at Risk

IFN B-1a	64	58	55	52	47	40	40	37	10
DMF	71	64	61	57	49	47	42	40	16

NOTE 1: Plot uses Kaplan-Meier product-limit method.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109ms306_table51_tt_kmplot_disability_improvement_n=135_ban012722.sas DATE: 04FEB2022

Sub groups

Progression

109MS306_table51_TTE_12_Week_progression_DESCRIBE__age13to14

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks - mITT Population, Aged 13 years or older (n=135). Subgroup analysis for AGES 13 TO 14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Number of subjects with progression of disability (a)	2 (11)	1 (7)	3 (9)
Number of subjects without disability progression (a)	16 (89)	13 (93)	29 (91)
Time to progression of disability (weeks) (b)			
10th percentile	83.6	NA	83.6
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects with disability progression at (b)			
12 weeks, n (%)	1 (5.9)	0 (0.0)	1 (3.4)
12 weeks, 95% CI	(0.9, 35.0)	NA	(0.5, 22.1)
24 weeks, n (%)	1 (5.9)	0 (0.0)	1 (3.4)
24 weeks, 95% CI	(0.9, 35.0)	NA	(0.5, 22.1)
36 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
36 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
48 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
48 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
60 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
60 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
72 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
72 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
84 weeks, n (%)	2 (12.2)	1 (10.0)	3 (11.5)
84 weeks, 95% CI	(3.2, 40.5)	(1.5, 52.7)	(3.8, 31.8)
96 weeks, n (%)	2 (12.2)	1 (10.0)	3 (11.5)
96 weeks, 95% CI	(3.2, 40.5)	(1.5, 52.7)	(3.8, 31.8)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects without disability progressioin at (b)			
12 weeks, n (%)	16 (94.1)	12 (NA)	28 (96.6)
12 weeks, 95% CI	(65.0, 99.1)	NA	(77.9, 99.5)
24 weeks, n (%)	15 (94.1)	10 (NA)	25 (96.6)
24 weeks, 95% CI	(65.0, 99.1)	NA	(77.9, 99.5)
36 weeks, n (%)	15 (94.1)	9 (90.0)	24 (92.7)
36 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
48 weeks, n (%)	15 (94.1)	9 (90.0)	24 (92.7)
48 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
60 weeks, n (%)	15 (94.1)	8 (90.0)	23 (92.7)
60 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
72 weeks, n (%)	15 (94.1)	8 (90.0)	23 (92.7)
72 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
84 weeks, n (%)	14 (87.8)	7 (90.0)	21 (88.5)
84 weeks, 95% CI	(59.5, 96.8)	(47.3, 98.5)	(68.2, 96.2)
96 weeks, n (%)	8 (87.8)	2 (90.0)	10 (88.5)
96 weeks, 95% CI	(59.5, 96.8)	(47.3, 98.5)	(68.2, 96.2)
Hazard ratio (DMF vs IFN B-1a) (c)	1.223		
95% CI (c)	(0.107, 13.960)		
p-value (c)	0.8713		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

109MS306_table51_TTE_12_Week_progression_DESCRIBE__age15to17

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks - mITT Population, Aged 13 years or older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Number of subjects with progression of disability (a)	4 (8)	3 (6)	7 (7)
Number of subjects without disability progression (a)	49 (92)	47 (94)	96 (93)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects with disability progression at (b)			
12 weeks, n (%)	1 (2.0)	1 (2.0)	2 (2.0)
12 weeks, 95% CI	(0.3, 13.4)	(0.3, 13.6)	(0.5, 7.9)
24 weeks, n (%)	3 (6.0)	1 (2.0)	4 (4.1)
24 weeks, 95% CI	(2.0, 17.5)	(0.3, 13.6)	(1.6, 10.6)
36 weeks, n (%)	3 (6.0)	2 (4.2)	5 (5.2)
36 weeks, 95% CI	(2.0, 17.5)	(1.1, 15.8)	(2.2, 12.0)
48 weeks, n (%)	4 (8.1)	2 (4.2)	6 (6.3)
48 weeks, 95% CI	(3.1, 20.1)	(1.1, 15.8)	(2.9, 13.5)
60 weeks, n (%)	4 (8.1)	2 (4.2)	6 (6.3)
60 weeks, 95% CI	(3.1, 20.1)	(1.1, 15.8)	(2.9, 13.5)
72 weeks, n (%)	4 (8.1)	2 (4.2)	6 (6.3)
72 weeks, 95% CI	(3.1, 20.1)	(1.1, 15.8)	(2.9, 13.5)

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
84 weeks, n (%)	4 (8.1)	3 (7.1)	7 (7.7)
84 weeks, 95% CI	(3.1, 20.1)	(2.3, 20.8)	(3.7, 15.5)
96 weeks, n (%)	4 (8.1)	3 (7.1)	7 (7.7)
96 weeks, 95% CI	(3.1, 20.1)	(2.3, 20.8)	(3.7, 15.5)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects without disability progressioin at (b)			
12 weeks, n (%)	49 (98.0)	45 (98.0)	94 (98.0)
12 weeks, 95% CI	(86.6, 99.7)	(86.4, 99.7)	(92.1, 99.5)
24 weeks, n (%)	46 (94.0)	45 (98.0)	91 (95.9)
24 weeks, 95% CI	(82.5, 98.0)	(86.4, 99.7)	(89.4, 98.4)
36 weeks, n (%)	45 (94.0)	41 (95.8)	86 (94.8)
36 weeks, 95% CI	(82.5, 98.0)	(84.2, 98.9)	(88.0, 97.8)
48 weeks, n (%)	42 (91.9)	37 (95.8)	79 (93.7)
48 weeks, 95% CI	(79.9, 96.9)	(84.2, 98.9)	(86.5, 97.1)
60 weeks, n (%)	39 (91.9)	33 (95.8)	72 (93.7)
60 weeks, 95% CI	(79.9, 96.9)	(84.2, 98.9)	(86.5, 97.1)
72 weeks, n (%)	35 (91.9)	33 (95.8)	68 (93.7)
72 weeks, 95% CI	(79.9, 96.9)	(84.2, 98.9)	(86.5, 97.1)
84 weeks, n (%)	33 (91.9)	30 (92.9)	63 (92.3)
84 weeks, 95% CI	(79.9, 96.9)	(79.2, 97.7)	(84.5, 96.3)
96 weeks, n (%)	15 (91.9)	10 (92.9)	25 (92.3)
96 weeks, 95% CI	(79.9, 96.9)	(79.2, 97.7)	(84.5, 96.3)
Hazard ratio (DMF vs IFN B-1a) (c)	1.205		
95% CI (c)	(0.268, 5.414)		
p-value (c)	0.8082		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

109MS306_table51_TTE_12_Week_progression_DESCRIBE__female

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks - mITT Population, Aged 13 years or older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Number of subjects with progression of disability (a)	5 (10)	3 (7)	8 (8)
Number of subjects without disability progression (a)	45 (90)	43 (93)	88 (92)
Time to progression of disability (weeks) (b)			
10th percentile	83.6	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects with disability progression at (b)			
12 weeks, n (%)	2 (4.3)	1 (2.2)	3 (3.3)
12 weeks, 95% CI	(1.1, 16.0)	(0.3, 14.4)	(1.1, 9.9)
24 weeks, n (%)	3 (6.4)	1 (2.2)	4 (4.4)
24 weeks, 95% CI	(2.1, 18.5)	(0.3, 14.4)	(1.7, 11.4)
36 weeks, n (%)	3 (6.4)	3 (7.4)	6 (6.8)
36 weeks, 95% CI	(2.1, 18.5)	(2.4, 21.3)	(3.1, 14.6)
48 weeks, n (%)	4 (8.6)	3 (7.4)	7 (8.1)
48 weeks, 95% CI	(3.3, 21.4)	(2.4, 21.3)	(3.9, 16.2)
60 weeks, n (%)	4 (8.6)	3 (7.4)	7 (8.1)
60 weeks, 95% CI	(3.3, 21.4)	(2.4, 21.3)	(3.9, 16.2)
72 weeks, n (%)	4 (8.6)	3 (7.4)	7 (8.1)
72 weeks, 95% CI	(3.3, 21.4)	(2.4, 21.3)	(3.9, 16.2)

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
84 weeks, n (%)	5 (11.5)	3 (7.4)	8 (9.6)
84 weeks, 95% CI	(4.9, 25.6)	(2.4, 21.3)	(4.9, 18.4)
96 weeks, n (%)	5 (11.5)	3 (7.4)	8 (9.6)
96 weeks, 95% CI	(4.9, 25.6)	(2.4, 21.3)	(4.9, 18.4)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects without disability progressioin at (b)			
12 weeks, n (%)	45 (95.7)	40 (97.8)	85 (96.7)
12 weeks, 95% CI	(84.0, 98.9)	(85.6, 99.7)	(90.1, 98.9)
24 weeks, n (%)	42 (93.6)	38 (97.8)	80 (95.6)
24 weeks, 95% CI	(81.5, 97.9)	(85.6, 99.7)	(88.6, 98.3)
36 weeks, n (%)	42 (93.6)	34 (92.6)	76 (93.2)
36 weeks, 95% CI	(81.5, 97.9)	(78.7, 97.6)	(85.4, 96.9)
48 weeks, n (%)	39 (91.4)	32 (92.6)	71 (91.9)
48 weeks, 95% CI	(78.6, 96.7)	(78.7, 97.6)	(83.8, 96.1)
60 weeks, n (%)	37 (91.4)	29 (92.6)	66 (91.9)
60 weeks, 95% CI	(78.6, 96.7)	(78.7, 97.6)	(83.8, 96.1)
72 weeks, n (%)	33 (91.4)	29 (92.6)	62 (91.9)
72 weeks, 95% CI	(78.6, 96.7)	(78.7, 97.6)	(83.8, 96.1)
84 weeks, n (%)	31 (88.5)	28 (92.6)	59 (90.4)
84 weeks, 95% CI	(74.4, 95.1)	(78.7, 97.6)	(81.6, 95.1)
96 weeks, n (%)	15 (88.5)	8 (92.6)	23 (90.4)
96 weeks, 95% CI	(74.4, 95.1)	(78.7, 97.6)	(81.6, 95.1)
Hazard ratio (DMF vs IFN B-1a) (c)	1.430		
95% CI (c)	(0.340, 6.010)		
p-value (c)	0.6250		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

109MS306_table51_TTE_12_Week_progression_DESCRIBE__male

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks - mITT Population, Aged 13 years or older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Number of subjects with progression of disability (a)	1 (5)	1 (6)	2 (5)
Number of subjects without disability progression (a)	20 (95)	17 (94)	37 (95)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects with disability progression at (b)			
12 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	1 (5.0)	0 (0.0)	1 (2.7)
24 weeks, 95% CI	(0.7, 30.5)	NA	(0.4, 17.7)
36 weeks, n (%)	1 (5.0)	0 (0.0)	1 (2.7)
36 weeks, 95% CI	(0.7, 30.5)	NA	(0.4, 17.7)
48 weeks, n (%)	1 (5.0)	0 (0.0)	1 (2.7)
48 weeks, 95% CI	(0.7, 30.5)	NA	(0.4, 17.7)
60 weeks, n (%)	1 (5.0)	0 (0.0)	1 (2.7)
60 weeks, 95% CI	(0.7, 30.5)	NA	(0.4, 17.7)
72 weeks, n (%)	1 (5.0)	0 (0.0)	1 (2.7)
72 weeks, 95% CI	(0.7, 30.5)	NA	(0.4, 17.7)

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
84 weeks, n (%)	1 (5.0)	1 (8.3)	2 (6.1)
84 weeks, 95% CI	(0.7, 30.5)	(1.2, 46.1)	(1.5, 22.3)
96 weeks, n (%)	1 (5.0)	1 (8.3)	2 (6.1)
96 weeks, 95% CI	(0.7, 30.5)	(1.2, 46.1)	(1.5, 22.3)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

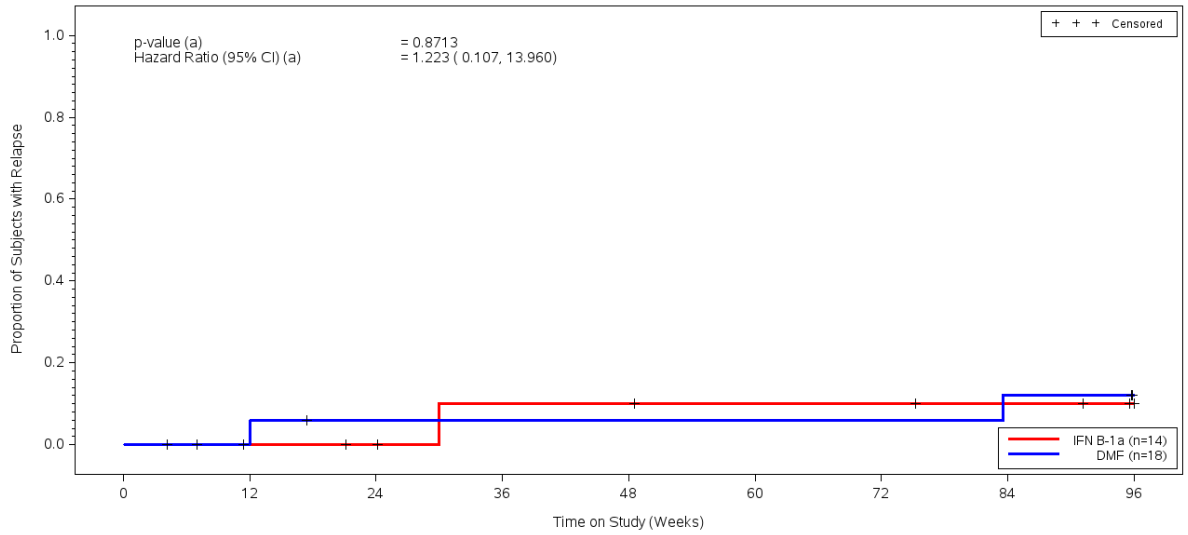
	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects without disability progressioin at (b)			
12 weeks, n (%)	20 (NA)	17 (NA)	37 (NA)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	19 (95.0)	17 (NA)	36 (97.3)
24 weeks, 95% CI	(69.5, 99.3)	NA	(82.3, 99.6)
36 weeks, n (%)	18 (95.0)	16 (NA)	34 (97.3)
36 weeks, 95% CI	(69.5, 99.3)	NA	(82.3, 99.6)
48 weeks, n (%)	18 (95.0)	14 (NA)	32 (97.3)
48 weeks, 95% CI	(69.5, 99.3)	NA	(82.3, 99.6)
60 weeks, n (%)	17 (95.0)	12 (NA)	29 (97.3)
60 weeks, 95% CI	(69.5, 99.3)	NA	(82.3, 99.6)
72 weeks, n (%)	17 (95.0)	12 (NA)	29 (97.3)
72 weeks, 95% CI	(69.5, 99.3)	NA	(82.3, 99.6)
84 weeks, n (%)	16 (95.0)	9 (91.7)	25 (93.9)
84 weeks, 95% CI	(69.5, 99.3)	(53.9, 98.8)	(77.7, 98.5)
96 weeks, n (%)	8 (95.0)	4 (91.7)	12 (93.9)
96 weeks, 95% CI	(69.5, 99.3)	(53.9, 98.8)	(77.7, 98.5)
Hazard ratio (DMF vs IFN B-1a) (c)	0.952		
95% CI (c)	(0.051, 17.738)		
p-value (c)	0.9740		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TTE_12_Week_progression_DESCRIBE_SubGr_ban020922.sas date: 09FEB2022

109MS306_Table51_TTE_12_Week_progression_KMPLOT_Age13_14

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks, Aged 13 years or older

Subgroup analysis for Age13_14



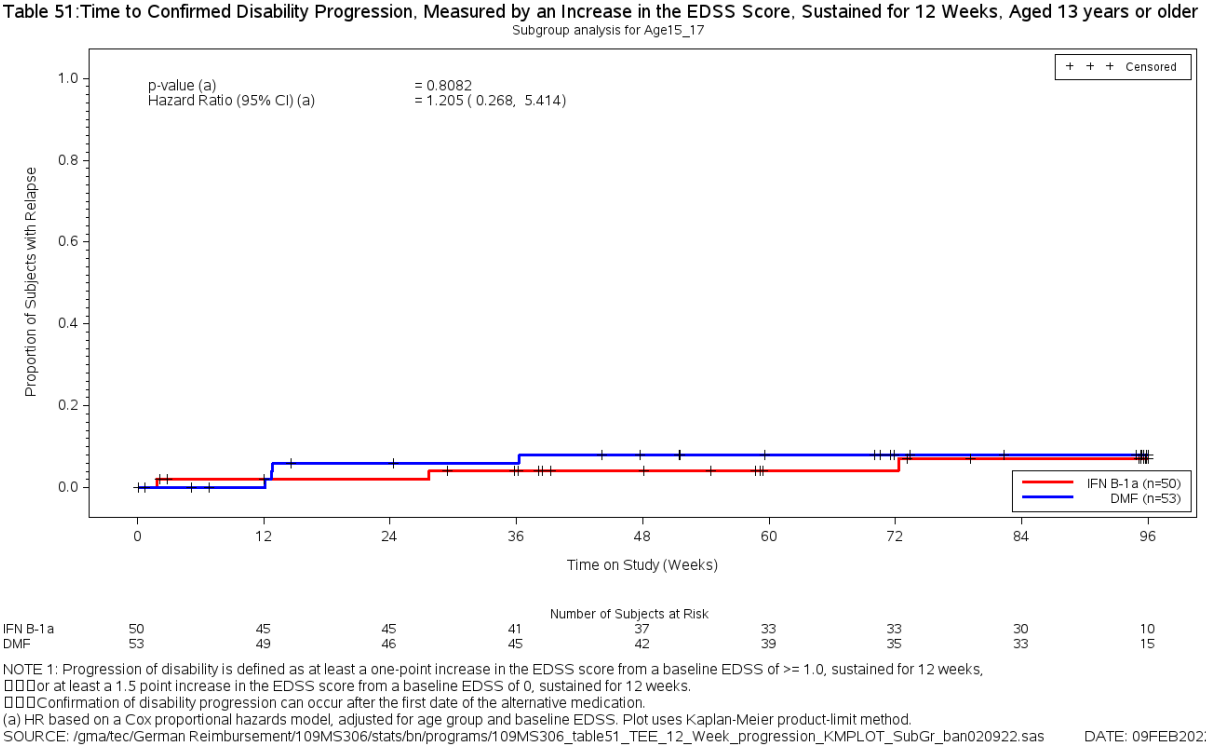
Number of Subjects at Risk

IFN B-1a	14	12	10	9	9	8	8	7	2
DMF	18	16	15	15	15	15	15	14	8

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TEE_12_Week_progression_KMPLOT_SubGr_ban020922.sas DATE: 09FEB2022

109MS306_Table51_TTE_12_Week_progression_KMPLOT_Age15_17

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks, Aged 13 years or older



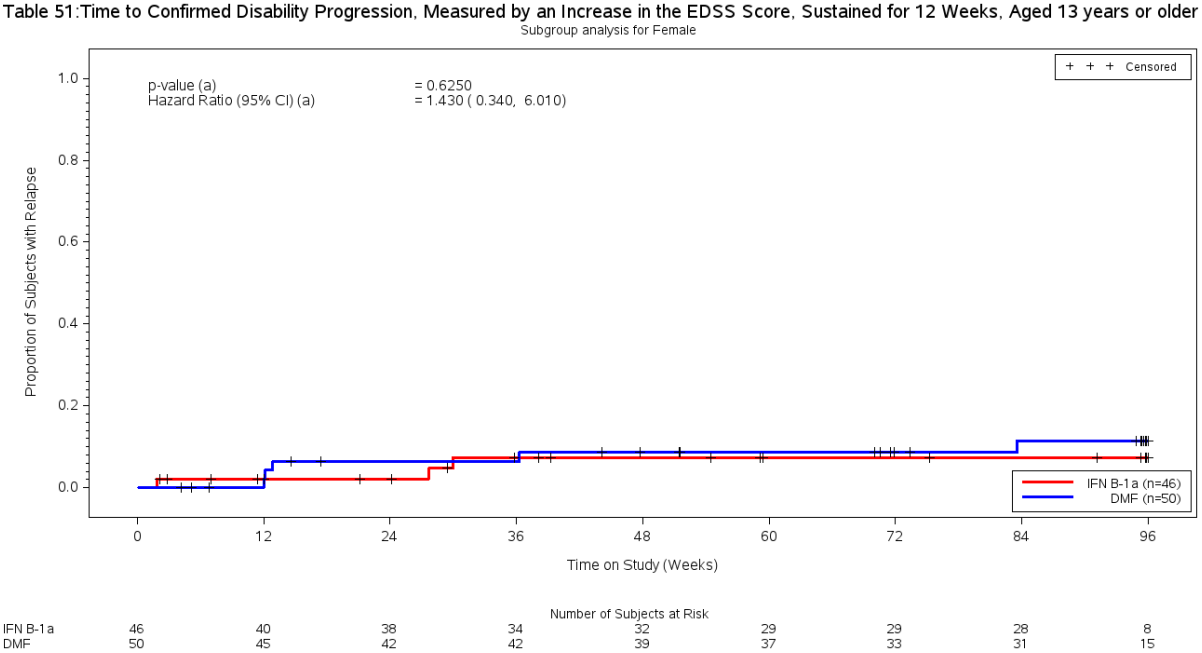
Number of Subjects at Risk

IFN B-1a	50	45	45	41	37	33	33	30	10
DMF	53	49	46	45	42	39	35	33	15

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TEE_12_Week_progression_KMPLOT_SubGr_ban020922.sas DATE: 09FEB2022

109MS306_Table51_TTE_12_Week_progression_KMPLOT_Female

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks, Aged 13 years or older



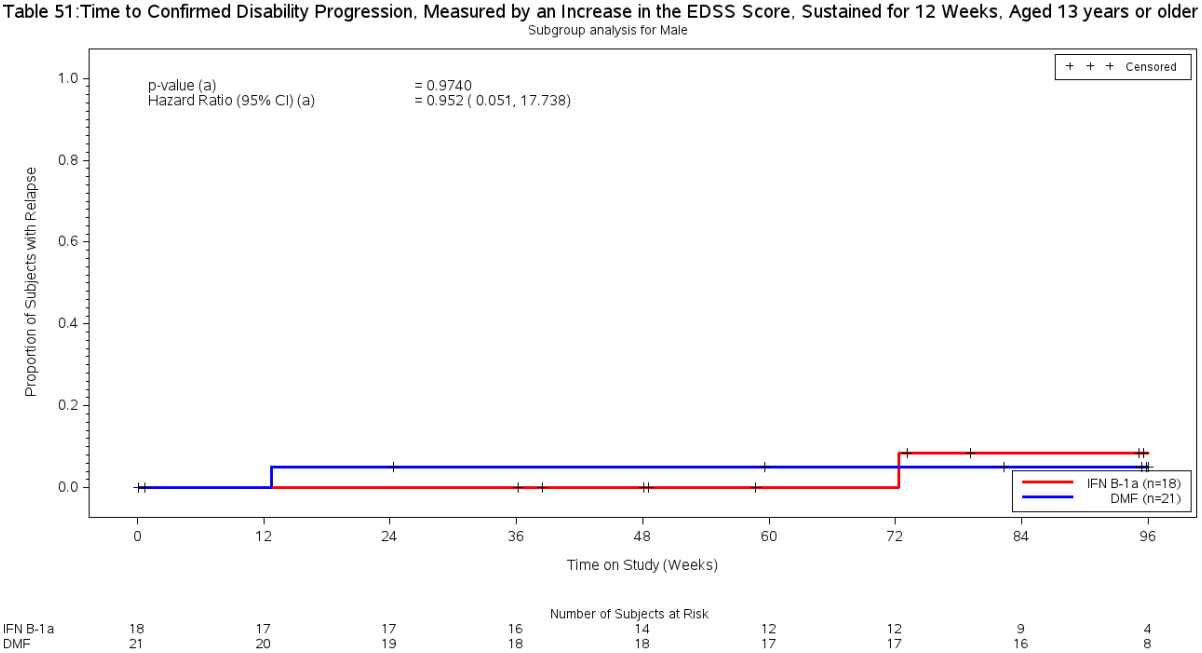
Number of Subjects at Risk

IFN B-1a	46	40	38	34	32	29	29	28	8
DMF	50	45	42	42	39	37	33	31	15

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TEE_12_Week_progression_KMPLOT_SubGr_ban020922.sas DATE: 09FEB2022

109MS306_Table51_TTE_12_Week_progression_KMPLOT_Male

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 12 Weeks, Aged 13 years or older



Number of Subjects at Risk

IFN B-1a	18	17	17	16	14	12	12	9	4
DMF	21	20	19	18	18	17	17	16	8

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 12 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 12 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_TEE_12_Week_progression_KMPLOT_SubGr_ban020922.sas DATE: 09FEB2022

109MS306_table51_TTE_24_Week_progression_DESCRIBE_Age13_14

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks - mITT Population. Subgroup analysis for Age13_14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Number of subjects with progression of disability (a)	1 (6)	1 (7)	2 (6)
Number of subjects without disability progression (a)	17 (94)	13 (93)	30 (94)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated proportion of subjects with disability progression at (b)			
12 weeks, n (%)	1 (5.9)	0 (0.0)	1 (3.4)
12 weeks, 95% CI	(0.9, 35.0)	NA	(0.5, 22.1)
24 weeks, n (%)	1 (5.9)	0 (0.0)	1 (3.4)
24 weeks, 95% CI	(0.9, 35.0)	NA	(0.5, 22.1)
36 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
36 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
48 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
48 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
60 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
60 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
72 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
72 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
84 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
84 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)
96 weeks, n (%)	1 (5.9)	1 (10.0)	2 (7.3)
96 weeks, 95% CI	(0.9, 35.0)	(1.5, 52.7)	(1.9, 26.3)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas
date: 08FEB2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated proportion of subjects without disability progression at (b)			
12 weeks, n (%)	16 (94.1)	12 (NA)	28 (96.6)
12 weeks, 95% CI	(65.0, 99.1)	NA	(77.9, 99.5)
24 weeks, n (%)	15 (94.1)	10 (NA)	25 (96.6)
24 weeks, 95% CI	(65.0, 99.1)	NA	(77.9, 99.5)
36 weeks, n (%)	15 (94.1)	9 (90.0)	24 (92.7)
36 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
48 weeks, n (%)	15 (94.1)	9 (90.0)	24 (92.7)
48 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
60 weeks, n (%)	15 (94.1)	8 (90.0)	23 (92.7)
60 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
72 weeks, n (%)	15 (94.1)	8 (90.0)	23 (92.7)
72 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
84 weeks, n (%)	15 (94.1)	7 (90.0)	22 (92.7)
84 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
96 weeks, n (%)	8 (94.1)	2 (90.0)	10 (92.7)
96 weeks, 95% CI	(65.0, 99.1)	(47.3, 98.5)	(73.7, 98.1)
Hazard ratio (DMF vs IFN B-1a) (c)	0.631		
95% CI (c)	(0.035, 11.394)		
p-value (c)	0.7550		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas date: 08FEB2022

109MS306_table51_TTE_24_Week_progression_DESCRIBE_Age15_17

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks - mITT Population. Subgroup analysis for Age15_17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Number of subjects with progression of disability (a)	2 (4)	3 (6)	5 (5)
Number of subjects without disability progression (a)	51 (96)	47 (94)	98 (95)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated proportion of subjects with disability progression at (b)			
12 weeks, n (%)	1 (2.0)	0 (0.0)	1 (1.0)
12 weeks, 95% CI	(0.3, 13.4)	NA	(0.1, 7.2)
24 weeks, n (%)	2 (4.0)	1 (2.2)	3 (3.1)
24 weeks, 95% CI	(1.0, 15.1)	(0.3, 14.4)	(1.0, 9.4)
36 weeks, n (%)	2 (4.0)	2 (4.3)	4 (4.2)
36 weeks, 95% CI	(1.0, 15.1)	(1.1, 16.3)	(1.6, 10.8)
48 weeks, n (%)	2 (4.0)	2 (4.3)	4 (4.2)
48 weeks, 95% CI	(1.0, 15.1)	(1.1, 16.3)	(1.6, 10.8)
60 weeks, n (%)	2 (4.0)	2 (4.3)	4 (4.2)
60 weeks, 95% CI	(1.0, 15.1)	(1.1, 16.3)	(1.6, 10.8)
72 weeks, n (%)	2 (4.0)	2 (4.3)	4 (4.2)
72 weeks, 95% CI	(1.0, 15.1)	(1.1, 16.3)	(1.6, 10.8)

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
84 weeks, n (%)	2 (4.0)	3 (7.2)	5 (5.6)
84 weeks, 95% CI	(1.0, 15.1)	(2.4, 21.1)	(2.3, 12.9)
96 weeks, n (%)	2 (4.0)	3 (7.2)	5 (5.6)
96 weeks, 95% CI	(1.0, 15.1)	(2.4, 21.1)	(2.3, 12.9)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas
date: 08FEB2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated proportion of subjects without disability progression at (b)			
12 weeks, n (%)	49 (98.0)	46 (NA)	95 (99.0)
12 weeks, 95% CI	(86.6, 99.7)	NA	(92.8, 99.9)
24 weeks, n (%)	47 (96.0)	45 (97.8)	92 (96.9)
24 weeks, 95% CI	(84.9, 99.0)	(85.6, 99.7)	(90.6, 99.0)
36 weeks, n (%)	46 (96.0)	41 (95.7)	87 (95.8)
36 weeks, 95% CI	(84.9, 99.0)	(83.7, 98.9)	(89.2, 98.4)
48 weeks, n (%)	44 (96.0)	38 (95.7)	82 (95.8)
48 weeks, 95% CI	(84.9, 99.0)	(83.7, 98.9)	(89.2, 98.4)
60 weeks, n (%)	42 (96.0)	33 (95.7)	75 (95.8)
60 weeks, 95% CI	(84.9, 99.0)	(83.7, 98.9)	(89.2, 98.4)
72 weeks, n (%)	37 (96.0)	33 (95.7)	70 (95.8)
72 weeks, 95% CI	(84.9, 99.0)	(83.7, 98.9)	(89.2, 98.4)
84 weeks, n (%)	35 (96.0)	30 (92.8)	65 (94.4)
84 weeks, 95% CI	(84.9, 99.0)	(78.9, 97.6)	(87.1, 97.7)
96 weeks, n (%)	15 (96.0)	10 (92.8)	25 (94.4)
96 weeks, 95% CI	(84.9, 99.0)	(78.9, 97.6)	(87.1, 97.7)
Hazard ratio (DMF vs IFN B-1a) (c)	0.570		
95% CI (c)	(0.094, 3.469)		
p-value (c)	0.5415		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas date: 08FEB2022

109MS306_table51_TTE_24_Week_progression_DESCRIBE_Female

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks - mITT Population. Subgroup analysis for Female

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Number of subjects with progression of disability (a)	3 (6)	3 (7)	6 (6)
Number of subjects without disability progression (a)	47 (94)	43 (93)	90 (94)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated proportion of subjects with disability progression at (b)			
12 weeks, n (%)	2 (4.3)	0 (0.0)	2 (2.3)
12 weeks, 95% CI	(1.1, 16.0)	NA	(0.6, 8.7)
24 weeks, n (%)	3 (6.4)	1 (2.4)	4 (4.5)
24 weeks, 95% CI	(2.1, 18.5)	(0.3, 16.1)	(1.7, 11.6)
36 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)
36 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)
48 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)
48 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)
60 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)
60 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)
72 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)
72 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)
84 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
84 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)
96 weeks, n (%)	3 (6.4)	3 (7.6)	6 (6.9)
96 weeks, 95% CI	(2.1, 18.5)	(2.5, 21.7)	(3.2, 14.8)

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas
date: 08FEB2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated proportion of subjects without disability progression at (b)			
12 weeks, n (%)	45 (95.7)	41 (NA)	86 (97.7)
12 weeks, 95% CI	(84.0, 98.9)	NA	(91.3, 99.4)
24 weeks, n (%)	42 (93.6)	38 (97.6)	80 (95.5)
24 weeks, 95% CI	(81.5, 97.9)	(83.9, 99.7)	(88.4, 98.3)
36 weeks, n (%)	42 (93.6)	34 (92.4)	76 (93.1)
36 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
48 weeks, n (%)	40 (93.6)	32 (92.4)	72 (93.1)
48 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
60 weeks, n (%)	38 (93.6)	29 (92.4)	67 (93.1)
60 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
72 weeks, n (%)	34 (93.6)	29 (92.4)	63 (93.1)
72 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
84 weeks, n (%)	33 (93.6)	28 (92.4)	61 (93.1)
84 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
96 weeks, n (%)	15 (93.6)	8 (92.4)	23 (93.1)
96 weeks, 95% CI	(81.5, 97.9)	(78.3, 97.5)	(85.2, 96.8)
Hazard ratio (DMF vs IFN B-1a) (c)	0.800		
95% CI (c)	(0.156, 4.108)		
p-value (c)	0.7891		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas date: 08FEB2022

109MS306_table51_TTE_24_Week_progression_DESCRIBE_Male

Table 51: Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks - mITT Population. Subgroup analysis for Male

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Number of subjects with progression of disability (a)	0	1 (6)	1 (3)
Number of subjects without disability progression (a)	21 (100)	17 (94)	38 (97)
Time to progression of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated proportion of subjects with disability progression at (b)			
12 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	0 (0.0)	1 (8.3)	1 (3.3)

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
84 weeks, 95% CI	NA	(1.2, 46.1)	(0.5, 21.4)
96 weeks, n (%)	0 (0.0)	1 (8.3)	1 (3.3)
96 weeks, 95% CI	NA	(1.2, 46.1)	(0.5, 21.4)

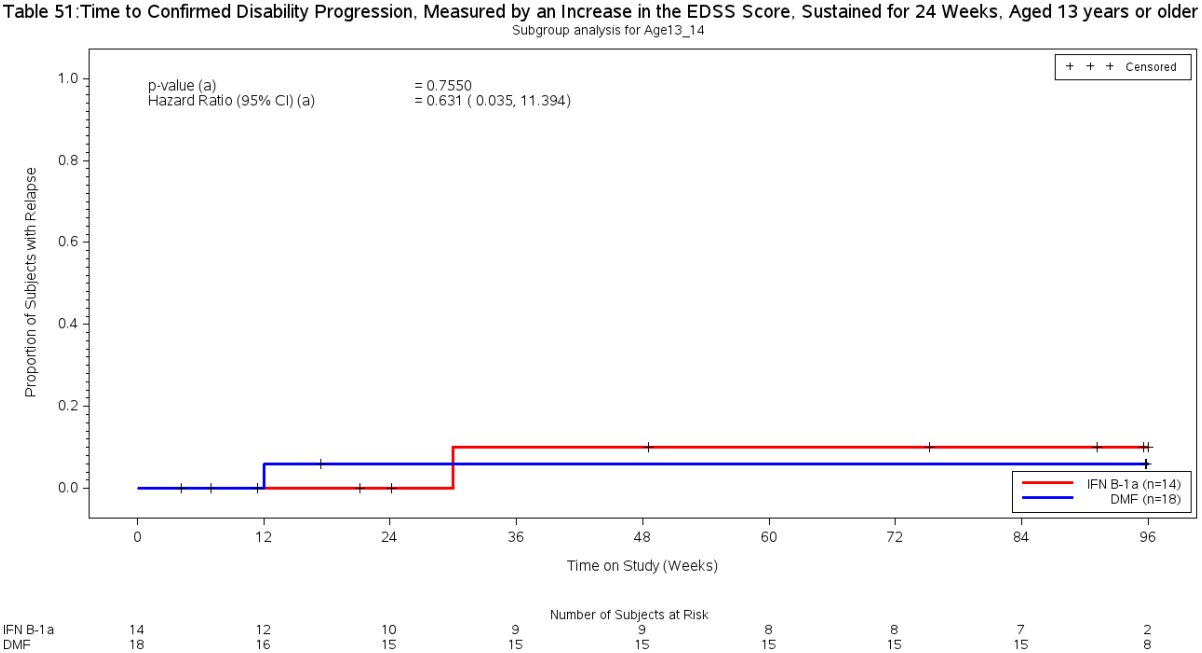
(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas
date: 08FEB2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated proportion of subjects without disability progression at (b)			
12 weeks, n (%)	20 (NA)	17 (NA)	37 (NA)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	20 (NA)	17 (NA)	37 (NA)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	19 (NA)	16 (NA)	35 (NA)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	19 (NA)	15 (NA)	34 (NA)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	19 (NA)	12 (NA)	31 (NA)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	18 (NA)	12 (NA)	30 (NA)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	17 (NA)	9 (91.7)	26 (96.7)
84 weeks, 95% CI	NA	(53.9, 98.8)	(78.6, 99.5)
96 weeks, n (%)	8 (NA)	4 (91.7)	12 (96.7)
96 weeks, 95% CI	NA	(53.9, 98.8)	(78.6, 99.5)
Hazard ratio (DMF vs IFN B-1a) (c)	0.000		
95% CI (c)	(0.000, NA)		
p-value (c)	0.9993		

(a) Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks, or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks. Confirmation of disability progression can occur after the first date of the alternative medication.
(b) Time to disability progression and estimated proportion of subjects with disability progression are based on Kaplan-Meier product limit method
(c) Hazard ratio, 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: .../109MS306_table51_TTE_24_Week_progression_DESCRIBE_subgroups.sas date: 08FEB2022

109MS306_Table51_TTE_24_Week_progression_KMPLOT_Age13_14

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks, Aged 13 years or older



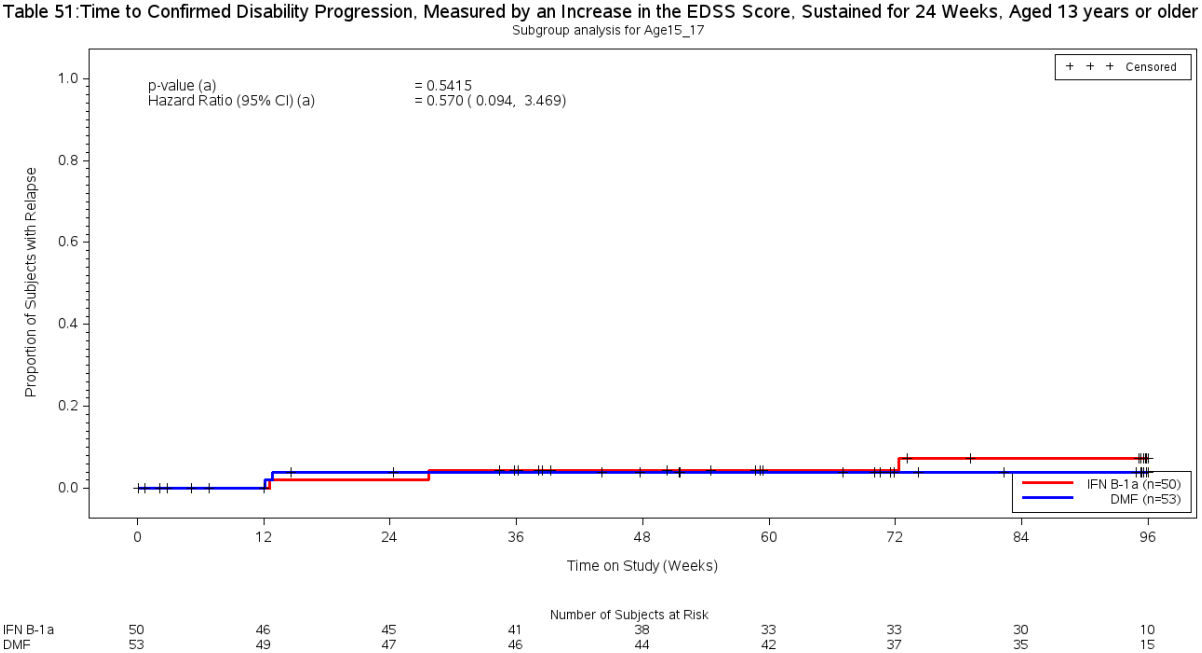
Number of Subjects at Risk

IFN B-1a	14	12	10	9	9	8	8	7	2
DMF	18	16	15	15	15	15	15	15	8

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_TABLE51_TTE_24_Week_progression_KMPLOT_subgroups.sas DATE: 09FEB2022

109MS306_Table51_TTE_24_Week_progression_KMPLOT_Age15_17

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks, Aged 13 years or older



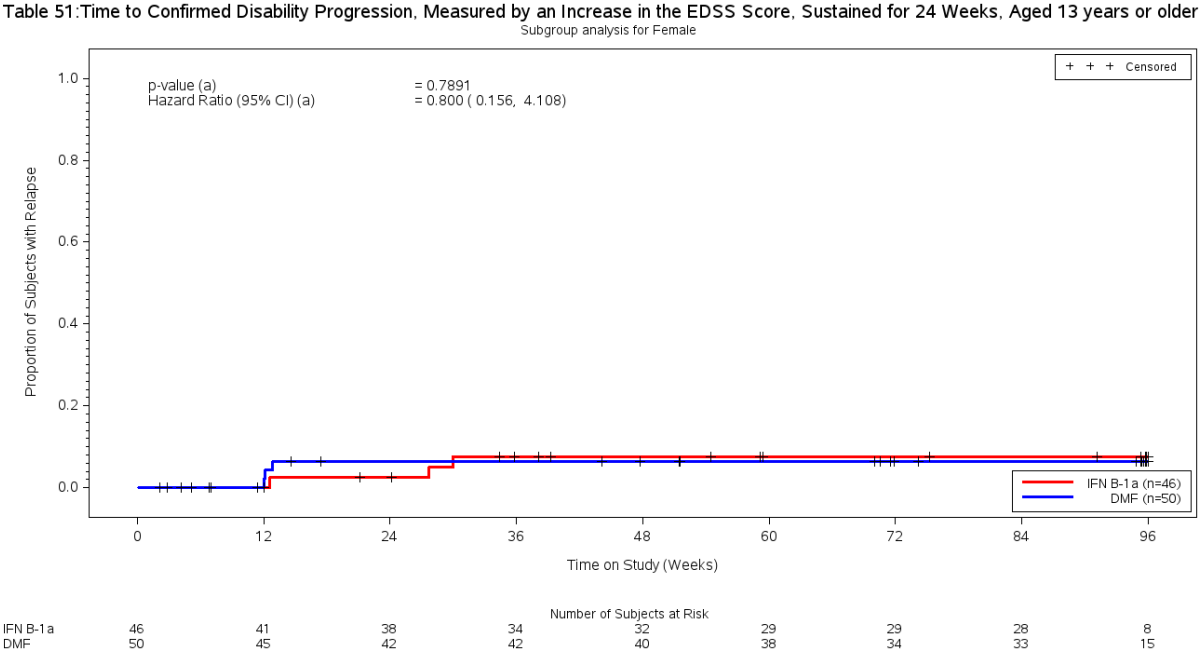
Number of Subjects at Risk

IFN B-1 a	50	46	45	41	38	33	33	30	10
DMF	53	49	47	46	44	42	37	35	15

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_TABLE51_TTE_24_Week_progression_KMPLOT_subgroups.sas DATE: 09FEB2022

109MS306_Table51_TTE_24_Week_progression_KMPLOT_Female

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks, Aged 13 years or older



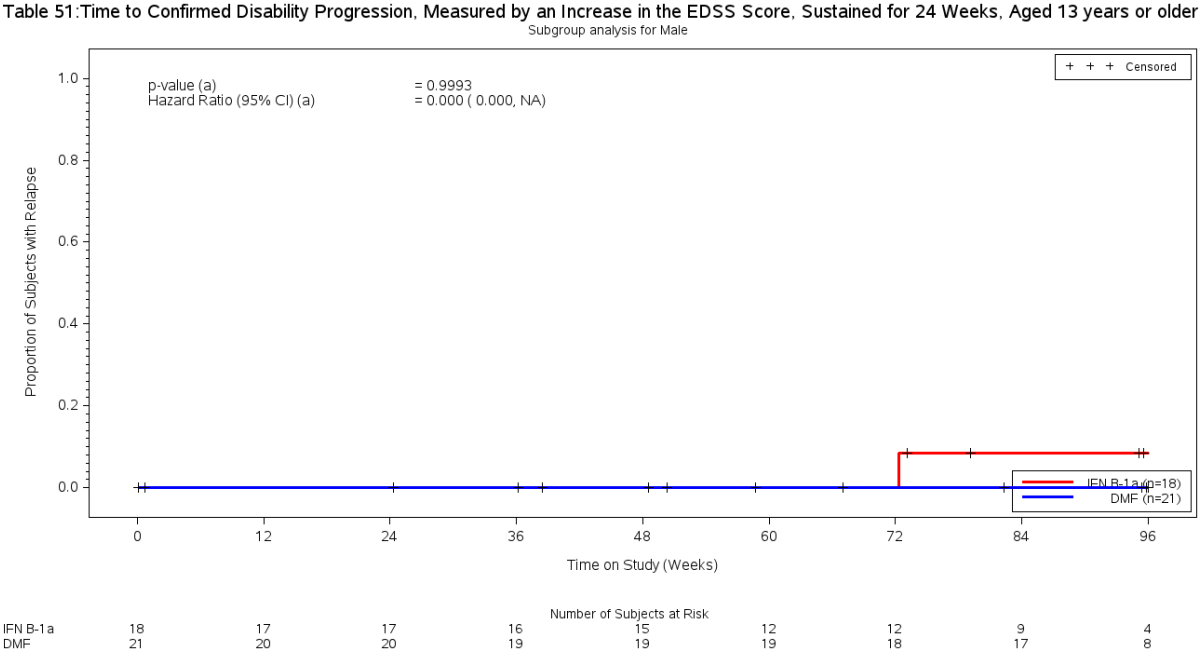
Number of Subjects at Risk

IFN B-1a	46	41	38	34	32	29	29	28	8
DMF	50	45	42	42	40	38	34	33	15

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_TABLE51_TTE_24_Week_progression_KMPLOT_subgroups.sas DATE: 09FEB2022

109MS306_Table51_TTE_24_Week_progression_KMPLOT_Male

Table 51:Time to Confirmed Disability Progression, Measured by an Increase in the EDSS Score, Sustained for 24 Weeks, Aged 13 years or older



Number of Subjects at Risk

IFN B-1a	18	17	17	16	15	12	12	9	4
DMF	21	20	20	19	19	19	18	17	8

NOTE 1: Progression of disability is defined as at least a one-point increase in the EDSS score from a baseline EDSS of >= 1.0, sustained for 24 weeks,
□□□or at least a 1.5 point increase in the EDSS score from a baseline EDSS of 0, sustained for 24 weeks.
□□□Confirmation of disability progression can occur after the first date of the alternative medication.
(a) HR based on a Cox proportional hazards model, adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_TABLE51_TTE_24_Week_progression_KMPLOT_subgroups.sas DATE: 09FEB2022

Verbesserung

109MS306_Table51_TTE_improvement_DESCRIBE_male

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for male sex

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	4 (19)	3 (17)	7 (18)
Number of subjects without confirmed improvement of disability (a)	17 (81)	15 (83)	32 (82)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	11.6	24.4	23.4
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	3 (15.0)	0 (0.0)	3 (8.1)
12 weeks, 95% CI	(5.1, 39.6)	NA	(2.7, 23.1)
24 weeks, n (%)	4 (20.0)	1 (5.9)	5 (13.5)
24 weeks, 95% CI	(8.0, 44.9)	(0.9, 35.0)	(5.9, 29.5)
36 weeks, n (%)	4 (20.0)	2 (11.8)	6 (16.3)
36 weeks, 95% CI	(8.0, 44.9)	(3.1, 39.4)	(7.7, 32.7)
48 weeks, n (%)	4 (20.0)	2 (11.8)	6 (16.3)
48 weeks, 95% CI	(8.0, 44.9)	(3.1, 39.4)	(7.7, 32.7)
60 weeks, n (%)	4 (20.0)	2 (11.8)	6 (16.3)
60 weeks, 95% CI	(8.0, 44.9)	(3.1, 39.4)	(7.7, 32.7)
72 weeks, n (%)	4 (20.0)	2 (11.8)	6 (16.3)
72 weeks, 95% CI	(8.0, 44.9)	(3.1, 39.4)	(7.7, 32.7)
84 weeks, n (%)	4 (20.0)	3 (20.6)	7 (19.9)
84 weeks, 95% CI	(8.0, 44.9)	(6.9, 52.4)	(10.0, 37.6)
96 weeks, n (%)	4 (20.0)	3 (20.6)	7 (19.9)
96 weeks, 95% CI	(8.0, 44.9)	(6.9, 52.4)	(10.0, 37.6)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	17 (85.0)	17 (NA)	34 (91.9)
12 weeks, 95% CI	(60.4, 94.9)	NA	(76.9, 97.3)
24 weeks, n (%)	16 (80.0)	16 (94.1)	32 (86.5)
24 weeks, 95% CI	(55.1, 92.0)	(65.0, 99.1)	(70.5, 94.1)
36 weeks, n (%)	15 (80.0)	14 (88.2)	29 (83.7)
36 weeks, 95% CI	(55.1, 92.0)	(60.6, 96.9)	(67.3, 92.3)
48 weeks, n (%)	15 (80.0)	14 (88.2)	29 (83.7)
48 weeks, 95% CI	(55.1, 92.0)	(60.6, 96.9)	(67.3, 92.3)
60 weeks, n (%)	15 (80.0)	12 (88.2)	27 (83.7)
60 weeks, 95% CI	(55.1, 92.0)	(60.6, 96.9)	(67.3, 92.3)
72 weeks, n (%)	14 (80.0)	12 (88.2)	26 (83.7)
72 weeks, 95% CI	(55.1, 92.0)	(60.6, 96.9)	(67.3, 92.3)
84 weeks, n (%)	13 (80.0)	9 (79.4)	22 (80.1)
84 weeks, 95% CI	(55.1, 92.0)	(47.6, 93.1)	(62.4, 90.0)
96 weeks, n (%)	5 (80.0)	4 (79.4)	9 (80.1)
96 weeks, 95% CI	(55.1, 92.0)	(47.6, 93.1)	(62.4, 90.0)
Hazard ratio (DMF vs IFN B-1a) (c)	1.157		
95% CI (c)	(0.254, 5.283)		
p-value (c)	0.8504		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	3 (14)	0	3 (8)
Number of subjects without confirmed improvement of disability (a)	18 (86)	18 (100)	36 (92)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	12.1	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	2 (10.0)	0 (0.0)	2 (5.4)
12 weeks, 95% CI	(2.6, 34.4)	NA	(1.4, 19.9)
24 weeks, n (%)	2 (10.0)	0 (0.0)	2 (5.4)
24 weeks, 95% CI	(2.6, 34.4)	NA	(1.4, 19.9)
36 weeks, n (%)	2 (10.0)	0 (0.0)	2 (5.4)
36 weeks, 95% CI	(2.6, 34.4)	NA	(1.4, 19.9)
48 weeks, n (%)	3 (15.3)	0 (0.0)	3 (8.4)
48 weeks, 95% CI	(5.2, 40.3)	NA	(2.8, 23.8)
60 weeks, n (%)	3 (15.3)	0 (0.0)	3 (8.4)
60 weeks, 95% CI	(5.2, 40.3)	NA	(2.8, 23.8)
72 weeks, n (%)	3 (15.3)	0 (0.0)	3 (8.4)
72 weeks, 95% CI	(5.2, 40.3)	NA	(2.8, 23.8)
84 weeks, n (%)	3 (15.3)	0 (0.0)	3 (8.4)
84 weeks, 95% CI	(5.2, 40.3)	NA	(2.8, 23.8)
96 weeks, n (%)	3 (15.3)	0 (0.0)	3 (8.4)
96 weeks, 95% CI	(5.2, 40.3)	NA	(2.8, 23.8)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	18 (90.0)	17 (NA)	35 (94.6)
12 weeks, 95% CI	(65.6, 97.4)	NA	(80.1, 98.6)
24 weeks, n (%)	18 (90.0)	17 (NA)	35 (94.6)
24 weeks, 95% CI	(65.6, 97.4)	NA	(80.1, 98.6)
36 weeks, n (%)	17 (90.0)	16 (NA)	33 (94.6)
36 weeks, 95% CI	(65.6, 97.4)	NA	(80.1, 98.6)
48 weeks, n (%)	16 (84.7)	15 (NA)	31 (91.6)
48 weeks, 95% CI	(59.7, 94.8)	NA	(76.2, 97.2)
60 weeks, n (%)	16 (84.7)	12 (NA)	28 (91.6)
60 weeks, 95% CI	(59.7, 94.8)	NA	(76.2, 97.2)
72 weeks, n (%)	15 (84.7)	12 (NA)	27 (91.6)
72 weeks, 95% CI	(59.7, 94.8)	NA	(76.2, 97.2)
84 weeks, n (%)	14 (84.7)	10 (NA)	24 (91.6)
84 weeks, 95% CI	(59.7, 94.8)	NA	(76.2, 97.2)
96 weeks, n (%)	6 (84.7)	5 (NA)	11 (91.6)
96 weeks, 95% CI	(59.7, 94.8)	NA	(76.2, 97.2)
Hazard ratio (DMF vs IFN B-1a) (c)	909E5		
95% CI (c)	(0.000, NA)		
p-value (c)	0.9975		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

109MS306_Table51_TTE_improvement_DESCRIBE_female

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for female sex

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	14 (28)	4 (9)	18 (19)
Number of subjects without confirmed improvement of disability (a)	36 (72)	42 (91)	78 (81)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	36.0	73.7	36.4
25th percentile	48.1	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	2 (4.3)	0 (0.0)	2 (2.2)
12 weeks, 95% CI	(1.1, 16.0)	NA	(0.6, 8.6)
24 weeks, n (%)	3 (6.5)	2 (5.0)	5 (5.8)
24 weeks, 95% CI	(2.1, 18.8)	(1.3, 18.6)	(2.4, 13.3)
36 weeks, n (%)	6 (13.2)	2 (5.0)	8 (9.4)
36 weeks, 95% CI	(6.1, 27.0)	(1.3, 18.6)	(4.8, 18.0)
48 weeks, n (%)	12 (26.9)	3 (8.0)	15 (18.4)
48 weeks, 95% CI	(16.2, 42.5)	(2.6, 22.8)	(11.5, 28.7)
60 weeks, n (%)	12 (26.9)	3 (8.0)	15 (18.4)
60 weeks, 95% CI	(16.2, 42.5)	(2.6, 22.8)	(11.5, 28.7)
72 weeks, n (%)	13 (29.6)	3 (8.0)	16 (19.9)
72 weeks, 95% CI	(18.3, 45.6)	(2.6, 22.8)	(12.7, 30.5)
84 weeks, n (%)	13 (29.6)	4 (11.4)	17 (21.4)
84 weeks, 95% CI	(18.3, 45.6)	(4.4, 27.8)	(13.8, 32.3)
96 weeks, n (%)	14 (32.4)	4 (11.4)	18 (23.0)
96 weeks, 95% CI	(20.5, 48.8)	(4.4, 27.8)	(15.1, 34.1)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	45 (95.7)	41 (NA)	86 (97.8)
12 weeks, 95% CI	(84.0, 98.9)	NA	(91.4, 99.4)
24 weeks, n (%)	42 (93.5)	37 (95.0)	79 (94.2)
24 weeks, 95% CI	(81.2, 97.9)	(81.4, 98.7)	(86.7, 97.6)
36 weeks, n (%)	39 (86.8)	35 (95.0)	74 (90.6)
36 weeks, 95% CI	(73.0, 93.9)	(81.4, 98.7)	(82.0, 95.2)
48 weeks, n (%)	31 (73.1)	31 (92.0)	62 (81.6)
48 weeks, 95% CI	(57.5, 83.8)	(77.2, 97.4)	(71.3, 88.5)
60 weeks, n (%)	29 (73.1)	27 (92.0)	56 (81.6)
60 weeks, 95% CI	(57.5, 83.8)	(77.2, 97.4)	(71.3, 88.5)
72 weeks, n (%)	26 (70.4)	27 (92.0)	53 (80.1)
72 weeks, 95% CI	(54.4, 81.7)	(77.2, 97.4)	(69.5, 87.3)
84 weeks, n (%)	25 (70.4)	25 (88.6)	50 (78.6)
84 weeks, 95% CI	(54.4, 81.7)	(72.2, 95.6)	(67.7, 86.2)
96 weeks, n (%)	9 (67.6)	5 (88.6)	14 (77.0)
96 weeks, 95% CI	(51.2, 79.5)	(72.2, 95.6)	(65.9, 84.9)
Hazard ratio (DMF vs IFN B-1a) (c)	3.183		
95% CI (c)	(1.045, 9.694)		
p-value (c)	0.0416		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	11 (22)	2 (4)	13 (14)
Number of subjects without confirmed improvement of disability (a)	39 (78)	44 (96)	83 (86)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	36.1	NA	47.6
25th percentile	72.1	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	1 (2.1)	0 (0.0)	1 (1.1)
12 weeks, 95% CI	(0.3, 14.2)	NA	(0.2, 7.6)
24 weeks, n (%)	2 (4.4)	1 (2.4)	3 (3.4)
24 weeks, 95% CI	(1.1, 16.3)	(0.3, 16.1)	(1.1, 10.3)
36 weeks, n (%)	5 (11.0)	1 (2.4)	6 (7.1)
36 weeks, 95% CI	(4.7, 24.5)	(0.3, 16.1)	(3.2, 15.1)
48 weeks, n (%)	10 (22.5)	2 (5.4)	12 (14.8)
48 weeks, 95% CI	(12.8, 37.8)	(1.4, 20.0)	(8.7, 24.6)
60 weeks, n (%)	10 (22.5)	2 (5.4)	12 (14.8)
60 weeks, 95% CI	(12.8, 37.8)	(1.4, 20.0)	(8.7, 24.6)
72 weeks, n (%)	11 (25.2)	2 (5.4)	13 (16.3)
72 weeks, 95% CI	(14.8, 41.0)	(1.4, 20.0)	(9.8, 26.5)
84 weeks, n (%)	11 (25.2)	2 (5.4)	13 (16.3)
84 weeks, 95% CI	(14.8, 41.0)	(1.4, 20.0)	(9.8, 26.5)
96 weeks, n (%)	11 (25.2)	2 (5.4)	13 (16.3)
96 weeks, 95% CI	(14.8, 41.0)	(1.4, 20.0)	(9.8, 26.5)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	46 (97.9)	41 (NA)	87 (98.9)
12 weeks, 95% CI	(85.8, 99.7)	NA	(92.4, 99.8)
24 weeks, n (%)	43 (95.6)	38 (97.6)	81 (96.6)
24 weeks, 95% CI	(83.7, 98.9)	(83.9, 99.7)	(89.7, 98.9)
36 weeks, n (%)	40 (89.0)	36 (97.6)	76 (92.9)
36 weeks, 95% CI	(75.5, 95.3)	(83.9, 99.7)	(84.9, 96.8)
48 weeks, n (%)	33 (77.5)	32 (94.6)	65 (85.2)
48 weeks, 95% CI	(62.2, 87.2)	(80.0, 98.6)	(75.4, 91.3)
60 weeks, n (%)	31 (77.5)	28 (94.6)	59 (85.2)
60 weeks, 95% CI	(62.2, 87.2)	(80.0, 98.6)	(75.4, 91.3)
72 weeks, n (%)	27 (74.8)	28 (94.6)	55 (83.7)
72 weeks, 95% CI	(59.0, 85.2)	(80.0, 98.6)	(73.5, 90.2)
84 weeks, n (%)	26 (74.8)	27 (94.6)	53 (83.7)
84 weeks, 95% CI	(59.0, 85.2)	(80.0, 98.6)	(73.5, 90.2)
96 weeks, n (%)	10 (74.8)	5 (94.6)	15 (83.7)
96 weeks, 95% CI	(59.0, 85.2)	(80.0, 98.6)	(73.5, 90.2)
Hazard ratio (DMF vs IFN B-1a) (c)	4.958		
95% CI (c)	(1.097, 22.414)		
p-value (c)	0.0375		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

109MS306_Table51_TTE_improvement_DESCRIBE_age15to17

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for Ages 15 to 17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	14 (26)	6 (12)	20 (19)
Number of subjects without confirmed improvement of disability (a)	39 (74)	44 (88)	83 (81)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	24.1	73.7	36.0
25th percentile	72.1	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	4 (8.0)	0 (0.0)	4 (4.1)
12 weeks, 95% CI	(3.1, 19.9)	NA	(1.6, 10.6)
24 weeks, n (%)	5 (10.0)	2 (4.3)	7 (7.3)
24 weeks, 95% CI	(4.3, 22.5)	(1.1, 16.3)	(3.5, 14.7)
36 weeks, n (%)	8 (16.3)	3 (6.5)	11 (11.6)
36 weeks, 95% CI	(8.5, 30.0)	(2.2, 18.9)	(6.6, 20.0)
48 weeks, n (%)	12 (24.9)	4 (9.0)	16 (17.4)
48 weeks, 95% CI	(15.0, 39.7)	(3.5, 22.4)	(11.0, 26.9)
60 weeks, n (%)	12 (24.9)	4 (9.0)	16 (17.4)
60 weeks, 95% CI	(15.0, 39.7)	(3.5, 22.4)	(11.0, 26.9)
72 weeks, n (%)	13 (27.5)	4 (9.0)	17 (18.8)
72 weeks, 95% CI	(16.9, 42.8)	(3.5, 22.4)	(12.1, 28.5)
84 weeks, n (%)	13 (27.5)	6 (15.0)	19 (21.6)
84 weeks, 95% CI	(16.9, 42.8)	(7.0, 30.8)	(14.3, 31.9)
96 weeks, n (%)	14 (30.3)	6 (15.0)	20 (23.0)
96 weeks, 95% CI	(19.1, 46.0)	(7.0, 30.8)	(15.4, 33.6)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	46 (92.0)	46 (NA)	92 (95.9)
12 weeks, 95% CI	(80.1, 96.9)	NA	(89.4, 98.4)
24 weeks, n (%)	44 (90.0)	44 (95.7)	88 (92.7)
24 weeks, 95% CI	(77.5, 95.7)	(83.7, 98.9)	(85.3, 96.5)
36 weeks, n (%)	40 (83.7)	40 (93.5)	80 (88.4)
36 weeks, 95% CI	(70.0, 91.5)	(81.1, 97.8)	(80.0, 93.4)
48 weeks, n (%)	34 (75.1)	36 (91.0)	70 (82.6)
48 weeks, 95% CI	(60.3, 85.0)	(77.6, 96.5)	(73.1, 89.0)
60 weeks, n (%)	32 (75.1)	32 (91.0)	64 (82.6)
60 weeks, 95% CI	(60.3, 85.0)	(77.6, 96.5)	(73.1, 89.0)
72 weeks, n (%)	28 (72.5)	32 (91.0)	60 (81.2)
72 weeks, 95% CI	(57.2, 83.1)	(77.6, 96.5)	(71.5, 87.9)
84 weeks, n (%)	26 (72.5)	28 (85.0)	54 (78.4)
84 weeks, 95% CI	(57.2, 83.1)	(69.2, 93.0)	(68.1, 85.7)
96 weeks, n (%)	9 (69.7)	7 (85.0)	16 (77.0)
96 weeks, 95% CI	(54.0, 80.9)	(69.2, 93.0)	(66.4, 84.6)
Hazard ratio (DMF vs IFN B-1a) (c)	2.265		
95% CI (c)	(0.865, 5.932)		
p-value (c)	0.0960		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	12 (23)	1 (2)	13 (13)
Number of subjects without confirmed improvement of disability (a)	41 (77)	49 (98)	90 (87)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	35.6	NA	47.6
25th percentile	72.1	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	3 (6.0)	0 (0.0)	3 (3.1)
12 weeks, 95% CI	(2.0, 17.5)	NA	(1.0, 9.3)
24 weeks, n (%)	4 (8.0)	0 (0.0)	4 (4.2)
24 weeks, 95% CI	(3.1, 20.0)	NA	(1.6, 10.7)
36 weeks, n (%)	7 (14.3)	0 (0.0)	7 (7.4)
36 weeks, 95% CI	(7.1, 27.7)	NA	(3.6, 14.9)
48 weeks, n (%)	11 (22.9)	1 (2.6)	12 (13.2)
48 weeks, 95% CI	(13.4, 37.6)	(0.4, 16.8)	(7.7, 22.2)
60 weeks, n (%)	11 (22.9)	1 (2.6)	12 (13.2)
60 weeks, 95% CI	(13.4, 37.6)	(0.4, 16.8)	(7.7, 22.2)
72 weeks, n (%)	12 (25.6)	1 (2.6)	13 (14.6)
72 weeks, 95% CI	(15.3, 40.7)	(0.4, 16.8)	(8.7, 24.0)
84 weeks, n (%)	12 (25.6)	1 (2.6)	13 (14.6)
84 weeks, 95% CI	(15.3, 40.7)	(0.4, 16.8)	(8.7, 24.0)
96 weeks, n (%)	12 (25.6)	1 (2.6)	13 (14.6)
96 weeks, 95% CI	(15.3, 40.7)	(0.4, 16.8)	(8.7, 24.0)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	47 (94.0)	46 (NA)	93 (96.9)
12 weeks, 95% CI	(82.5, 98.0)	NA	(90.7, 99.0)
24 weeks, n (%)	45 (92.0)	46 (NA)	91 (95.8)
24 weeks, 95% CI	(80.0, 96.9)	NA	(89.3, 98.4)
36 weeks, n (%)	41 (85.7)	43 (NA)	84 (92.6)
36 weeks, 95% CI	(72.3, 92.9)	NA	(85.1, 96.4)
48 weeks, n (%)	35 (77.1)	38 (97.4)	73 (86.8)
48 weeks, 95% CI	(62.4, 86.6)	(83.2, 99.6)	(77.8, 92.3)
60 weeks, n (%)	33 (77.1)	33 (97.4)	66 (86.8)
60 weeks, 95% CI	(62.4, 86.6)	(83.2, 99.6)	(77.8, 92.3)
72 weeks, n (%)	28 (74.4)	33 (97.4)	61 (85.4)
72 weeks, 95% CI	(59.3, 84.7)	(83.2, 99.6)	(76.0, 91.3)
84 weeks, n (%)	26 (74.4)	31 (97.4)	57 (85.4)
84 weeks, 95% CI	(59.3, 84.7)	(83.2, 99.6)	(76.0, 91.3)
96 weeks, n (%)	10 (74.4)	8 (97.4)	18 (85.4)
96 weeks, 95% CI	(59.3, 84.7)	(83.2, 99.6)	(76.0, 91.3)
Hazard ratio (DMF vs IFN B-1a) (c)	12.08		
95% CI (c)	(1.567, 93.124)		
p-value (c)	0.0168		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

109MS306_Table51_TTE_improvement_DESCRIBE_age13to14

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for Ages 13 to 14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	4 (22)	1 (7)	5 (16)
Number of subjects without confirmed improvement of disability (a)	14 (78)	13 (93)	27 (84)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	23.4	NA	23.4
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	1 (5.9)	0 (0.0)	1 (3.4)
12 weeks, 95% CI	(0.9, 35.0)	NA	(0.5, 22.1)
24 weeks, n (%)	2 (12.2)	1 (8.3)	3 (10.8)
24 weeks, 95% CI	(3.2, 40.5)	(1.2, 46.1)	(3.6, 29.9)
36 weeks, n (%)	2 (12.2)	1 (8.3)	3 (10.8)
36 weeks, 95% CI	(3.2, 40.5)	(1.2, 46.1)	(3.6, 29.9)
48 weeks, n (%)	4 (24.7)	1 (8.3)	5 (18.5)
48 weeks, 95% CI	(10.1, 53.2)	(1.2, 46.1)	(8.1, 39.1)
60 weeks, n (%)	4 (24.7)	1 (8.3)	5 (18.5)
60 weeks, 95% CI	(10.1, 53.2)	(1.2, 46.1)	(8.1, 39.1)
72 weeks, n (%)	4 (24.7)	1 (8.3)	5 (18.5)
72 weeks, 95% CI	(10.1, 53.2)	(1.2, 46.1)	(8.1, 39.1)
84 weeks, n (%)	4 (24.7)	1 (8.3)	5 (18.5)
84 weeks, 95% CI	(10.1, 53.2)	(1.2, 46.1)	(8.1, 39.1)
96 weeks, n (%)	4 (24.7)	1 (8.3)	5 (18.5)
96 weeks, 95% CI	(10.1, 53.2)	(1.2, 46.1)	(8.1, 39.1)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	16 (94.1)	12 (NA)	28 (96.6)
12 weeks, 95% CI	(65.0, 99.1)	NA	(77.9, 99.5)
24 weeks, n (%)	14 (87.8)	9 (91.7)	23 (89.2)
24 weeks, 95% CI	(59.5, 96.8)	(53.9, 98.8)	(70.1, 96.4)
36 weeks, n (%)	14 (87.8)	9 (91.7)	23 (89.2)
36 weeks, 95% CI	(59.5, 96.8)	(53.9, 98.8)	(70.1, 96.4)
48 weeks, n (%)	12 (75.3)	9 (91.7)	21 (81.5)
48 weeks, 95% CI	(46.8, 89.9)	(53.9, 98.8)	(60.9, 91.9)
60 weeks, n (%)	12 (75.3)	7 (91.7)	19 (81.5)
60 weeks, 95% CI	(46.8, 89.9)	(53.9, 98.8)	(60.9, 91.9)
72 weeks, n (%)	12 (75.3)	7 (91.7)	19 (81.5)
72 weeks, 95% CI	(46.8, 89.9)	(53.9, 98.8)	(60.9, 91.9)
84 weeks, n (%)	12 (75.3)	6 (91.7)	18 (81.5)
84 weeks, 95% CI	(46.8, 89.9)	(53.9, 98.8)	(60.9, 91.9)
96 weeks, n (%)	5 (75.3)	2 (91.7)	7 (81.5)
96 weeks, 95% CI	(46.8, 89.9)	(53.9, 98.8)	(60.9, 91.9)
Hazard ratio (DMF vs IFN B-1a) (c)	2.844		
95% CI (c)	(0.317, 25.497)		
p-value (c)	0.3503		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.

(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	2 (11)	1 (7)	3 (9)
Number of subjects without confirmed improvement of disability (a)	16 (89)	13 (93)	29 (91)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	48.1	NA	48.1
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,
or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.
Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	0 (0.0)	1 (8.3)	1 (3.4)
24 weeks, 95% CI	NA	(1.2, 46.1)	(0.5, 22.1)
36 weeks, n (%)	0 (0.0)	1 (8.3)	1 (3.4)
36 weeks, 95% CI	NA	(1.2, 46.1)	(0.5, 22.1)
48 weeks, n (%)	2 (12.5)	1 (8.3)	3 (11.2)
48 weeks, 95% CI	(3.3, 41.4)	(1.2, 46.1)	(3.7, 30.8)
60 weeks, n (%)	2 (12.5)	1 (8.3)	3 (11.2)
60 weeks, 95% CI	(3.3, 41.4)	(1.2, 46.1)	(3.7, 30.8)
72 weeks, n (%)	2 (12.5)	1 (8.3)	3 (11.2)
72 weeks, 95% CI	(3.3, 41.4)	(1.2, 46.1)	(3.7, 30.8)
84 weeks, n (%)	2 (12.5)	1 (8.3)	3 (11.2)
84 weeks, 95% CI	(3.3, 41.4)	(1.2, 46.1)	(3.7, 30.8)
96 weeks, n (%)	2 (12.5)	1 (8.3)	3 (11.2)
96 weeks, 95% CI	(3.3, 41.4)	(1.2, 46.1)	(3.7, 30.8)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	17 (NA)	12 (NA)	29 (NA)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	16 (NA)	9 (91.7)	25 (96.6)
24 weeks, 95% CI	NA	(53.9, 98.8)	(77.9, 99.5)
36 weeks, n (%)	16 (NA)	9 (91.7)	25 (96.6)
36 weeks, 95% CI	NA	(53.9, 98.8)	(77.9, 99.5)
48 weeks, n (%)	14 (87.5)	9 (91.7)	23 (88.8)
48 weeks, 95% CI	(58.6, 96.7)	(53.9, 98.8)	(69.2, 96.3)
60 weeks, n (%)	14 (87.5)	7 (91.7)	21 (88.8)
60 weeks, 95% CI	(58.6, 96.7)	(53.9, 98.8)	(69.2, 96.3)
72 weeks, n (%)	14 (87.5)	7 (91.7)	21 (88.8)
72 weeks, 95% CI	(58.6, 96.7)	(53.9, 98.8)	(69.2, 96.3)
84 weeks, n (%)	14 (87.5)	6 (91.7)	20 (88.8)
84 weeks, 95% CI	(58.6, 96.7)	(53.9, 98.8)	(69.2, 96.3)
96 weeks, n (%)	6 (87.5)	2 (91.7)	8 (88.8)
96 weeks, 95% CI	(58.6, 96.7)	(53.9, 98.8)	(69.2, 96.3)
Hazard ratio (DMF vs IFN B-1a) (c)	1.283		
95% CI (c)	(0.116, 14.220)		
p-value (c)	0.8393		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or were without improvement, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5,

or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks.

Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.

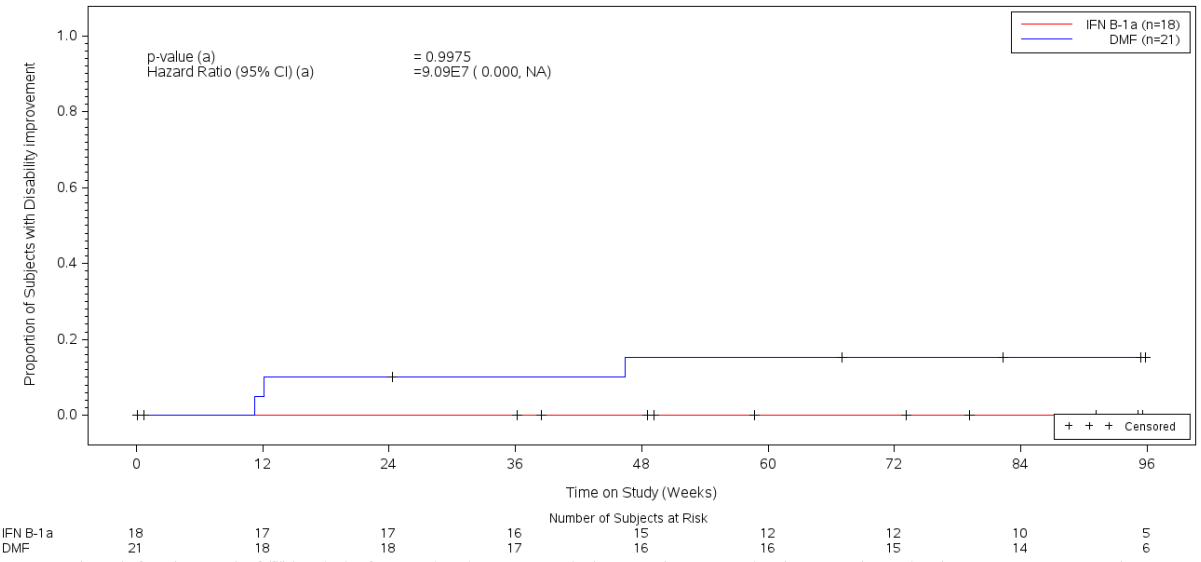
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban031722.sas date: 18MAR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_male

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for male sex



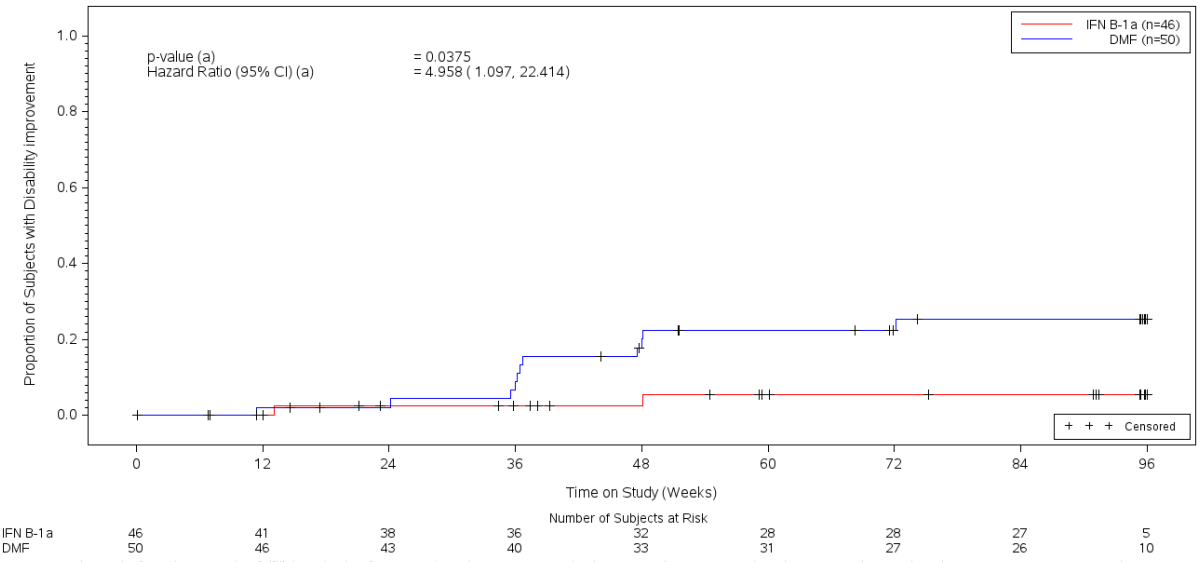
Number of Subjects at Risk

IFN B-1a	18	17	17	16	15	12	12	10	5
DMF	21	18	18	17	16	16	15	14	6

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_female

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for female sex



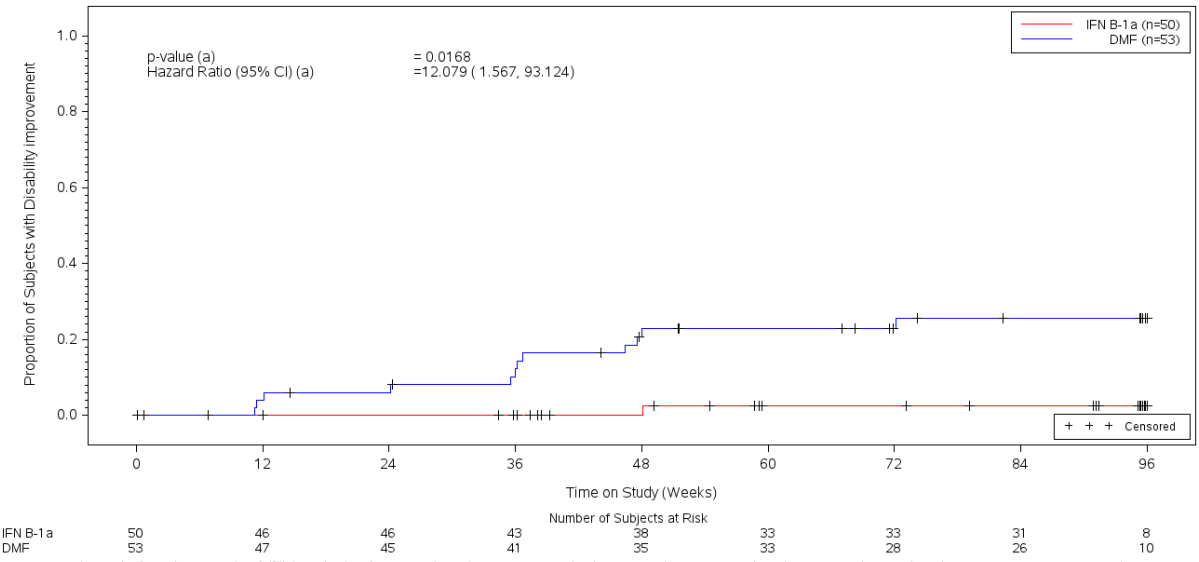
Number of Subjects at Risk

IFN B-1a	46	41	38	36	32	28	28	27	5
DMF	50	46	43	40	33	31	27	26	10

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_age15to17

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for Ages 15 to 17



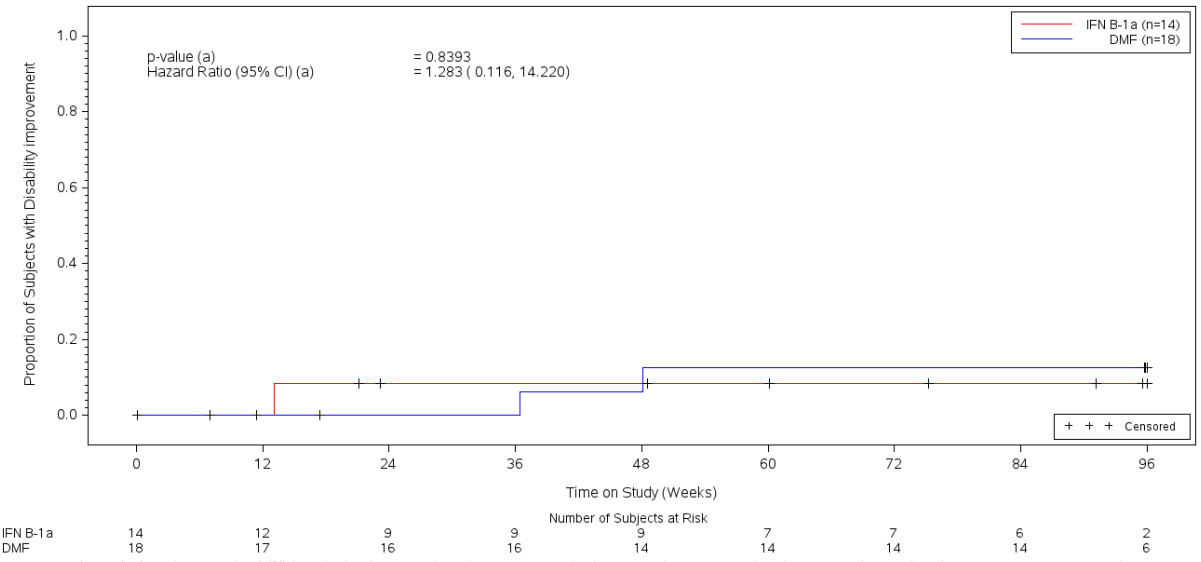
Number of Subjects at Risk

IFN B-1a	50	46	46	43	38	33	33	31	8
DMF	53	47	45	41	35	33	28	26	10

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_age13to14

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for ages 13 to 14



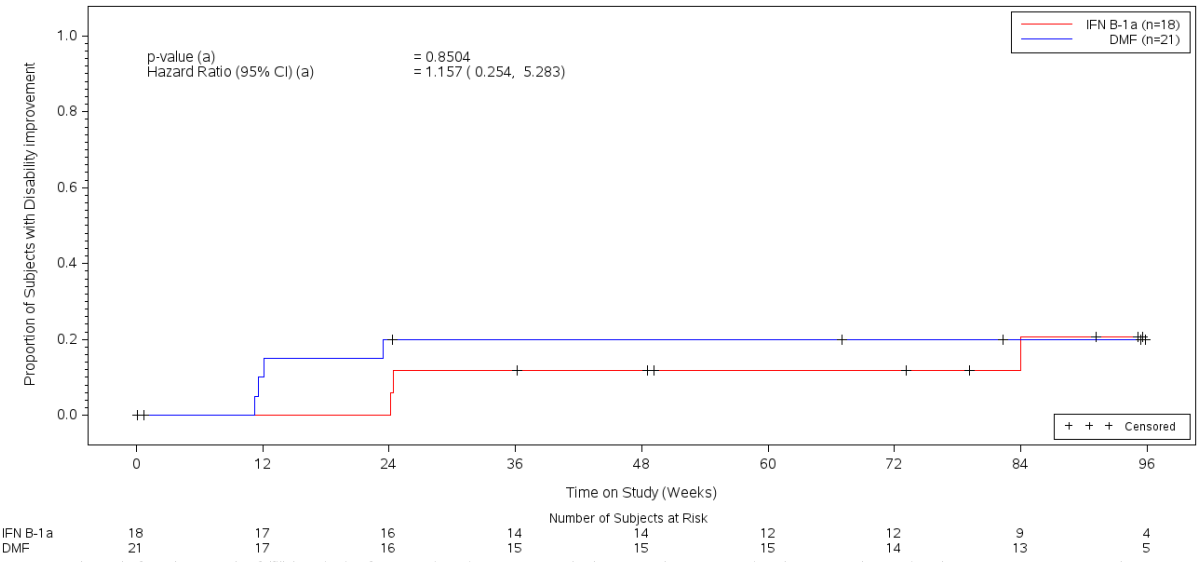
Number of Subjects at Risk

IFN B-1a	14	12	9	9	9	7	7	6	2
DMF	18	17	16	16	14	14	14	14	6

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_male

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for male sex



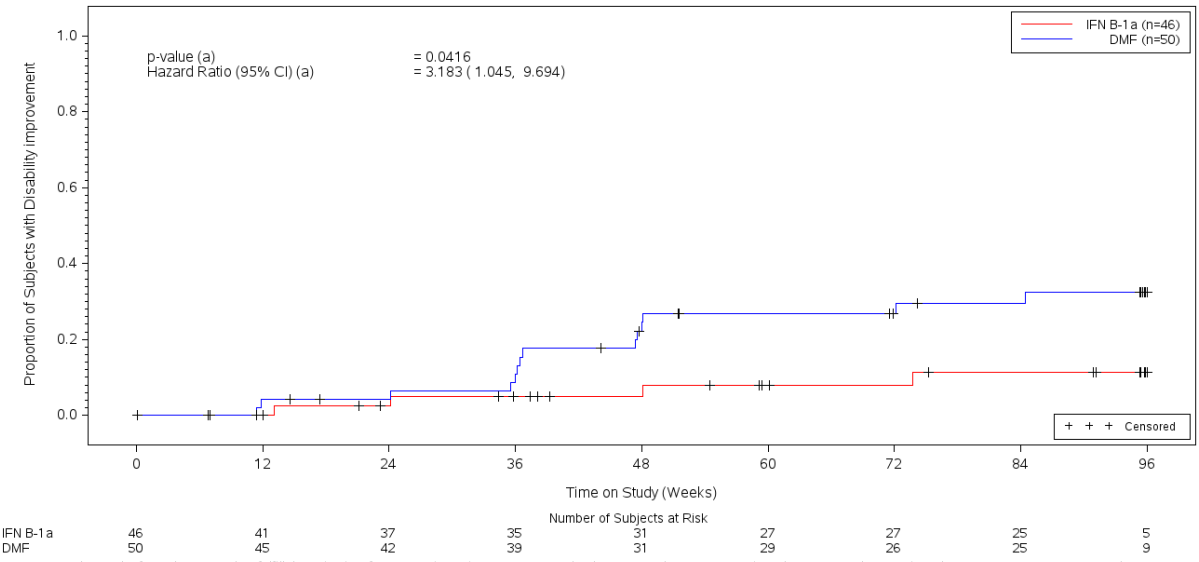
Number of Subjects at Risk

IFN B-1a	18	17	16	14	14	12	12	9	4
DMF	21	17	16	15	15	15	14	13	5

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_female

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for female sex



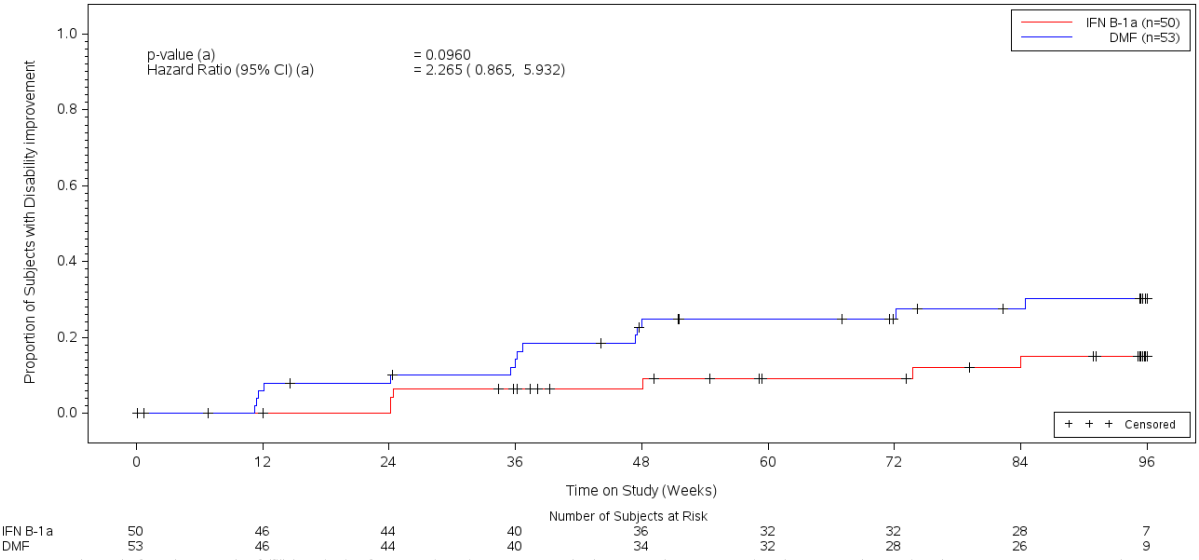
Number of Subjects at Risk

IFN B-1a	46	41	37	35	31	27	27	25	5
DMF	50	45	42	39	31	29	26	25	9

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.rtf DATE: 18MAR2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_age15to17

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for Ages 15 to 17



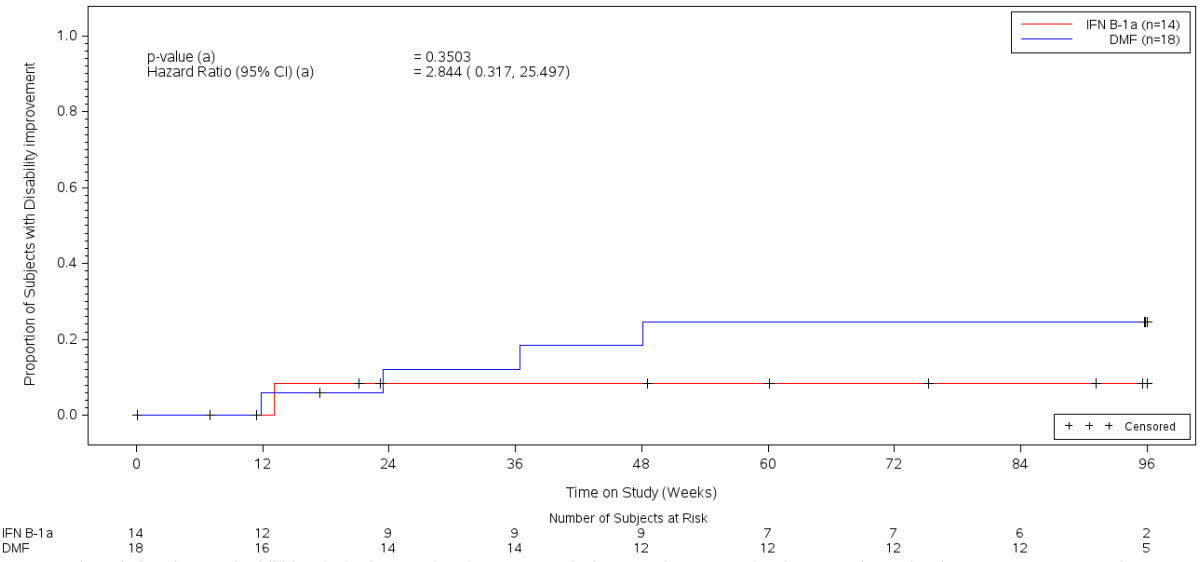
Number of Subjects at Risk

IFN B-1a	50	46	44	40	36	32	32	28	7
DMF	53	46	44	40	34	32	28	26	9

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_age13to14

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for ages 13 to 14



Number of Subjects at Risk

IFN B-1a	14	12	9	9	9	7	7	6	2
DMF	18	16	14	14	12	12	12	12	5

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects with or without improvement, n represents number of people at timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier. When you have censoring or no event, % is not able to be estimated and represented with an NA.
Where there is an estimate at a previous timepoint, but not at current timepoint, n and % are carried forward.
(a) HR based on a Cox proportional hazards model adjusted for age group and baseline EDSS. Plot uses Kaplan-Meier product-limit method
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban01.RTF: 18MAR2022

BVMT-R

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	37 (52)	37 (58)	74 (55)
Mean (SD)	0.4 (2.28)	0.4 (2.08)	0.4 (2.16)
Median	0.0	0.0	0.0
Q1, Q3	-2.0, 2.0	-1.0, 2.0	-1.0, 2.0
Min, Max	-4, 5	-3, 6	-4, 6
Week 96 change from baseline			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	0.5 (2.16)	0.6 (2.75)	0.5 (2.42)
Median	0.0	1.0	0.5
Q1, Q3	-1.0, 2.0	-1.0, 1.0	-1.0, 2.0
Min, Max	-4, 5	-5, 7	-5, 7

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_CHG_DESCRIBE_banupdate012622.sas DATE: 01FEB2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	37 (52)	37 (58)	74 (55)
Mean (SD)	0.6 (2.20)	1.1 (2.18)	0.9 (2.19)
Median	0.0	1.0	1.0
Q1, Q3	-1.0, 2.0	0.0, 2.0	-1.0, 2.0
Min, Max	-4, 6	-5, 6	-5, 6
Week 96 change from baseline			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	0.9 (1.73)	1.0 (2.21)	0.9 (1.94)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 2.0	-1.0, 2.0	-1.0, 2.0
Min, Max	-2, 5	-3, 6	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_CHG_DESCRIBE_banupdate012622.sas DATE: 01FEB2022

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	37 (52)	37 (58)	74 (55)
Mean (SD)	0.4 (1.50)	1.3 (1.97)	0.9 (1.79)
Median	1.0	1.0	1.0
Q1, Q3	0.0, 1.0	0.0, 3.0	0.0, 2.0
Min, Max	-4, 4	-2, 7	-4, 7
Week 96 change from baseline			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	0.7 (2.00)	0.2 (1.56)	0.5 (1.82)
Median	1.0	0.0	1.0
Q1, Q3	-1.0, 2.0	-1.0, 1.0	-1.0, 1.5
Min, Max	-3, 6	-3, 3	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_CHG_DESCRIBE_banupdate012622.sas DATE: 01FEB2022

109MS306_table52_CHG_DESCRIBE

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	41 (58)	37 (58)	78 (58)
Mean (SD)	6.8 (2.51)	5.9 (2.15)	6.4 (2.38)
Median	6.0	6.0	6.0
Q1, Q3	6.0, 9.0	4.0, 7.0	5.0, 8.0
Min, Max	1, 11	2, 12	1, 12
Week 48			
n (%)	50 (70)	44 (69)	94 (70)
Mean (SD)	6.6 (2.58)	6.1 (2.56)	6.4 (2.57)
Median	6.0	6.0	6.0
Q1, Q3	5.0, 9.0	4.0, 8.0	4.0, 8.0
Min, Max	1, 11	2, 12	1, 12
Week 96			
n (%)	51 (72)	40 (63)	91 (67)
Mean (SD)	7.1 (2.59)	6.8 (2.70)	6.9 (2.63)
Median	8.0	6.5	7.0
Q1, Q3	5.0, 9.0	5.0, 9.0	5.0, 9.0
Min, Max	0, 12	3, 12	0, 12

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	41 (58)	37 (58)	78 (58)
Mean (SD)	8.6 (2.45)	7.8 (2.20)	8.3 (2.35)
Median	9.0	8.0	8.0
Q1, Q3	7.0, 11.0	6.0, 9.0	7.0, 10.0
Min, Max	3, 12	3, 12	3, 12
Week 48			
n (%)	50 (70)	44 (69)	94 (70)
Mean (SD)	8.8 (2.26)	8.7 (2.82)	8.8 (2.52)
Median	9.0	10.0	9.0
Q1, Q3	8.0, 10.0	7.0, 11.0	7.0, 10.0
Min, Max	2, 12	1, 12	1, 12
Week 96			
n (%)	51 (72)	40 (63)	91 (67)
Mean (SD)	9.5 (2.25)	9.0 (2.46)	9.2 (2.34)
Median	10.0	10.0	10.0
Q1, Q3	8.0, 11.0	6.0, 11.0	7.0, 11.0
Min, Max	3, 12	5, 12	3, 12

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	41 (58)	37 (58)	78 (58)
Mean (SD)	9.5 (2.05)	8.8 (2.14)	9.1 (2.11)
Median	10.0	9.0	10.0
Q1, Q3	8.0, 11.0	7.0, 10.0	8.0, 11.0
Min, Max	5, 12	4, 12	4, 12
Week 48			
n (%)	50 (70)	44 (69)	94 (70)
Mean (SD)	9.5 (2.23)	9.8 (2.18)	9.7 (2.20)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 11.0	9.0, 11.0	9.0, 11.0
Min, Max	2, 12	4, 12	2, 12
Week 96			
n (%)	51 (72)	40 (63)	91 (67)
Mean (SD)	10.0 (1.80)	9.4 (2.10)	9.7 (1.95)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 12.0	8.0, 11.0	8.0, 11.0
Min, Max	5, 12	5, 12	5, 12

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

109MS306_table52_CHG_HEDGESCI

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-Hedge's CI

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
BVMT101	48 Weeks	-0.037	-0.493	0.418
	96 Weeks	-0.048	-0.575	0.479
BVMT102	48 Weeks	-0.197	-0.654	0.259
	96 Weeks	-0.046	-0.572	0.481
BVMT103	48 Weeks	-0.479	-0.941	-0.017
	96 Weeks	0.276	-0.253	0.805

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T52/109MS306_table52_CHG_HEDGESCI.sasdate: 16FEB2022

109MS306_table52_CHG_LSMEANS_Brief Visuospatial Memory Test-Revised - Trial 1

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
48	n (%)	37 (52)	37 (58)
	Lsmean (SE)	00.44 (0.374)	00.31 (0.378)
	Lsmean_95 % CI	(-0.306, 01.184)	(-0.439, 01.068)
	Diffrence (95% CI)	0.12 (-0.845, 1.094)	
	SE_Difference	0.4860	
	p-value	0.7985	
96	n (%)	31 (44)	25 (39)
	Lsmean (SE)	00.49 (0.453)	00.21 (0.531)
	Lsmean_95 % CI	(-0.417, 01.401)	(-0.855, 01.275)
	Diffrence (95% CI)	0.28 (-1.008, 1.572)	
	SE_Difference	0.6429	
	p-value	0.6630	

109MS306_table52_CHG_LSMEANS_Brief Visuospatial Memory Test-Revised - Trial 2

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
48	n (%)	37 (52)	37 (58)
	Lsmean (SE)	00.85 (0.348)	01.04 (0.354)
	Lsmean_95 % CI	(00.158, 01.545)	(00.338, 01.750)
	Diffrence (95% CI)	-0.19 (-1.098, 0.713)	
	SE_Difference	0.4538	
	p-value	0.6729	
96	n (%)	31 (44)	25 (39)
	Lsmean (SE)	00.89 (0.327)	00.52 (0.390)
	Lsmean_95 % CI	(00.232, 01.543)	(-0.260, 01.305)
	Diffrence (95% CI)	0.36 (-0.577, 1.307)	
	SE_Difference	0.4694	
	p-value	0.4405	

109MS306_table52_CHG_LSMEANS_Brief Visuospatial Memory Test-Revised - Trial 3

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
48	n (%)	37 (52)	37 (58)
	Lsmean (SE)	00.45 (0.286)	01.10 (0.290)
	Lsmean_95 % CI	(-0.119, 01.021)	(00.525, 01.683)
	Diffrence (95% CI)	-0.65 (-1.396, 0.0895)	
	SE_Difference	0.3723	
	p-value	0.0838	
96	n (%)	31 (44)	25 (39)
	Lsmean (SE)	00.73 (0.304)	-0.01 (0.359)
	Lsmean_95 % CI	(00.116, 01.336)	(-0.736, 00.706)
	Diffrence (95% CI)	0.74 (-0.123, 1.605)	
	SE_Difference	0.4306	
	p-value	0.0911	

109MS306_Table52_MCID_15PCT_EFFECTMEASURES

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135)

OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% decrease from baseline	Effect measure	1.667	1.504	0.082
	95% CI	(0.540, 5.149)	(0.606, 3.734)	(-0.095, 0.259)
	p-value	0.3747	0.3790	0.3658
Trial 1 Week 96 >=15% decrease from baseline	Effect measure	0.889	0.902	-0.013
	95% CI	(0.236, 3.354)	(0.284, 2.871)	(-0.162, 0.136)
	p-value	0.8620	0.8620	0.8622
Trial 2 Week 48 >=15% decrease from baseline	Effect measure	1.943	1.805	0.065
	95% CI	(0.449, 8.400)	(0.486, 6.707)	(-0.074, 0.205)
	p-value	0.3739	0.3780	0.3589
Trial 2 Week 96 >=15% decrease from baseline	Effect measure	0.897	0.902	-0.005
	95% CI	(0.120, 6.714)	(0.134, 6.088)	(-0.104, 0.093)
	p-value	0.9161	0.9161	0.9162
Trial 3 Week 48 >=15% decrease from baseline	Effect measure	0.895	0.902	-0.008
	95% CI	(0.169, 4.733)	(0.194, 4.198)	(-0.127, 0.111)
	p-value	0.8959	0.8959	0.8961
Trial 3 Week 96 >=15% decrease from baseline	Effect measure	1.892	1.805	0.044
	95% CI	(0.326, 10.987)	(0.351, 9.287)	(-0.073, 0.160)
	p-value	0.4775	0.4799	0.4640

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sasdate: 28JAN2022

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% increase from baseline	Effect measure	0.862	0.902	-0.032
	95% CI	(0.329, 2.257)	(0.464, 1.755)	(-0.237, 0.174)
	p-value	0.7625	0.7624	0.7626
Trial 1 Week 96 >=15% increase from baseline	Effect measure	1.894	1.654	0.106
	95% CI	(0.622, 5.773)	(0.679, 4.029)	(-0.074, 0.286)
	p-value	0.2610	0.2675	0.2486
Trial 2 Week 48 >=15% increase from baseline	Effect measure	0.607	0.722	-0.113
	95% CI	(0.237, 1.553)	(0.390, 1.336)	(-0.323, 0.098)
	p-value	0.2977	0.2994	0.2945
Trial 2 Week 96 >=15% increase from baseline	Effect measure	0.867	0.902	-0.029
	95% CI	(0.323, 2.326)	(0.445, 1.831)	(-0.229, 0.171)
	p-value	0.7763	0.7762	0.7765
Trial 3 Week 48 >=15% increase from baseline	Effect measure	0.270	0.395	-0.262
	95% CI	(0.095, 0.766)	(0.183, 0.852)	(-0.459, -0.065)
	p-value	0.0138	0.0179	0.0092
Trial 3 Week 96 >=15% increase from baseline	Effect measure	1.800	1.624	0.084
	95% CI	(0.543, 5.964)	(0.598, 4.410)	(-0.084, 0.252)
	p-value	0.3362	0.3411	0.3246

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)

NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sasdate: 28JAN2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135)

N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
BVMT Trial 1 Week 48 >=15% decrease from baseline				
	Yes	10 (14)	6 (9)	16 (12)
	No	31 (44)	31 (48)	62 (46)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 1 Week 96 >=15% decrease from baseline				
	Yes	5 (7)	5 (8)	10 (7)
	No	36 (51)	32 (50)	68 (50)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 2 Week 48 >=15% decrease from baseline				
	Yes	6 (8)	3 (5)	9 (7)
	No	35 (49)	34 (53)	69 (51)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 2 Week 96 >=15% decrease from baseline				
	Yes	2 (3)	2 (3)	4 (3)
	No	39 (55)	35 (55)	74 (55)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 3 Week 48 >=15% decrease from baseline				
	Yes	3 (4)	3 (5)	6 (4)
	No	38 (54)	34 (53)	72 (53)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 3 Week 96 >=15% decrease from baseline				

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
	Yes	4 (6)	2 (3)	6 (4)
	No	37 (52)	35 (55)	72 (53)
	Missing	30 (42)	27 (42)	57 (42)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sasdate: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
BVMT Trial 1 Week 48 >=15% increase from baseline				
	Yes	12 (17)	12 (19)	24 (18)
	No	29 (41)	25 (39)	54 (40)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 1 Week 96 >=15% increase from baseline				
	Yes	11 (15)	6 (9)	17 (13)
	No	30 (42)	31 (48)	61 (45)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 2 Week 48 >=15% increase from baseline				
	Yes	12 (17)	15 (23)	27 (20)
	No	29 (41)	22 (34)	51 (38)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 2 Week 96 >=15% increase from baseline				
	Yes	11 (15)	11 (17)	22 (16)
	No	30 (42)	26 (41)	56 (41)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 3 Week 48 >=15% increase from baseline				
	Yes	7 (10)	16 (25)	23 (17)
	No	34 (48)	21 (33)	55 (41)
	Missing	30 (42)	27 (42)	57 (42)
BVMT Trial 3 Week 96 >=15% increase from baseline				
	Yes	9 (13)	5 (8)	14 (10)
	No	32 (45)	32 (50)	64 (47)
	Missing	30 (42)	27 (42)	57 (42)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sasdate: 28JAN2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135)

N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
BVMT Trial 1 scale Week 0				
	Yes	41 (58)	37 (58)	78 (58)
	No	30 (42)	27 (42)	57 (42)
BVMT Trial 1 scale Week 48				
	Yes	50 (70)	44 (69)	94 (70)
	No	21 (30)	20 (31)	41 (30)
BVMT Trial 1 scale Week 96				
	Yes	51 (72)	40 (63)	91 (67)
	No	20 (28)	24 (38)	44 (33)
BVMT Trial 2 scale Week 0				
	Yes	41 (58)	37 (58)	78 (58)
	No	30 (42)	27 (42)	57 (42)
BVMT Trial 2 scale Week 48				
	Yes	50 (70)	44 (69)	94 (70)
	No	21 (30)	20 (31)	41 (30)
BVMT Trial 2 scale Week 96				
	Yes	51 (72)	40 (63)	91 (67)
	No	20 (28)	24 (38)	44 (33)
BVMT Trial 3 scale Week 0				
	Yes	41 (58)	37 (58)	78 (58)

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
	No	30 (42)	27 (42)	57 (42)
BVMT Trial 3 scale Week 48				
	Yes	50 (70)	44 (69)	94 (70)
	No	21 (30)	20 (31)	41 (30)
BVMT Trial 3 scale Week 96				
	Yes	51 (72)	40 (63)	91 (67)
	No	20 (28)	24 (38)	44 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sasdate: 28JAN2022

Sub groups

Change

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	9 (50)	8 (57)	17 (53)
Mean (SD)	0.3 (2.35)	0.1 (1.96)	0.2 (2.11)
Median	1.0	-0.5	0.0
Q1, Q3	-1.0, 2.0	-1.0, 1.0	-1.0, 2.0
Min, Max	-4, 3	-2, 4	-4, 4
Week 96 change from baseline			
n (%)	9 (50)	4 (29)	13 (41)
Mean (SD)	-0.7 (2.55)	1.0 (2.16)	-0.2 (2.48)
Median	-1.0	0.5	-1.0
Q1, Q3	-2.0, 1.0	-0.5, 2.5	-2.0, 1.0
Min, Max	-4, 4	-1, 4	-4, 4

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	9 (50)	8 (57)	17 (53)
Mean (SD)	1.3 (2.87)	0.9 (1.46)	1.1 (2.26)
Median	1.0	1.5	1.0
Q1, Q3	0.0, 3.0	0.0, 2.0	0.0, 2.0
Min, Max	-4, 6	-2, 2	-4, 6
Week 96 change from baseline			
n (%)	9 (50)	4 (29)	13 (41)
Mean (SD)	0.6 (2.40)	0.3 (1.26)	0.5 (2.07)
Median	0.0	0.0	0.0
Q1, Q3	-1.0, 2.0	-0.5, 1.0	-1.0, 2.0
Min, Max	-2, 5	-1, 2	-2, 5

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	9 (50)	8 (57)	17 (53)
Mean (SD)	0.7 (1.22)	0.5 (1.77)	0.6 (1.46)
Median	1.0	0.5	1.0
Q1, Q3	0.0, 1.0	-1.0, 2.0	0.0, 2.0
Min, Max	-2, 2	-2, 3	-2, 3
Week 96 change from baseline			
n (%)	9 (50)	4 (29)	13 (41)
Mean (SD)	0.3 (2.18)	-0.5 (2.08)	0.1 (2.10)
Median	0.0	-0.5	0.0
Q1, Q3	-1.0, 1.0	-2.0, 1.0	-1.0, 1.0
Min, Max	-3, 4	-3, 2	-3, 4

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	28 (53)	29 (58)	57 (55)
Mean (SD)	0.4 (2.30)	0.5 (2.13)	0.4 (2.20)
Median	0.0	1.0	1.0
Q1, Q3	-2.0, 2.0	-1.0, 2.0	-1.0, 2.0
Min, Max	-4, 5	-3, 6	-4, 6
Week 96 change from baseline			
n (%)	22 (42)	21 (42)	43 (42)
Mean (SD)	1.0 (1.84)	0.5 (2.89)	0.7 (2.39)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 2.0	-1.0, 1.0	-1.0, 2.0
Min, Max	-2, 5	-5, 7	-5, 7

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=53)	**IFN B-1a (N=50)**	**Total (N=103)**
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	28 (53)	29 (58)	57 (55)
Mean (SD)	0.4 (1.95)	1.1 (2.36)	0.8 (2.18)
Median	0.0	1.0	1.0
Q1, Q3	-1.0, 2.0	0.0, 2.0	-1.0, 2.0
Min, Max	-3, 5	-5, 6	-5, 6
Week 96 change from baseline			
n (%)	22 (42)	21 (42)	43 (42)
Mean (SD)	1.0 (1.41)	1.1 (2.34)	1.0 (1.90)
Median	1.0	1.0	1.0
Q1, Q3	0.0, 2.0	-1.0, 3.0	0.0, 2.0
Min, Max	-1, 4	-3, 6	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	28 (53)	29 (58)	57 (55)
Mean (SD)	0.4 (1.59)	1.5 (1.99)	0.9 (1.88)
Median	0.5	1.0	1.0
Q1, Q3	-1.0, 1.0	0.0, 3.0	0.0, 2.0
Min, Max	-4, 4	-2, 7	-4, 7
Week 96 change from baseline			
n (%)	22 (42)	21 (42)	43 (42)
Mean (SD)	0.9 (1.95)	0.4 (1.47)	0.7 (1.73)
Median	1.0	0.0	1.0
Q1, Q3	0.0, 2.0	-1.0, 1.0	-1.0, 2.0
Min, Max	-2, 6	-3, 3	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	28 (56)	25 (54)	53 (55)
Mean (SD)	0.6 (2.28)	0.6 (2.02)	0.6 (2.14)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 2.0	-1.0, 2.0	-1.0, 2.0
Min, Max	-4, 5	-3, 4	-4, 5
Week 96 change from baseline			
n (%)	25 (50)	16 (35)	41 (43)
Mean (SD)	0.9 (2.04)	0.4 (2.42)	0.7 (2.18)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 2.0	-0.5, 1.0	-1.0, 2.0
Min, Max	-3, 5	-5, 5	-5, 5

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	28 (56)	25 (54)	53 (55)
Mean (SD)	0.6 (2.11)	0.7 (2.15)	0.7 (2.11)
Median	0.0	1.0	1.0
Q1, Q3	-1.0, 2.0	0.0, 2.0	-1.0, 2.0
Min, Max	-3, 6	-5, 5	-5, 6
Week 96 change from baseline			
n (%)	25 (50)	16 (35)	41 (43)
Mean (SD)	1.2 (1.59)	0.9 (1.88)	1.1 (1.69)
Median	1.0	1.5	1.0
Q1, Q3	0.0, 2.0	-0.5, 2.0	0.0, 2.0
Min, Max	-1, 5	-3, 4	-3, 5

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=50)	**IFN B-1a (N=46)**	**Total (N=96)**
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	28 (56)	25 (54)	53 (55)
Mean (SD)	0.4 (1.62)	0.9 (1.89)	0.7 (1.75)
Median	1.0	1.0	1.0
Q1, Q3	-0.5, 1.0	0.0, 2.0	0.0, 1.0
Min, Max	-4, 4	-2, 7	-4, 7
Week 96 change from baseline			
n (%)	25 (50)	16 (35)	41 (43)
Mean (SD)	1.0 (1.55)	0.1 (1.44)	0.6 (1.56)
Median	1.0	0.0	1.0
Q1, Q3	0.0, 2.0	-1.0, 1.0	-1.0, 1.0
Min, Max	-2, 4	-3, 3	-3, 4

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	-0.6 (2.13)	0.2 (2.25)	-0.1 (2.17)
Median	0.0	-0.5	0.0
Q1, Q3	-2.0, 1.0	-1.0, 1.0	-1.0, 1.0
Min, Max	-4, 3	-3, 6	-4, 6
Week 96 change from baseline			
n (%)	6 (29)	9 (50)	15 (38)
Mean (SD)	-1.3 (1.75)	1.0 (3.39)	0.1 (3.01)
Median	-1.5	0.0	0.0
Q1, Q3	-2.0, 0.0	-1.0, 4.0	-2.0, 1.0
Min, Max	-4, 1	-3, 7	-4, 7

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	0.8 (2.59)	1.8 (2.12)	1.4 (2.33)
Median	1.0	2.0	2.0
Q1, Q3	0.0, 3.0	0.5, 2.5	0.0, 3.0
Min, Max	-4, 4	-1, 6	-4, 6
Week 96 change from baseline			
n (%)	6 (29)	9 (50)	15 (38)
Mean (SD)	-0.7 (1.51)	1.0 (2.83)	0.3 (2.47)
Median	-1.0	0.0	0.0
Q1, Q3	-2.0, 0.0	-1.0, 3.0	-1.0, 2.0
Min, Max	-2, 2	-3, 6	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

	DMF (N=21)	**IFN B-1a (N=18)**	**Total (N=39)**
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	0.4 (1.13)	2.0 (2.00)	1.3 (1.83)
Median	0.0	2.5	2.0
Q1, Q3	0.0, 1.0	1.0, 3.5	0.0, 3.0
Min, Max	-1, 2	-2, 4	-2, 4
Week 96 change from baseline			
n (%)	6 (29)	9 (50)	15 (38)
Mean (SD)	-0.3 (3.27)	0.6 (1.81)	0.2 (2.43)
Median	-1.5	1.0	0.0
Q1, Q3	-2.0, 0.0	0.0, 2.0	-2.0, 2.0
Min, Max	-3, 6	-3, 3	-3, 6

NOTE: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 09FEB2022
Note: This is based on Change variable (CHG)

109MS306_table52_CHG_DESCRIBE_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	7.9 (2.13)	5.4 (2.56)	6.8 (2.60)
Median	7.0	5.5	7.0
Q1, Q3	6.0, 10.0	3.0, 8.0	5.0, 8.0
Min, Max	5, 11	2, 8	2, 11
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	7.2 (2.44)	5.3 (2.11)	6.3 (2.44)
Median	8.0	5.5	6.0
Q1, Q3	6.0, 9.0	4.0, 7.0	4.0, 9.0
Min, Max	2, 10	2, 9	2, 10
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	6.2 (3.34)	7.3 (3.09)	6.5 (3.23)
Median	6.0	8.0	7.5
Q1, Q3	4.0, 8.0	3.0, 9.0	4.0, 9.0
Min, Max	0, 12	3, 11	0, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	8.9 (2.96)	7.5 (2.56)	8.3 (2.80)
Median	9.0	8.5	9.0
Q1, Q3	8.0, 11.0	5.5, 9.5	6.0, 10.0
Min, Max	3, 12	3, 10	3, 12
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	9.2 (2.49)	8.0 (4.22)	8.7 (3.32)
Median	9.0	10.0	10.0
Q1, Q3	9.0, 10.0	5.0, 11.0	8.0, 11.0
Min, Max	2, 12	1, 12	1, 12
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	8.6 (2.77)	8.6 (2.51)	8.6 (2.63)
Median	9.0	10.0	9.5
Q1, Q3	7.0, 11.0	6.0, 11.0	7.0, 11.0
Min, Max	3, 12	5, 11	3, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	9.9 (1.91)	8.4 (2.45)	9.2 (2.24)
Median	10.5	8.5	9.5
Q1, Q3	9.0, 11.0	6.5, 10.0	8.0, 11.0
Min, Max	6, 12	5, 12	5, 12
Week 48			
n (%)	1 (72)	1 (71)	2 (72)
Mean (SD)	9.8 (2.70)	8.8 (2.78)	9.4 (2.73)
Median	11.0	10.0	10.0
Q1, Q3	10.0, 11.0	6.0, 11.0	9.0, 11.0
Min, Max	2, 12	4, 12	2, 12
Week 96			
n (%)	1 (83)	(50)	2 (69)
Mean (SD)	9.0 (2.27)	9.3 (2.29)	9.1 (2.22)
Median	8.0	10.0	8.5
Q1, Q3	7.0, 12.0	7.0, 11.0	7.0, 11.0
Min, Max	5, 12	6, 12	5, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_DESCRIBE_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	31 (58)	29 (58)	60 (58)
Mean (SD)	6.5 (2.55)	6.1 (2.05)	6.3 (2.31)
Median	6.0	6.0	6.0
Q1, Q3	5.0, 8.0	5.0, 7.0	5.0, 8.0
Min, Max	1, 11	3, 12	1, 12
Week 48			
n (%)	37 (70)	34 (68)	71 (69)
Mean (SD)	6.4 (2.63)	6.4 (2.65)	6.4 (2.62)
Median	6.0	6.0	6.0
Q1, Q3	5.0, 8.0	4.0, 8.0	4.0, 8.0
Min, Max	1, 11	2, 12	1, 12
Week 96			
n (%)	36 (68)	33 (66)	69 (67)
Mean (SD)	7.4 (2.16)	6.6 (2.64)	7.1 (2.42)
Median	8.0	6.0	7.0
Q1, Q3	6.0, 9.0	5.0, 8.0	5.0, 9.0
Min, Max	3, 11	3, 12	3, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	31 (58)	29 (58)	60 (58)
Mean (SD)	8.5 (2.31)	7.9 (2.14)	8.3 (2.23)
Median	9.0	8.0	8.0
Q1, Q3	7.0, 10.0	7.0, 9.0	7.0, 10.0
Min, Max	3, 12	4, 12	3, 12
Week 48			
n (%)	37 (70)	34 (68)	71 (69)
Mean (SD)	8.7 (2.19)	8.9 (2.31)	8.8 (2.23)
Median	9.0	9.5	9.0
Q1, Q3	7.0, 10.0	7.0, 11.0	7.0, 10.0
Min, Max	2, 12	4, 12	2, 12
Week 96			
n (%)	36 (68)	33 (66)	69 (67)
Mean (SD)	9.8 (1.92)	9.0 (2.48)	9.4 (2.23)
Median	10.5	10.0	10.0
Q1, Q3	9.0, 11.0	6.0, 11.0	8.0, 11.0
Min, Max	4, 12	5, 12	4, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	31 (58)	29 (58)	60 (58)
Mean (SD)	9.3 (2.10)	8.9 (2.08)	9.1 (2.08)
Median	10.0	9.0	10.0
Q1, Q3	7.0, 11.0	7.0, 11.0	7.0, 11.0
Min, Max	5, 12	4, 12	4, 12
Week 48			
n (%)	37 (70)	34 (68)	71 (69)
Mean (SD)	9.4 (2.08)	10.1 (1.93)	9.7 (2.02)
Median	10.0	11.0	10.0
Q1, Q3	7.0, 11.0	9.0, 12.0	9.0, 11.0
Min, Max	6, 12	5, 12	5, 12
Week 96			
n (%)	36 (68)	33 (66)	69 (67)
Mean (SD)	10.4 (1.40)	9.4 (2.09)	9.9 (1.82)
Median	11.0	10.0	10.0
Q1, Q3	9.0, 12.0	8.0, 11.0	9.0, 11.0
Min, Max	8, 12	5, 12	5, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_DESCRIBE_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	32 (64)	25 (54)	57 (59)
Mean (SD)	7.0 (2.55)	6.1 (2.33)	6.6 (2.47)
Median	6.5	6.0	6.0
Q1, Q3	6.0, 9.0	5.0, 8.0	5.0, 8.0
Min, Max	1, 11	2, 12	1, 12
Week 48			
n (%)	36 (72)	31 (67)	67 (70)
Mean (SD)	7.1 (2.31)	6.4 (2.81)	6.8 (2.56)
Median	7.0	6.0	7.0
Q1, Q3	5.5, 9.0	4.0, 8.0	5.0, 9.0
Min, Max	2, 11	2, 12	2, 12
Week 96			
n (%)	38 (76)	28 (61)	66 (69)
Mean (SD)	7.6 (2.57)	7.0 (2.69)	7.3 (2.62)
Median	8.0	7.0	8.0
Q1, Q3	6.0, 9.0	5.0, 9.0	6.0, 9.0
Min, Max	0, 12	3, 12	0, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=50)	**IFN B-1a (N=46)**	**Total (N=96)**
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	32 (64)	25 (54)	57 (59)
Mean (SD)	8.7 (2.45)	8.2 (2.37)	8.5 (2.41)
Median	9.0	8.0	9.0
Q1, Q3	7.0, 11.0	7.0, 10.0	7.0, 10.0
Min, Max	3, 12	3, 12	3, 12
Week 48			
n (%)	36 (72)	31 (67)	67 (70)
Mean (SD)	9.1 (1.79)	8.6 (3.21)	8.9 (2.54)
Median	9.5	10.0	10.0
Q1, Q3	8.5, 10.0	6.0, 11.0	7.0, 10.0
Min, Max	5, 12	1, 12	1, 12
Week 96			
n (%)	38 (76)	28 (61)	66 (69)
Mean (SD)	9.9 (2.09)	9.6 (2.18)	9.8 (2.12)
Median	11.0	10.0	10.0
Q1, Q3	9.0, 11.0	8.5, 11.0	9.0, 11.0
Min, Max	4, 12	5, 12	4, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=50)	**IFN B-1a (N=46)**	**Total (N=96)**
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	32 (64)	25 (54)	57 (59)
Mean (SD)	9.4 (1.97)	9.1 (2.26)	9.3 (2.09)
Median	10.0	10.0	10.0
Q1, Q3	8.0, 11.0	8.0, 11.0	8.0, 11.0
Min, Max	5, 12	4, 12	4, 12
Week 48			
n (%)	36 (72)	31 (67)	67 (70)
Mean (SD)	9.7 (2.00)	9.7 (2.40)	9.7 (2.18)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 11.0	8.0, 12.0	9.0, 11.0
Min, Max	6, 12	4, 12	4, 12
Week 96			
n (%)	38 (76)	28 (61)	66 (69)
Mean (SD)	10.2 (1.67)	9.9 (2.01)	10.1 (1.81)
Median	10.5	10.5	10.5
Q1, Q3	9.0, 12.0	9.0, 11.0	9.0, 12.0
Min, Max	7, 12	5, 12	5, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_DESCRIBE_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	6.3 (2.45)	5.6 (1.78)	5.9 (2.07)
Median	6.0	6.0	6.0
Q1, Q3	5.0, 7.0	4.0, 7.0	4.0, 7.0
Min, Max	3, 10	3, 8	3, 10
Week 48			
n (%)	14 (67)	13 (72)	27 (69)
Mean (SD)	5.2 (2.81)	5.6 (1.80)	5.4 (2.34)
Median	5.5	5.0	5.0
Q1, Q3	3.0, 7.0	4.0, 7.0	4.0, 7.0
Min, Max	1, 10	4, 9	1, 10
Week 96			
n (%)	13 (62)	12 (67)	25 (64)
Mean (SD)	5.6 (2.10)	6.3 (2.77)	5.9 (2.41)
Median	5.0	5.5	5.0
Q1, Q3	5.0, 8.0	4.5, 8.0	5.0, 8.0
Min, Max	1, 8	3, 11	1, 11

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	8.3 (2.55)	7.0 (1.60)	7.6 (2.11)
Median	9.0	7.5	8.0
Q1, Q3	6.0, 10.0	6.0, 8.0	6.0, 9.0
Min, Max	5, 12	4, 9	4, 12
Week 48			
n (%)	14 (67)	13 (72)	27 (69)
Mean (SD)	8.1 (3.13)	8.9 (1.66)	8.5 (2.52)
Median	8.5	9.0	9.0
Q1, Q3	7.0, 10.0	7.0, 10.0	7.0, 10.0
Min, Max	2, 12	7, 11	2, 12
Week 96			
n (%)	13 (62)	12 (67)	25 (64)
Mean (SD)	8.2 (2.31)	7.3 (2.39)	7.8 (2.35)
Median	9.0	6.5	8.0
Q1, Q3	7.0, 10.0	6.0, 8.0	6.0, 9.0
Min, Max	3, 11	5, 12	3, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

	DMF (N=21)	**IFN B-1a (N=18)**	**Total (N=39)**
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	9 (43)	12 (67)	21 (54)
Mean (SD)	9.6 (2.46)	8.1 (1.73)	8.7 (2.15)
Median	11.0	8.0	9.0
Q1, Q3	9.0, 11.0	7.0, 9.5	7.0, 11.0
Min, Max	5, 12	5, 11	5, 12
Week 48			
n (%)	14 (67)	13 (72)	27 (69)
Mean (SD)	9.2 (2.81)	10.0 (1.63)	9.6 (2.31)
Median	10.0	10.0	10.0
Q1, Q3	7.0, 11.0	9.0, 11.0	9.0, 11.0
Min, Max	2, 12	6, 12	2, 12
Week 96			
n (%)	13 (62)	12 (67)	25 (64)
Mean (SD)	9.3 (2.06)	8.3 (1.91)	8.8 (2.02)
Median	9.0	8.0	9.0
Q1, Q3	8.0, 11.0	7.5, 9.0	8.0, 11.0
Min, Max	5, 12	5, 12	5, 12

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_HEDGESCI_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	0.096	-0.857	1.049
	96 Weeks	-0.68	-1.892	0.531
Trial 2	48 Weeks	0.197	-0.758	1.152
	96 Weeks	0.142	-1.037	1.321
Trial 3	48 Weeks	0.111	-0.842	1.064
	96 Weeks	0.387	-0.802	1.576

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 18FEB2022

109MS306_table52_CHG_HEDGESCI_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	-0.072	-0.592	0.447
	96 Weeks	0.179	-0.420	0.778
Trial 2	48 Weeks	-0.327	-0.850	0.196
	96 Weeks	-0.049	-0.648	0.549
Trial 3	48 Weeks	-0.623	-1.155	-0.091
	96 Weeks	0.305	-0.296	0.907

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 18FEB2022

109MS306_table52_CHG_HEDGESCI_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	0.039	-0.491	0.568
	96 Weeks	0.22	-0.393	0.834
Trial 2	48 Weeks	-0.019	-0.549	0.510
	96 Weeks	0.124	-0.488	0.736
Trial 3	48 Weeks	-0.314	-0.847	0.218
	96 Weeks	0.567	-0.056	1.191

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 18FEB2022

109MS306_table52_CHG_HEDGESCI_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	0.036	-0.723	0.796
	96 Weeks	-0.629	-1.547	0.289
Trial 2	48 Weeks	-0.303	-1.067	0.461
	96 Weeks	-0.169	-1.066	0.727
Trial 3	48 Weeks	-0.865	-1.661	-0.069
	96 Weeks	-0.383	-1.286	0.521

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 18FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL1_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1

Subgroup analysis for AGES 13 TO 14

TIME POINTS	STATISTICS	DMF(N=18)	IFN B-1a (N=14)
48	n (%)	9 (50)	8 (57)
	Lsmean (SE)	0.93 (0.640)	-0.55 (0.683)
	Lsmean_95 % CI	(-0.441, 2.303)	(-2.013, 0.918)
	Diffrence (95% CI)	1.48 (-0.646, 3.602)	
	SE_Difference	0.9903	
	p-value	0.1577	
96	n (%)	9 (50)	4 (29)
	Lsmean (SE)	-0.65 (0.877)	0.95 (1.353)
	Lsmean_95 % CI	(-2.600, 1.307)	(-2.061, 3.970)
	Diffrence (95% CI)	-1.60 (-5.304, 2.104)	
	SE_Difference	1.6623	
	p-value	0.3584	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL1_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1. Subgroup analysis for AGES 15 TO 17

TIME POINTS	STATISTICS	DMF(N=53)	IFN B-1a (N=50)
48	n (%)	28 (53)	29 (58)
	Lsmean (SE)	0.37 (0.403)	0.50 (0.396)
	Lsmean_95 % CI	(-0.435, 1.182)	(-0.293, 1.296)
	Diffrence (95% CI)	-0.13 (-1.262, 1.006)	
	SE_Difference	0.5656	
	p-value	0.8214	
96	n (%)	22 (42)	21 (42)
	Lsmean (SE)	1.06 (0.481)	0.41 (0.493)
	Lsmean_95 % CI	(0.089, 2.035)	(-0.585, 1.407)
	Diffrence (95% CI)	0.65 (-0.746, 2.048)	
	SE_Difference	0.6913	
	p-value	0.3519	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL1_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1. Subgroup analysis for FEMALE SEX

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=46)
48	n (%)	28 (56)	25 (54)
	Lsmean (SE)	0.70 (0.455)	0.45 (0.468)
	Lsmean_95 % CI	(-0.211, 1.617)	(-0.487, 1.395)
	Diffrence (95% CI)	0.25 (-0.900, 1.398)	
	SE_Difference	0.5716	
	p-value	0.6651	
96	n (%)	25 (50)	16 (35)
	Lsmean (SE)	1.04 (0.468)	0.29 (0.603)
	Lsmean_95 % CI	(0.087, 1.985)	(-0.932, 1.511)
	Diffrence (95% CI)	0.75 (-0.617, 2.110)	
	SE_Difference	0.6730	
	p-value	0.2747	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL1_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1. Subgroup analysis for MALE SEX

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=18)
48	n (%)	9 (43)	12 (67)
	Lsmean (SE)	-0.29 (0.710)	0.21 (0.652)
	Lsmean_95 % CI	(-1.790, 1.208)	(-1.163, 1.588)
	Diffrence (95% CI)	-0.50 (-2.500, 1.492)	
	SE_Difference	0.9458	
	p-value	0.6011	
96	n (%)	6 (29)	9 (50)
	Lsmean (SE)	-1.13 (1.209)	0.48 (1.064)
	Lsmean_95 % CI	(-3.791, 1.532)	(-1.860, 2.825)
	Diffrence (95% CI)	-1.61 (-5.143, 1.919)	
	SE_Difference	1.6041	
	p-value	0.3365	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL2_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for AGES 13 TO 14

TIME POINTS	STATISTICS	DMF(N=18)	IFN B-1a (N=14)
48	n (%)	9 (50)	8 (57)
	Lsmean (SE)	1.52 (0.727)	0.67 (0.772)
	Lsmean_95 % CI	(-0.042, 3.076)	(-0.987, 2.324)
	Diffrence (95% CI)	0.85 (-1.449, 3.145)	
	SE_Difference	1.0710	
	p-value	0.4417	
96	n (%)	9 (50)	4 (29)
	Lsmean (SE)	0.63 (0.664)	0.09 (0.998)
	Lsmean_95 % CI	(-0.853, 2.106)	(-2.134, 2.314)
	Diffrence (95% CI)	0.54 (-2.142, 3.215)	
	SE_Difference	1.2021	
	p-value	0.6648	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL2_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for AGES 15 TO 17

TIME POINTS	STATISTICS	DMF(N=53)	IFN B-1a (N=50)
48	n (%)	28 (53)	29 (58)
	Lsmean (SE)	0.53 (0.354)	1.04 (0.348)
	Lsmean_95 % CI	(-0.180, 1.240)	(0.343, 1.738)
	Diffrence (95% CI)	-0.51 (-1.507, 0.487)	
	SE_Difference	0.4973	
	p-value	0.3093	
96	n (%)	22 (42)	21 (42)
	Lsmean (SE)	1.21 (0.356)	0.87 (0.364)
	Lsmean_95 % CI	(0.496, 1.933)	(0.135, 1.607)
	Diffrence (95% CI)	0.34 (-0.697, 1.385)	
	SE_Difference	0.5150	
	p-value	0.5083	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL2_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for FEMALE SEX

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=46)
48	n (%)	28 (56)	25 (54)
	Lsmean (SE)	0.64 (0.438)	0.70 (0.451)
	Lsmean_95 % CI	(-0.242, 1.520)	(-0.210, 1.603)
	Diffrence (95% CI)	-0.057 (-1.158, 1.043)	
	SE_Difference	0.5478	
	p-value	0.9169	
96	n (%)	25 (50)	16 (35)
	Lsmean (SE)	1.33 (0.292)	0.96 (0.378)
	Lsmean_95 % CI	(0.741, 1.922)	(0.194, 1.725)
	Diffrence (95% CI)	0.37 (-0.478, 1.222)	
	SE_Difference	0.4193	
	p-value	0.3808	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL2_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for MALE SEX

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=18)
48	n (%)	9 (43)	12 (67)
	Lsmean (SE)	1.50 (0.596)	1.69 (0.537)
	Lsmean_95 % CI	(0.246, 2.763)	(0.562, 2.826)
	Diffrence (95% CI)	-0.19 (-1.880, 1.502)	
	SE_Difference	0.8015	
	p-value	0.8163	
96	n (%)	6 (29)	9 (50)
	Lsmean (SE)	-0.28 (0.958)	0.27 (0.837)
	Lsmean_95 % CI	(-2.389, 1.828)	(-1.575, 2.110)
	Diffrence (95% CI)	-0.55 (-3.419, 2.324)	
	SE_Difference	1.3046	
	p-value	0.6826	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL3_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for AGES 13 TO 14

TIME POINTS	STATISTICS	DMF(N=18)	IFN B-1a (N=14)
48	n (%)	9 (50)	8 (57)
	Lsmean (SE)	0.86 (0.483)	0.29 (0.514)
	Lsmean_95 % CI	(-0.179, 1.893)	(-0.816, 1.388)
	Diffrence (95% CI)	0.57 (-0.981, 2.123)	
	SE_Difference	0.7238	
	p-value	0.4433	
96	n (%)	9 (50)	4 (29)
	Lsmean (SE)	0.30 (0.680)	-0.42 (1.020)
	Lsmean_95 % CI	(-1.215, 1.815)	(-2.698, 1.849)
	Diffrence (95% CI)	0.72 (-2.009, 3.459)	
	SE_Difference	1.2270	
	p-value	0.5679	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL3_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for AGES 15 TO 17

TIME POINTS	STATISTICS	DMF(N=53)	IFN B-1a (N=50)
48	n (%)	28 (53)	29 (58)
	Lsmean (SE)	0.40 (0.303)	1.44 (0.297)
	Lsmean_95 % CI	(-0.205, 1.008)	(0.844, 2.036)
	Diffrence (95% CI)	-1.04 (-1.889, -0.187)	
	SE_Difference	0.4244	
	p-value	0.0178	
96	n (%)	22 (42)	21 (42)
	Lsmean (SE)	1.01 (0.317)	0.27 (0.325)
	Lsmean_95 % CI	(0.374, 1.656)	(-0.386, 0.926)
	Diffrence (95% CI)	0.74 (-0.176, 1.665)	
	SE_Difference	0.4554	
	p-value	0.1100	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL3_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for FEMALE SEX

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=46)
48	n (%)	28 (56)	25 (54)
	Lsmean (SE)	0.22 (0.361)	0.71 (0.371)
	Lsmean_95 % CI	(-0.507, 0.944)	(-0.040, 1.451)
	Diffrence (95% CI)	-0.49 (-1.393, 0.419)	
	SE_Difference	0.4509	
	p-value	0.2853	
96	n (%)	25 (50)	16 (35)
	Lsmean (SE)	1.03 (0.314)	0.29 (0.408)
	Lsmean_95 % CI	(0.395, 1.669)	(-0.536, 1.117)
	Diffrence (95% CI)	0.74 (-0.179, 1.662)	
	SE_Difference	0.4544	
	p-value	0.1113	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

109MS306_table52_CHG_LSMEANS_TRIAL3_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for MALE SEX

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=18)
48	n (%)	9 (43)	12 (67)
	Lsmean (SE)	0.90 (0.511)	1.82 (0.456)
	Lsmean_95 % CI	(-0.179, 1.978)	(0.861, 2.784)
	Diffrence (95% CI)	-0.92 (-2.370, 0.524)	
	SE_Difference	0.6857	
	p-value	0.1960	
96	n (%)	6 (29)	9 (50)
	Lsmean (SE)	0.53 (0.834)	-0.41 (0.703)
	Lsmean_95 % CI	(-1.304, 2.366)	(-1.953, 1.142)
	Diffrence (95% CI)	0.94 (-1.543, 3.416)	
	SE_Difference	1.1263	
	p-value	0.4234	

Note: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 11FEB2022

MCID 15

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% increase from baseline	Effect measure	1.286	1.200	0.050
	95% CI	(0.158, 10.450)	(0.260, 5.535)	(-0.363, 0.463)
	p-value	0.8141	0.8152	0.8125
Trial 2 Week 48 >=15% increase from baseline	Effect measure	0.667	0.800	-0.100
	95% CI	(0.102, 4.354)	(0.286, 2.236)	(-0.561, 0.361)
	p-value	0.6719	0.6705	0.6705
Trial 2 Week 96 >=15% increase from baseline	Effect measure	3.000	2.400	0.175
	95% CI	(0.248, 36.325)	(0.305, 18.894)	(-0.190, 0.540)
	p-value	0.3879	0.4056	0.3473
Trial 3 Week 48 >=15% increase from baseline	Effect measure	0.417	0.533	-0.175
	95% CI	(0.051, 3.435)	(0.116, 2.460)	(-0.592, 0.242)
	p-value	0.4160	0.4203	0.4109

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% increase from baseline	Effect measure	0.777	0.842	-0.055
	95% CI	(0.261, 2.311)	(0.400, 1.773)	(-0.290, 0.181)
	p-value	0.6505	0.6507	0.6501
Trial 2 Week 48 >=15% increase from baseline	Effect measure	0.569	0.680	-0.121
	95% CI	(0.189, 1.710)	(0.319, 1.450)	(-0.356, 0.113)
	p-value	0.3153	0.3187	0.3105
Trial 2 Week 96 >=15% increase from baseline	Effect measure	0.661	0.748	-0.087
	95% CI	(0.218, 2.007)	(0.343, 1.632)	(-0.318, 0.145)
	p-value	0.4648	0.4663	0.4629
Trial 3 Week 48 >=15% increase from baseline	Effect measure	0.237	0.360	-0.287
	95% CI	(0.071, 0.790)	(0.146, 0.884)	(-0.510, -0.064)
	p-value	0.0191	0.0258	0.0115

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% increase from baseline	Effect measure	0.786	0.859	-0.056
	95% CI	(0.266, 2.320)	(0.436, 1.693)	(-0.309, 0.197)
	p-value	0.6624	0.6613	0.6629
Trial 1 Week 96 >=15% increase from baseline	Effect measure	3.841	2.865	0.224
	95% CI	(0.938, 15.729)	(0.894, 9.179)	(0.016, 0.432)
	p-value	0.0613	0.0765	0.0351
Trial 2 Week 96 >=15% increase from baseline	Effect measure	0.966	0.977	-0.008
	95% CI	(0.314, 2.974)	(0.453, 2.106)	(-0.251, 0.236)
	p-value	0.9518	0.9518	0.9518

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
Trial 1 Week 48 >=15% increase from baseline	Effect measure	0.625	0.667	-0.056
	95% CI	(0.048, 8.201)	(0.071, 6.259)	(-0.350, 0.239)
	p-value	0.7204	0.7227	0.7114
Trial 1 Week 96 >=15% increase from baseline	Effect measure	0.143	0.188	-0.250
	95% CI	(0.006, 3.161)	(0.011, 3.219)	(-0.592, 0.092)
	p-value	0.2181	0.2488	0.2216
Trial 2 Week 96 >=15% increase from baseline	Effect measure	0.375	0.444	-0.139
	95% CI	(0.032, 4.369)	(0.055, 3.599)	(-0.459, 0.181)
	p-value	0.4337	0.4473	0.3944

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15% (CODED AS YES). SCALES ARE 0 TO 12, SO 15%=1.8)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
BVMT Trial 1 Week 48 >=15% increase from baseline				
	Yes	3 (17)	2 (14)	5 (16)
	No	7 (39)	6 (43)	13 (41)
	Missing	8 (44)	6 (43)	14 (44)
BVMT Trial 2 Week 48 >=15% increase from baseline				
	Yes	4 (22)	4 (29)	8 (25)
	No	6 (33)	4 (29)	10 (31)
	Missing	8 (44)	6 (43)	14 (44)
BVMT Trial 2 Week 96 >=15% increase from baseline				
	Yes	3 (17)	1 (7)	4 (13)
	No	7 (39)	7 (50)	14 (44)
	Missing	8 (44)	6 (43)	14 (44)
BVMT Trial 3 Week 48 >=15% increase from baseline				
	Yes	2 (11)	3 (21)	5 (16)
	No	8 (44)	5 (36)	13 (41)
	Missing	8 (44)	6 (43)	14 (44)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
BVMT Trial 1 Week 48 >=15% increase from baseline				
	Yes	9 (17)	10 (20)	19 (18)
	No	22 (42)	19 (38)	41 (40)
	Missing	22 (42)	21 (42)	43 (42)
BVMT Trial 2 Week 48 >=15% increase from baseline				
	Yes	8 (15)	11 (22)	19 (18)
	No	23 (43)	18 (36)	41 (40)
	Missing	22 (42)	21 (42)	43 (42)
BVMT Trial 2 Week 96 >=15% increase from baseline				
	Yes	8 (15)	10 (20)	18 (17)
	No	23 (43)	19 (38)	42 (41)
	Missing	22 (42)	21 (42)	43 (42)
BVMT Trial 3 Week 48 >=15% increase from baseline				
	Yes	5 (9)	13 (26)	18 (17)
	No	26 (49)	16 (32)	42 (41)
	Missing	22 (42)	21 (42)	43 (42)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
BVMT Trial 1 Week 48 >=15% increase from baseline				
	Yes	11 (22)	10 (22)	21 (22)
	No	21 (42)	15 (33)	36 (38)
	Missing	18 (36)	21 (46)	39 (41)
BVMT Trial 1 Week 96 >=15% increase from baseline				
	Yes	11 (22)	3 (7)	14 (15)
	No	21 (42)	22 (48)	43 (45)
	Missing	18 (36)	21 (46)	39 (41)
BVMT Trial 2 Week 96 >=15% increase from baseline				
	Yes	10 (20)	8 (17)	18 (19)
	No	22 (44)	17 (37)	39 (41)
	Missing	18 (36)	21 (46)	39 (41)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
BVMT Trial 1 Week 48 >=15% increase from baseline				
	Yes	1 (5)	2 (11)	3 (8)
	No	8 (38)	10 (56)	18 (46)
	Missing	12 (57)	6 (33)	18 (46)
BVMT Trial 1 Week 96 >=15% increase from baseline				
	Yes	0 (0)	3 (17)	3 (8)
	No	9 (43)	9 (50)	18 (46)
	Missing	12 (57)	6 (33)	18 (46)
BVMT Trial 2 Week 96 >=15% increase from baseline				
	Yes	1 (5)	3 (17)	4 (10)
	No	8 (38)	9 (50)	17 (44)
	Missing	12 (57)	6 (33)	18 (46)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban030222.sas date: 30MAR2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_age13to14

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
BVMT Trial 1 scale Week 0				
	Yes	10 (56)	8 (57)	18 (56)
	No	8 (44)	6 (43)	14 (44)
BVMT Trial 1 scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
BVMT Trial 1 scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)
BVMT Trial 2 scale Week 0				
	Yes	10 (56)	8 (57)	18 (56)
	No	8 (44)	6 (43)	14 (44)
BVMT Trial 2 scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
BVMT Trial 2 scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)
BVMT Trial 3 scale Week 0				
	Yes	10 (56)	8 (57)	18 (56)
	No	8 (44)	6 (43)	14 (44)
BVMT Trial 3 scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
BVMT Trial 3 scale Week 96				

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban012922.sas date: 01FEB2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_age15to17

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
BVMT Trial 1 scale Week 0				
	Yes	31 (58)	29 (58)	60 (58)
	No	22 (42)	21 (42)	43 (42)
BVMT Trial 1 scale Week 48				
	Yes	37 (70)	34 (68)	71 (69)
	No	16 (30)	16 (32)	32 (31)
BVMT Trial 1 scale Week 96				
	Yes	36 (68)	33 (66)	69 (67)
	No	17 (32)	17 (34)	34 (33)
BVMT Trial 2 scale Week 0				
	Yes	31 (58)	29 (58)	60 (58)
	No	22 (42)	21 (42)	43 (42)
BVMT Trial 2 scale Week 48				
	Yes	37 (70)	34 (68)	71 (69)

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
	No	16 (30)	16 (32)	32 (31)
BVMT Trial 2 scale Week 96				
	Yes	36 (68)	33 (66)	69 (67)
	No	17 (32)	17 (34)	34 (33)
BVMT Trial 3 scale Week 0				
	Yes	31 (58)	29 (58)	60 (58)
	No	22 (42)	21 (42)	43 (42)
BVMT Trial 3 scale Week 48				
	Yes	37 (70)	34 (68)	71 (69)
	No	16 (30)	16 (32)	32 (31)
BVMT Trial 3 scale Week 96				
	Yes	36 (68)	33 (66)	69 (67)
	No	17 (32)	17 (34)	34 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban012922.sas date: 01FEB2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_female

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
BVMT Trial 1 scale Week 0				
	Yes	32 (64)	25 (54)	57 (59)
	No	18 (36)	21 (46)	39 (41)
BVMT Trial 1 scale Week 48				
	Yes	36 (72)	31 (67)	67 (70)
	No	14 (28)	15 (33)	29 (30)
BVMT Trial 1 scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)
BVMT Trial 2 scale Week 0				
	Yes	32 (64)	25 (54)	57 (59)
	No	18 (36)	21 (46)	39 (41)
BVMT Trial 2 scale Week 48				
	Yes	36 (72)	31 (67)	67 (70)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
	No	14 (28)	15 (33)	29 (30)
BVMT Trial 2 scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)
BVMT Trial 3 scale Week 0				
	Yes	32 (64)	25 (54)	57 (59)
	No	18 (36)	21 (46)	39 (41)
BVMT Trial 3 scale Week 48				
	Yes	36 (72)	31 (67)	67 (70)
	No	14 (28)	15 (33)	29 (30)
BVMT Trial 3 scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban012922.sas date: 01FEB2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_male

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

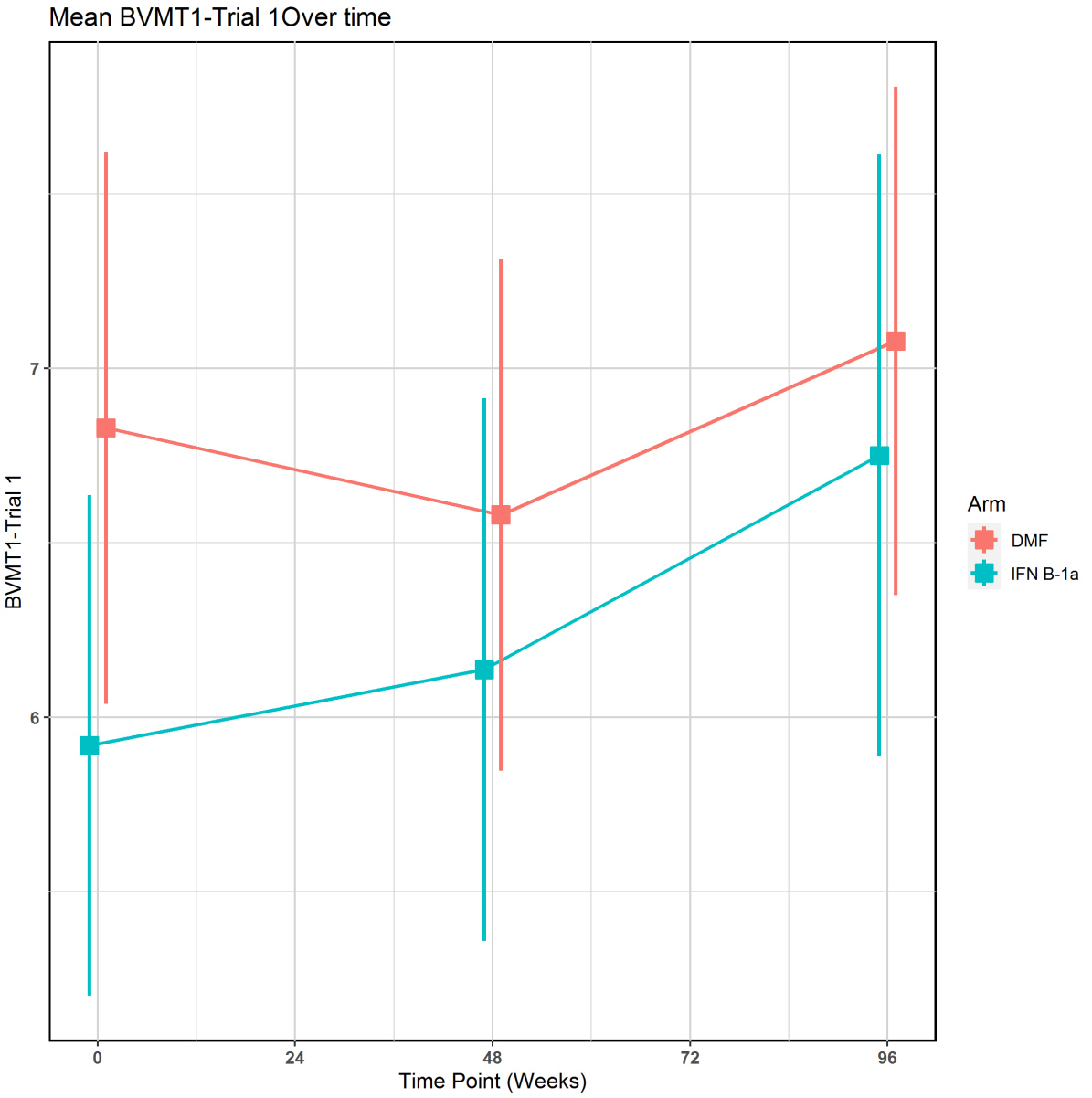
	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
BVMT Trial 1 scale Week 0				
	Yes	9 (43)	12 (67)	21 (54)
	No	12 (57)	6 (33)	18 (46)
BVMT Trial 1 scale Week 48				
	Yes	14 (67)	13 (72)	27 (69)
	No	7 (33)	5 (28)	12 (31)
BVMT Trial 1 scale Week 96				
	Yes	13 (62)	12 (67)	25 (64)
	No	8 (38)	6 (33)	14 (36)
BVMT Trial 2 scale Week 0				
	Yes	9 (43)	12 (67)	21 (54)
	No	12 (57)	6 (33)	18 (46)
BVMT Trial 2 scale Week 48				
	Yes	14 (67)	13 (72)	27 (69)

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
	No	7 (33)	5 (28)	12 (31)
BVMT Trial 2 scale Week 96				
	Yes	13 (62)	12 (67)	25 (64)
	No	8 (38)	6 (33)	14 (36)
BVMT Trial 3 scale Week 0				
	Yes	9 (43)	12 (67)	21 (54)
	No	12 (57)	6 (33)	18 (46)
BVMT Trial 3 scale Week 48				
	Yes	14 (67)	13 (72)	27 (69)
	No	7 (33)	5 (28)	12 (31)
BVMT Trial 3 scale Week 96				
	Yes	13 (62)	12 (67)	25 (64)
	No	8 (38)	6 (33)	14 (36)

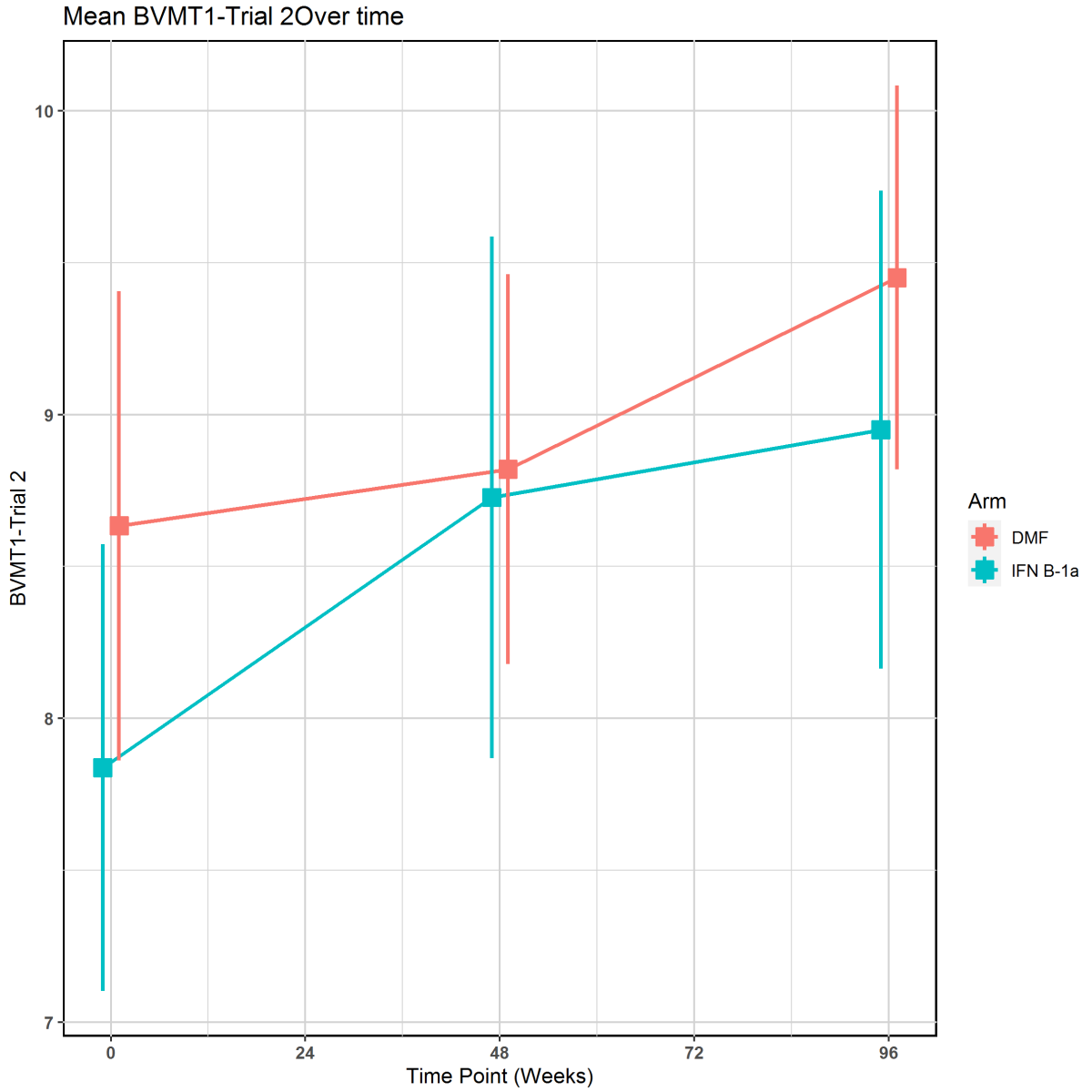
NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban012922.sas date: 01FEB2022

Graphics

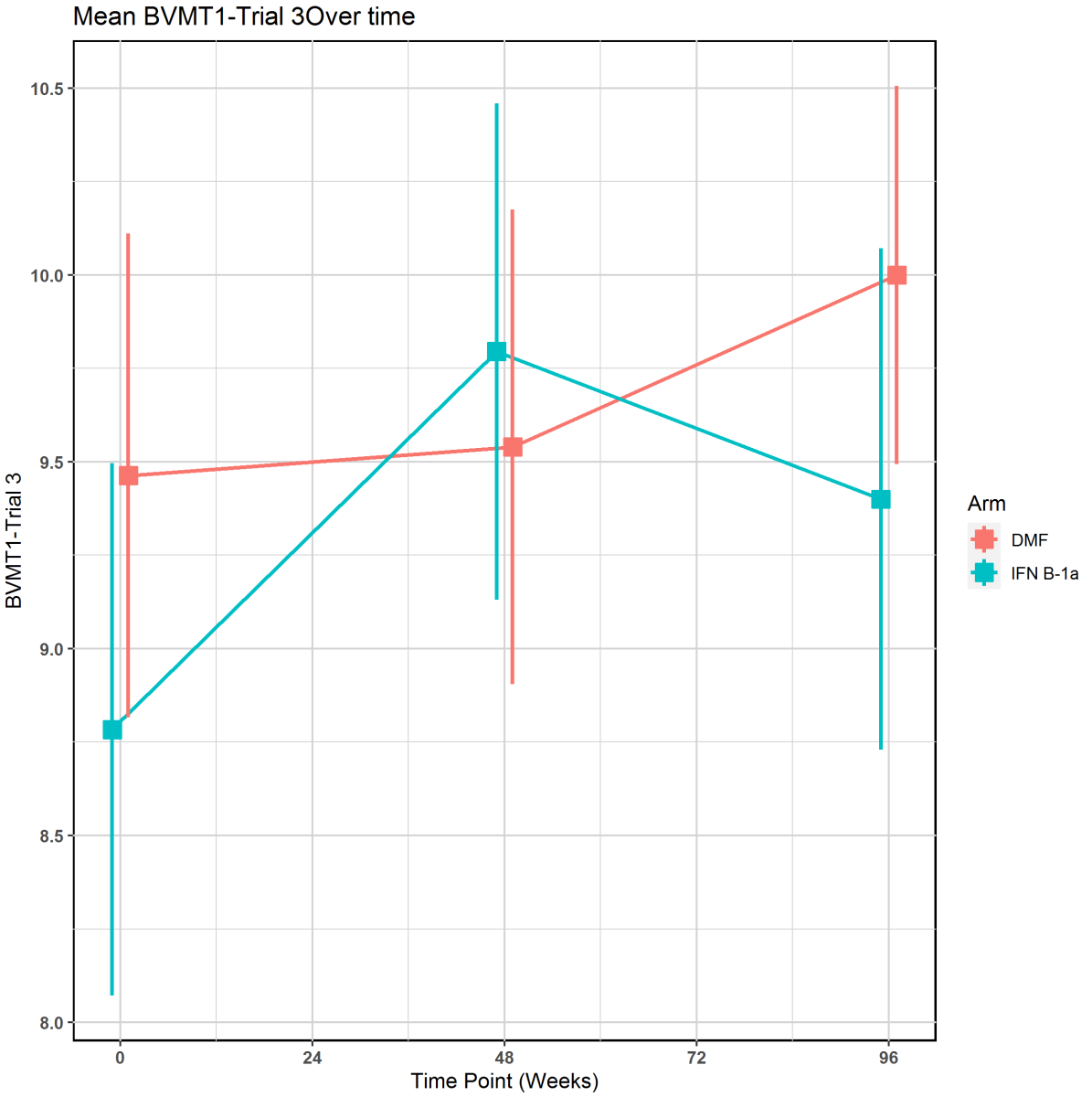
BVMT1-Trial 1



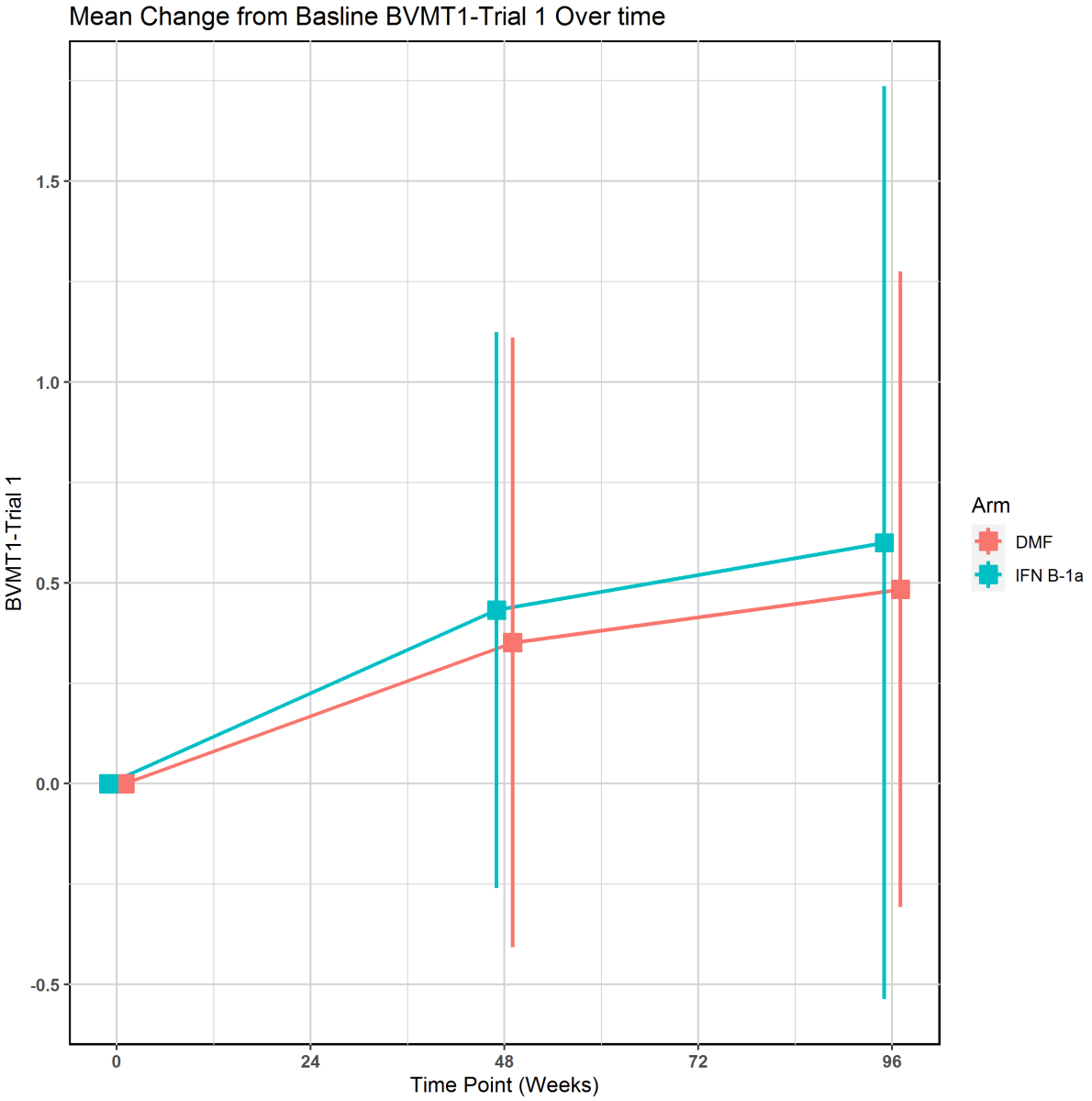
BVMT1-Trial 2



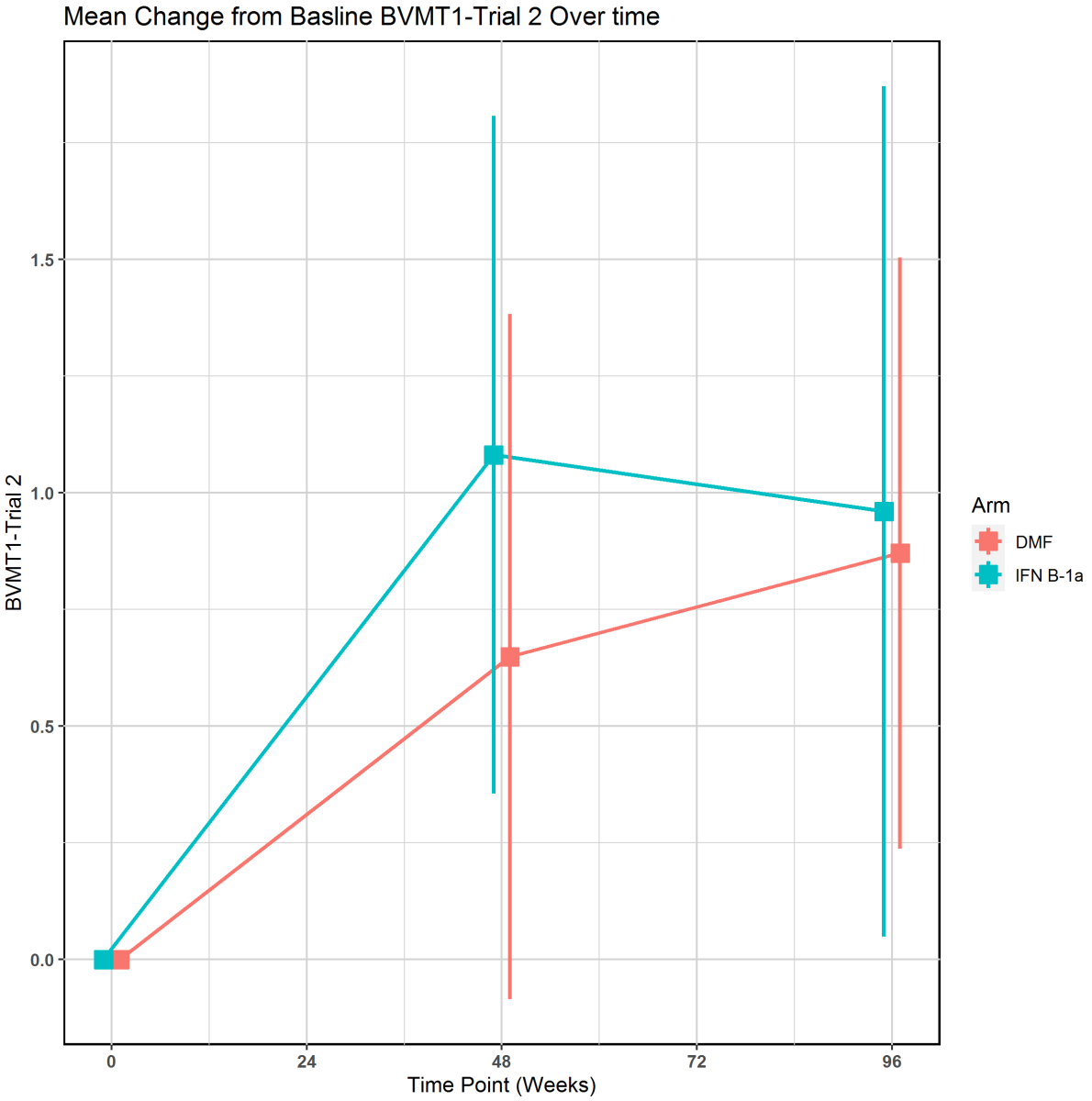
BVMT1-Trial 3



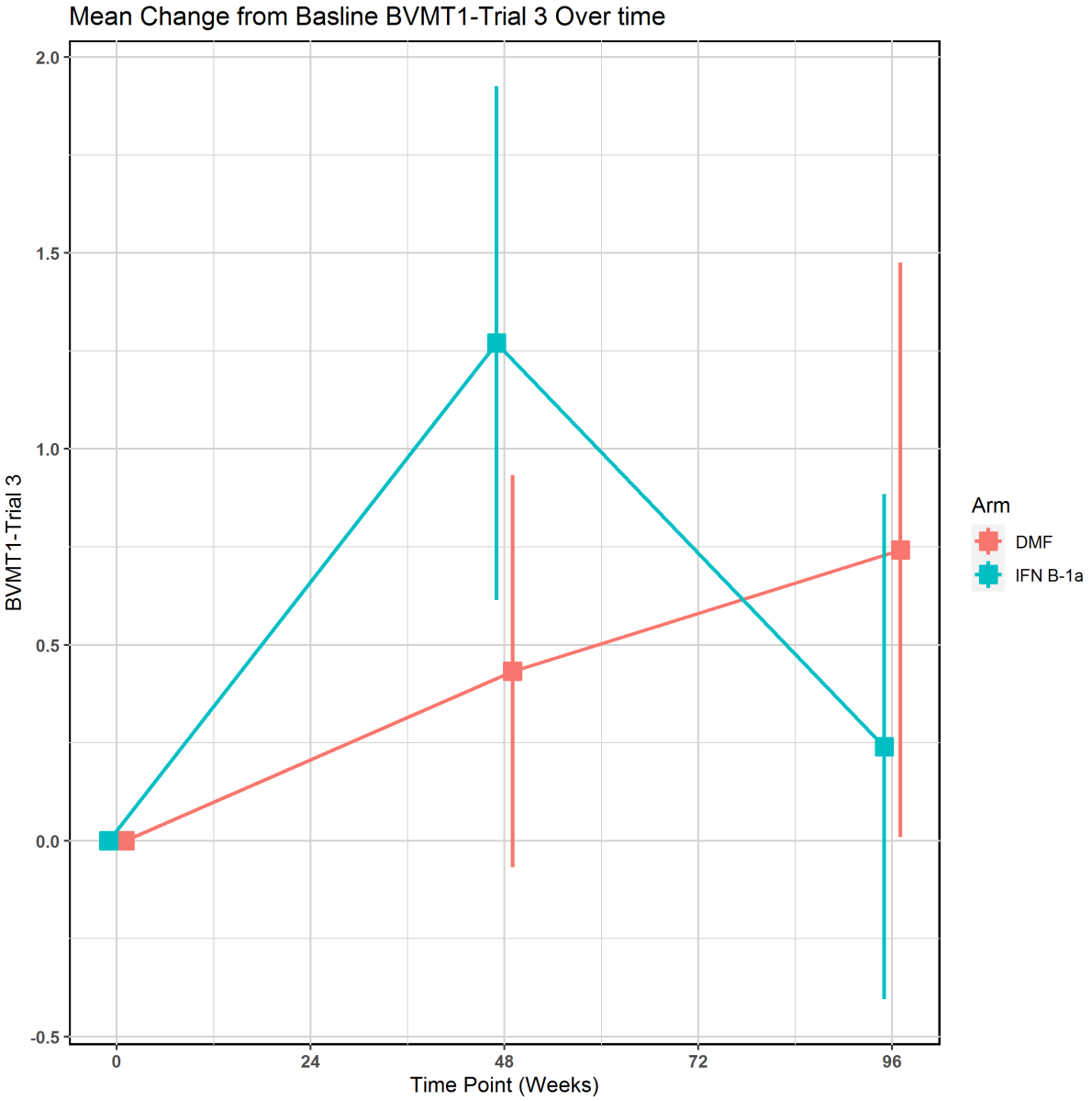
Change from baseline BVMT1-Trial 1



Change from baseline BVMT1-Trial 2



Change from baseline BVMT1-Trial 3



SDMT

109MS306_CSRTab53RelatedSDMT_effectmeasures

Effect Measure of SDMT scores

	Result	OR	RR	ARR
SDMT MCID increase ≥15% - Week 48	Effect measure	1.8	1.762	0.021
	95% CI	(0.157 , 20.7)	(0.166 , 18.65)	(-0.062 , 0.104)
	p-value	0.637	0.638	0.627
SDMT MCID increase ≥15% - Week 96	Effect measure	8.766	7.941	0.095
	95% CI	(0.456 , 168.529)	(0.442 , 142.689)	(-0.019 , 0.209)
	p-value	0.15	0.16	0.123
SDMT MCID decrease ≥15% - Week 48	Effect measure	0.116	0.126	-0.081
	95% CI	(0.006 , 2.322)	(0.007 , 2.362)	(-0.194 , 0.032)
	p-value	0.159	0.166	0.215
SDMT MCID decrease ≥15% - Week 96	Effect measure	0.427	0.44	-0.03
	95% CI	(0.037 , 4.909)	(0.042 , 4.663)	(-0.116 , 0.056)
	p-value	0.494	0.496	0.492

NOTE1: Scale of the measure is 0 to 110. Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab53RelatedSDMT_NPERCENT

Summary statistics SDMT scores

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SDMT MCID increase ≥15% - Week 48	Yes	2 (2.82)	1 (1.56)	3 (3.80)
	No	40 (56.34)	36 (56.25)	76 (96.20)
	Missing	29 (40.85)	27 (42.19)	56 (41.48)
SDMT MCID increase ≥15% - Week 96	Yes	4 (5.63)	0 (0.00)	4 (5.06)
	No	38 (53.52)	37 (57.81)	75 (94.94)
	Missing	29 (40.85)	27 (42.19)	56 (41.48)
SDMT MCID decrease ≥15% - Week 48	Yes	0 (0.00)	3 (4.69)	3 (3.80)
	No	42 (59.15)	34 (53.12)	76 (96.20)
	Missing	29 (40.85)	27 (42.19)	56 (41.48)
SDMT MCID decrease ≥15% - Week 96	Yes	1 (1.41)	2 (3.12)	3 (3.80)
	No	41 (57.75)	35 (54.69)	76 (96.20)
	Missing	29 (40.85)	27 (42.19)	56 (41.48)

NOTE1: Scale of the measure is 0 to 110.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab53RelatedSDMT_responsRate

Response Rate of SDMT scores

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SDMT Baseline	Yes	42 (59.15)	37 (57.81)	79 (58.52)
	No	29 (40.85)	27 (42.19)	56 (41.48)
SDMT Week 48	Yes	52 (73.24)	44 (68.75)	96 (71.11)
	No	19 (26.76)	20 (31.25)	39 (28.89)
SDMT Week 96	Yes	52 (73.24)	40 (62.50)	92 (68.15)
	No	19 (26.76)	24 (37.50)	43 (31.85)

NOTE1: Scale of the measure is 0 to 110.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_table53_CHG_DESCRIBE(CHG FROM BL)

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Week 48 change from baseline			
n (%)	39 (55)	37 (58)	76 (56)
Mean (SD)	3.8 (7.45)	1.8 (9.37)	2.9 (8.45)
Median	4.0	4.0	4.0
Q1, Q3	-1.0, 9.0	-3.0, 7.0	-2.0, 8.0
Min, Max	-11, 22	-26, 17	-26, 22
Week 96 change from baseline			
n (%)	33 (46)	26 (41)	59 (44)
Mean (SD)	7.6 (9.03)	1.5 (9.79)	4.9 (9.77)
Median	7.0	4.5	5.0
Q1, Q3	3.0, 13.0	-2.0, 9.0	1.0, 10.0
Min, Max	-19, 28	-28, 14	-28, 28

NOTE1: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE2: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_CHG_DESCRIBE_banupdate012622.sas date: 26JAN2022

109MS306_table53_CHG_DESCRIBE

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Baseline			
n (%)	42 (59)	37 (58)	79 (59)
Mean (SD)	57.1 (13.62)	57.3 (12.05)	57.2 (12.83)
Median	56.0	58.0	56.0
Q1, Q3	50.0, 66.0	52.0, 62.0	50.0, 63.0
Min, Max	26, 86	30, 87	26, 87
Week 48			
n (%)	52 (73)	44 (69)	96 (71)
Mean (SD)	57.4 (12.99)	58.2 (12.87)	57.8 (12.87)
Median	57.0	58.0	57.0
Q1, Q3	49.5, 65.0	52.5, 66.0	51.0, 65.5
Min, Max	28, 93	15, 86	15, 93
Week 96			
n (%)	52 (73)	40 (63)	92 (68)
Mean (SD)	60.7 (12.04)	59.0 (11.22)	60.0 (11.66)
Median	60.0	58.5	60.0
Q1, Q3	54.0, 67.5	51.0, 66.0	52.5, 66.5
Min, Max	25, 98	34, 95	25, 98

NOTE1: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE2: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_DESCRIBE_banupdate012622.sas date: 26JAN2022

109MS306_table53_CHG_HEDGESCI

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135)

Summary of Symbol Digit Modalities Test (SDMT Scores by Visit) - ITT Population (n=135)

Week	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
48 Weeks	0.241	-0.210	0.693
96 Weeks	0.644	0.117	1.171

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T53/109MS306_table53_CHG_HEDGESCI.sasdate: 16FEB2022

109MS306_table53_CHG_LSMEANS

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - mITT Population, Aged 13 years and older (n=135)

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
48	n (%)	39 (55)	37 (58)
	Lsmean (SE)	03.61 (1.411)	01.82 (1.473)
	Lsmean_95 % CI	(00.802, 06.428)	(-1.115, 04.759)
	Diffrence (95% CI)	1.79 (-1.929, 5.514)	
	SE_Difference	1.8667	
	p-value	0.3401	
96	n (%)	33 (46)	26 (41)
	Lsmean (SE)	08.28 (1.653)	03.39 (1.961)
	Lsmean_95 % CI	(04.964, 11.590)	(-0.543, 07.315)
	Diffrence (95% CI)	4.89 (0.244, 9.539)	
	SE_Difference	2.3190	
	p-value	0.0395	

Sub groups

Change

109MS306_table53_CHG_DESCRIBE (CHG FROM BL)_female

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Week 48 change from baseline			
n (%)	29 (58)	25 (54)	54 (56)
Mean (SD)	3.3 (7.44)	-0.3 (9.53)	1.6 (8.58)
Median	4.0	3.0	3.0
Q1, Q3	-1.0, 9.0	-4.0, 5.0	-4.0, 6.0
Min, Max	-11, 21	-26, 13	-26, 21
Week 96 change from baseline			
n (%)	26 (52)	17 (37)	43 (45)
Mean (SD)	7.7 (9.51)	0.3 (11.08)	4.8 (10.68)
Median	7.0	2.0	5.0
Q1, Q3	3.0, 13.0	-2.0, 8.0	0.0, 10.0
Min, Max	-19, 28	-28, 14	-28, 28

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
Note3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
Note4: This is based on Change variable (CHG)
SOURCE: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_DESCRIBE_(CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table53_CHG_DESCRIBE (CHG FROM BL)_male

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Week 48 change from baseline			
n (%)	10 (48)	12 (67)	22 (56)
Mean (SD)	5.5 (7.62)	6.2 (7.67)	5.9 (7.47)
Median	4.5	7.5	7.0
Q1, Q3	1.0, 9.0	3.0, 9.5	1.0, 9.0
Min, Max	-4, 22	-11, 17	-11, 22
Week 96 change from baseline			
n (%)	7 (33)	9 (50)	16 (41)
Mean (SD)	7.1 (7.65)	3.9 (6.68)	5.3 (7.07)
Median	6.0	6.0	6.0
Q1, Q3	1.0, 13.0	3.0, 9.0	2.0, 9.0
Min, Max	-4, 19	-11, 9	-11, 19

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
Note3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
Note4: This is based on Change variable (CHG)
SOURCE: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_DESCRIBE_(CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table53_CHG_DESCRIBE_female

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Baseline			
n (%)	32 (64)	25 (54)	57 (59)
Mean (SD)	59.2 (12.55)	58.7 (13.27)	59.0 (12.75)
Median	57.0	59.0	57.0
Q1, Q3	51.0, 67.5	52.0, 65.0	52.0, 66.0
Min, Max	26, 86	30, 87	26, 87
Week 48			
n (%)	38 (76)	31 (67)	69 (72)
Mean (SD)	58.3 (11.13)	57.3 (14.25)	57.8 (12.54)
Median	57.5	58.0	58.0
Q1, Q3	50.0, 65.0	52.0, 65.0	51.0, 65.0
Min, Max	34, 87	15, 86	15, 87
Week 96			
n (%)	39 (78)	28 (61)	67 (70)
Mean (SD)	62.7 (11.37)	60.3 (11.41)	61.7 (11.36)
Median	61.0	61.5	61.0
Q1, Q3	54.0, 70.0	51.0, 67.5	53.0, 69.0
Min, Max	45, 98	40, 95	40, 98

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_DESCRIBE_banupdate012622.sas date: 09MAR2022

109MS306_table53_CHG_DESCRIBE_male

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Baseline			
n (%)	10 (48)	12 (67)	22 (56)
Mean (SD)	50.4 (15.42)	54.3 (8.81)	52.5 (12.11)
Median	50.5	56.5	53.0
Q1, Q3	38.0, 58.0	47.0, 61.5	47.0, 61.0
Min, Max	27, 82	40, 68	27, 82
Week 48			
n (%)	14 (67)	13 (72)	27 (69)
Mean (SD)	55.1 (17.34)	60.5 (8.85)	57.7 (13.93)
Median	56.5	60.0	57.0
Q1, Q3	46.0, 64.0	53.0, 68.0	50.0, 68.0
Min, Max	28, 93	49, 75	28, 93
Week 96			
n (%)	13 (62)	12 (67)	25 (64)
Mean (SD)	54.8 (12.52)	55.9 (10.60)	55.4 (11.40)
Median	58.0	56.0	57.0
Q1, Q3	54.0, 61.0	49.5, 64.0	52.0, 62.0
Min, Max	25, 72	34, 70	25, 72

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_DESCRIBE_banupdate012622.sas date: 09MAR2022

109MS306_table53_CHG_HEDGESCI_female

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135). Subgroup analysis for FEMALE SEX

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
48	0.42	-0.121	0.961
96	0.729	0.097	1.360

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table53_CHG_HEDGESCI_male

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135). Subgroup analysis for MALE SEX

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
48	-0.087	-0.927	0.752
96	0.458	-0.545	1.460

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table53_CHG_LSMEANS_female

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=46)
48	n (%)	29 (58)	25 (54)
	Lsmean (SE)	2.80 (1.729)	-0.60 (1.832)
	Lsmean_95 % CI	(-0.671, 6.275)	(-4.282, 3.079)
	Diffrence (95% CI)	3.40 (-1.050, 7.857)	
	SE_Difference	2.2172	
	p-value	0.1310	
96	n (%)	26 (52)	17 (37)
	Lsmean (SE)	8.29 (2.131)	2.44 (2.711)
	Lsmean_95 % CI	(3.980, 12.600)	(-3.039, 7.927)
	Diffrence (95% CI)	5.85 (-0.244, 11.935)	
	SE_Difference	3.0107	
	p-value	0.0594	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_LSMEANS_SubGr.sas date: 09MAR2022

109MS306_table53_CHG_LSMEANS_male

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=18)
48	n (%)	10 (48)	12 (67)
	Lsmean (SE)	5.26 (2.556)	6.22 (2.523)
	Lsmean_95 % CI	(-0.113, 10.628)	(0.919, 11.522)
	Diffrence (95% CI)	-0.96 (-8.374, 6.449)	
	SE_Difference	3.5278	
	p-value	0.7881	
96	n (%)	7 (33)	9 (50)
	Lsmean (SE)	7.30 (2.623)	5.76 (2.522)
	Lsmean_95 % CI	(1.587, 13.018)	(0.267, 11.259)
	Diffrence (95% CI)	1.54 (-6.274, 9.353)	
	SE_Difference	3.5860	
	p-value	0.6753	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_LSMEANS_SubGr.sas date: 09MAR2022

MCID

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1314_effectmeasures

Effect Measure of SDMT scores

	Result	OR	RR	ARR
SDMT MCID increase ≥15% - Week 48	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A
SDMT MCID increase ≥15% - Week 96	Effect measure	5	4.048	0.2
	95% CI	(0.208 , 120.448)	(0.223 , 73.461)	(-0.16 , 0.56)
	p-value	0.321	0.344	0.489
SDMT MCID decrease ≥15% - Week 48	Effect measure	0.238	0.27	-0.125
	95% CI	(0.008 , 6.685)	(0.013 , 5.814)	(-0.467 , 0.217)
	p-value	0.399	0.403	0.915
SDMT MCID decrease ≥15% - Week 96	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A

NOTE1: Scale of the measure is 0 to 110. Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1314_NPERCENT

Summary statistics SDMT scores

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
SDMT MCID increase ≥15% - Week 48	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	10 (55.56)	8 (57.14)	18 (100.00)
	Missing	8 (44.44)	6 (42.86)	14 (43.75)
SDMT MCID increase ≥15% - Week 96	Yes	2 (11.11)	0 (0.00)	2 (11.11)
	No	8 (44.44)	8 (57.14)	16 (88.89)
	Missing	8 (44.44)	6 (42.86)	14 (43.75)
SDMT MCID decrease ≥15% - Week 48	Yes	0 (0.00)	1 (7.14)	1 (5.56)
	No	10 (55.56)	7 (50.00)	17 (94.44)
	Missing	8 (44.44)	6 (42.86)	14 (43.75)
SDMT MCID decrease ≥15% - Week 96	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	10 (55.56)	8 (57.14)	18 (100.00)
	Missing	8 (44.44)	6 (42.86)	14 (43.75)

NOTE1: Scale of the measure is 0 to 110.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1314_responsRate

Response Rate of SDMT scores

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
SDMT Baseline	Yes	10 (55.56)	8 (57.14)	18 (56.25)
	No	8 (44.44)	6 (42.86)	14 (43.75)
SDMT Week 48	Yes	15 (83.33)	10 (71.43)	25 (78.12)
	No	3 (16.67)	4 (28.57)	7 (21.88)
SDMT Week 96	Yes	14 (77.78)	7 (50.00)	21 (65.62)
	No	4 (22.22)	7 (50.00)	11 (34.38)

NOTE1: Scale of the measure is 0 to 110.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1517_effectmeasures

Effect Measure of SDMT scores

		Result	OR	RR	ARR
SDMT MCID increase ≥15% - Week 48		Effect measure	1.867	1.812	0.028
		95% CI	(0.16 , 21.743)	(0.173 , 18.954)	(-0.079 , 0.135)
		p-value	0.618	0.619	0.608
SDMT MCID increase ≥15% - Week 96		Effect measure	4.836	4.538	0.062
		95% CI	(0.223 , 105.048)	(0.227 , 90.724)	(-0.054 , 0.179)
		p-value	0.316	0.322	0.489
SDMT MCID decrease ≥15% - Week 48		Effect measure	0.169	0.182	-0.069
		95% CI	(0.008 , 3.677)	(0.009 , 3.629)	(-0.194 , 0.056)
		p-value	0.258	0.264	0.443
SDMT MCID decrease ≥15% - Week 96		Effect measure	0.435	0.453	-0.038
		95% CI	(0.037 , 5.073)	(0.043 , 4.739)	(-0.148 , 0.072)
		p-value	0.507	0.509	0.502

NOTE1: Scale of the measure is 0 to 110. Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1517_NPERCENT

Summary statistics SDMT scores

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
SDMT MCID increase ≥15% - Week 48	Yes	2 (3.77)	1 (2.00)	3 (4.92)
	No	30 (56.60)	28 (56.00)	58 (95.08)
	Missing	21 (39.62)	21 (42.00)	42 (40.78)
SDMT MCID increase ≥15% - Week 96	Yes	2 (3.77)	0 (0.00)	2 (3.28)
	No	30 (56.60)	29 (58.00)	59 (96.72)
	Missing	21 (39.62)	21 (42.00)	42 (40.78)
SDMT MCID decrease ≥15% - Week 48	Yes	0 (0.00)	2 (4.00)	2 (3.28)
	No	32 (60.38)	27 (54.00)	59 (96.72)
	Missing	21 (39.62)	21 (42.00)	42 (40.78)
SDMT MCID decrease ≥15% - Week 96	Yes	1 (1.89)	2 (4.00)	3 (4.92)
	No	31 (58.49)	27 (54.00)	58 (95.08)
	Missing	21 (39.62)	21 (42.00)	42 (40.78)

NOTE1: Scale of the measure is 0 to 110.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab53RelatedSDMT_AGEGRN_Age1517_responsRate

Response Rate of SDMT scores

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
SDMT Baseline	Yes	32 (60.38)	29 (58.00)	61 (59.22)
	No	21 (39.62)	21 (42.00)	42 (40.78)
SDMT Week 48	Yes	37 (69.81)	34 (68.00)	71 (68.93)
	No	16 (30.19)	16 (32.00)	32 (31.07)
SDMT Week 96	Yes	38 (71.70)	33 (66.00)	71 (68.93)
	No	15 (28.30)	17 (34.00)	32 (31.07)

NOTE1: Scale of the measure is 0 to 110.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab53RelatedSDMT_SEX_Female_effectmeasures

Effect Measure of SDMT scores

	Result	OR	RR	ARR
SDMT MCID increase ≥15% - Week 48	Effect measure	2.429	2.354	0.031
	95% CI	(0.095 , 62.195)	(0.1 , 55.392)	(-0.065 , 0.127)
	p-value	0.592	0.595	0.887
SDMT MCID increase ≥15% - Week 96	Effect measure	6.051	5.492	0.094
	95% CI	(0.298 , 122.788)	(0.297 , 101.583)	(-0.043 , 0.23)
	p-value	0.241	0.253	0.259
SDMT MCID decrease ≥15% - Week 48	Effect measure	0.099	0.112	-0.12
	95% CI	(0.005 , 2.01)	(0.006 , 2.073)	(-0.283 , 0.043)
	p-value	0.132	0.142	0.194
SDMT MCID decrease ≥15% - Week 96	Effect measure	0.371	0.391	-0.049
	95% CI	(0.032 , 4.344)	(0.038 , 4.067)	(-0.171 , 0.073)
	p-value	0.43	0.432	0.434

NOTE1: Scale of the measure is 0 to 110. Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab53RelatedSDMT_SEX_Female_NPERCENT

Summary statistics SDMT scores

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
SDMT MCID increase ≥15% - Week 48	Yes	1 (2.00)	0 (0.00)	1 (1.75)
	No	31 (62.00)	25 (54.35)	56 (98.25)
	Missing	18 (36.00)	21 (45.65)	39 (40.62)
SDMT MCID increase ≥15% - Week 96	Yes	3 (6.00)	0 (0.00)	3 (5.26)
	No	29 (58.00)	25 (54.35)	54 (94.74)
	Missing	18 (36.00)	21 (45.65)	39 (40.62)
SDMT MCID decrease ≥15% - Week 48	Yes	0 (0.00)	3 (6.52)	3 (5.26)
	No	32 (64.00)	22 (47.83)	54 (94.74)
	Missing	18 (36.00)	21 (45.65)	39 (40.62)
SDMT MCID decrease ≥15% - Week 96	Yes	1 (2.00)	2 (4.35)	3 (5.26)
	No	31 (62.00)	23 (50.00)	54 (94.74)
	Missing	18 (36.00)	21 (45.65)	39 (40.62)

NOTE1: Scale of the measure is 0 to 110.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab53RelatedSDMT_SEX_Female_responsRate

Response Rate of SDMT scores

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
SDMT Baseline	Yes	32 (64.00)	25 (54.35)	57 (59.38)
	No	18 (36.00)	21 (45.65)	39 (40.62)
SDMT Week 48	Yes	38 (76.00)	31 (67.39)	69 (71.88)
	No	12 (24.00)	15 (32.61)	27 (28.12)
SDMT Week 96	Yes	39 (78.00)	28 (60.87)	67 (69.79)
	No	11 (22.00)	18 (39.13)	29 (30.21)

NOTE1: Scale of the measure is 0 to 110.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab53RelatedSDMT_SEX_Male_effectmeasures

Effect Measure of SDMT scores

	Result	OR	RR	ARR
SDMT MCID increase ≥15% - Week 48	Effect measure	1.222	1.2	0.017
	95% CI	(0.067 , 22.402)	(0.085 , 16.846)	(-0.226 , 0.26)
	p-value	0.892	0.892	0.893
SDMT MCID increase ≥15% - Week 96	Effect measure	3.947	3.571	0.1
	95% CI	(0.144 , 108.097)	(0.162 , 78.782)	(-0.178 , 0.378)
	p-value	0.416	0.42	0.93
SDMT MCID decrease ≥15% - Week 48	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A
SDMT MCID decrease ≥15% - Week 96	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A

NOTE1: Scale of the measure is 0 to 110. Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab53RelatedSDMT_SEX_Male_NPERCENT

Summary statistics SDMT scores

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
SDMT MCID increase ≥15% - Week 48	Yes	1 (4.76)	1 (5.56)	2 (9.09)
	No	9 (42.86)	11 (61.11)	20 (90.91)
	Missing	11 (52.38)	6 (33.33)	17 (43.59)
SDMT MCID increase ≥15% - Week 96	Yes	1 (4.76)	0 (0.00)	1 (4.55)
	No	9 (42.86)	12 (66.67)	21 (95.45)
	Missing	11 (52.38)	6 (33.33)	17 (43.59)
SDMT MCID decrease ≥15% - Week 48	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	10 (47.62)	12 (66.67)	22 (100.00)
	Missing	11 (52.38)	6 (33.33)	17 (43.59)
SDMT MCID decrease ≥15% - Week 96	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	10 (47.62)	12 (66.67)	22 (100.00)
	Missing	11 (52.38)	6 (33.33)	17 (43.59)

NOTE1: Scale of the measure is 0 to 110.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab53RelatedSDMT_SEX_Male_responsRate

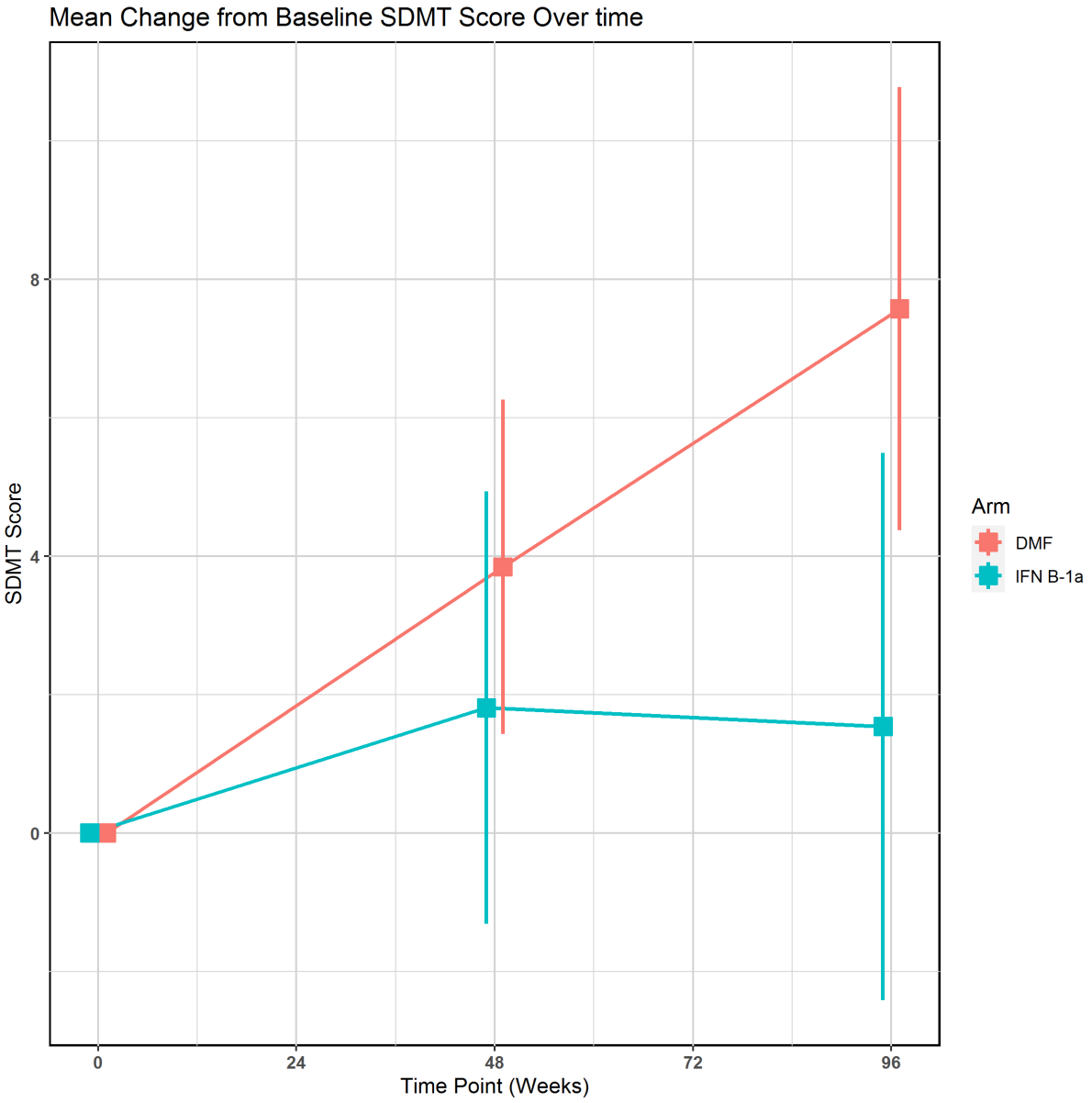
Response Rate of SDMT scores

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
SDMT Baseline	Yes	10 (47.62)	12 (66.67)	22 (56.41)
	No	11 (52.38)	6 (33.33)	17 (43.59)
SDMT Week 48	Yes	14 (66.67)	13 (72.22)	27 (69.23)
	No	7 (33.33)	5 (27.78)	12 (30.77)
SDMT Week 96	Yes	13 (61.90)	12 (66.67)	25 (64.10)
	No	8 (38.10)	6 (33.33)	14 (35.90)

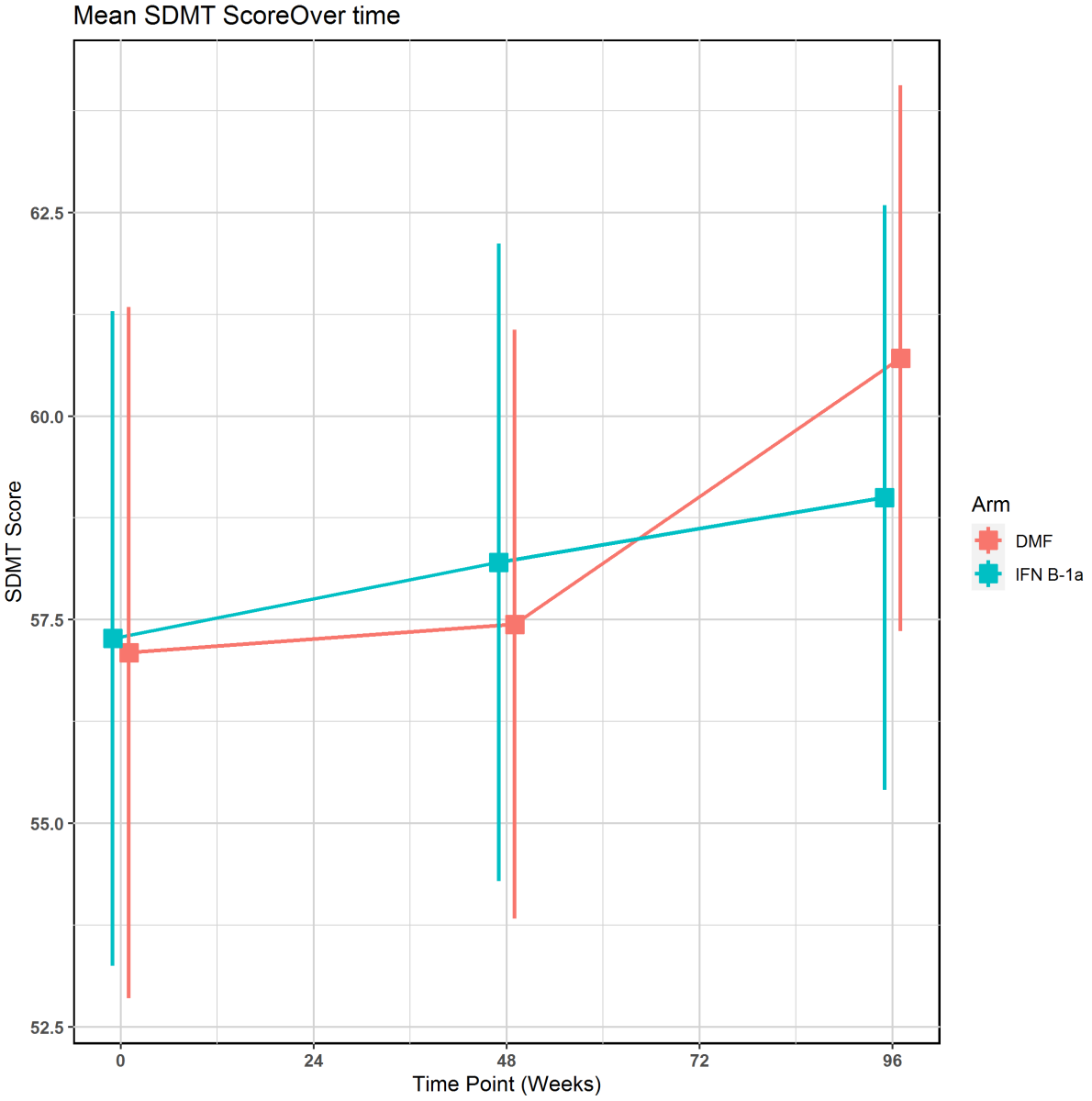
NOTE1: Scale of the measure is 0 to 110.Response rates are yes when patients report non-missing data for the given timepoint

Graphics

Change from baseline SDMT Score



SDMT Score


Mean SDMT ScoreOver time
SDMT Score
62.5
60.0
57.5
55.0
52.5
0
24
48
72
96
Time Point (Weeks)
Arm
DMF
IFN B-1a

PedsQL Fatique Parents

109MS306_CSRTab42_44Related_PedsQLFatigueParent_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale (Parent)

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.607	1.486	0.065
	95% CI	(0.559 , 4.619)	(0.614 , 3.598)	(-0.079 , 0.21)
	p-value	0.378	0.38	0.375
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	1.46	1.387	0.045
	95% CI	(0.468 , 4.558)	(0.518 , 3.712)	(-0.089 , 0.178)
	p-value	0.514	0.515	0.513
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.852	0.867	-0.015
	95% CI	(0.243 , 2.991)	(0.282 , 2.66)	(-0.136 , 0.105)
	p-value	0.802	0.803	0.802
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.333	0.347	-0.038
	95% CI	(0.034 , 3.317)	(0.037 , 3.223)	(-0.112 , 0.037)
	p-value	0.349	0.352	0.32
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	2.634	2.34	0.103
	95% CI	(0.755 , 9.188)	(0.77 , 7.115)	(-0.026 , 0.232)
	p-value	0.129	0.134	0.117
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	5.488	4.68	0.142
	95% CI	(1.123 , 26.827)	(1.063 , 20.604)	(0.023 , 0.26)
	p-value	0.035	0.041	0.019

	Result	OR	RR	ARR
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	4.083	3.467	0.142
	95% CI	(1.052 , 15.848)	(1.013 , 11.865)	(0.015 , 0.27)
	p-value	0.042	0.048	0.029
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.042	1.04	0.002
	95% CI	(0.141 , 7.694)	(0.152 , 7.102)	(-0.074 , 0.077)
	p-value	0.968	0.968	0.968
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.91	0.924	-0.013
	95% CI	(0.321 , 2.582)	(0.387 , 2.206)	(-0.158 , 0.131)
	p-value	0.859	0.859	0.859
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	1.953	1.82	0.063
	95% CI	(0.535 , 7.136)	(0.567 , 5.838)	(-0.057 , 0.183)
	p-value	0.311	0.314	0.305
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.852	0.867	-0.015
	95% CI	(0.243 , 2.991)	(0.282 , 2.66)	(-0.136 , 0.105)
	p-value	0.802	0.803	0.802
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.043	1.04	0.003
	95% CI	(0.246 , 4.421)	(0.275 , 3.934)	(-0.101 , 0.107)
	p-value	0.954	0.954	0.954
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.324	0.378	-0.132
	95% CI	(0.096 , 1.097)	(0.129 , 1.11)	(-0.266 , 0.003)
	p-value	0.07	0.077	0.054
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.351	0.39	-0.094
	95% CI	(0.088 , 1.408)	(0.11 , 1.387)	(-0.212 , 0.024)

	Result	OR	RR	ARR
	p-value	0.14	0.146	0.119
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.489	0.52	-0.055
	95% CI	(0.115 , 2.074)	(0.137 , 1.967)	(-0.164 , 0.054)
	p-value	0.332	0.335	0.319
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.131	0.149	-0.115
	95% CI	(0.016 , 1.108)	(0.019 , 1.165)	(-0.215 , -0.014)
	p-value	0.062	0.07	0.025
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	0.818	0.851	-0.032
	95% CI	(0.307 , 2.183)	(0.386 , 1.876)	(-0.185 , 0.122)
	p-value	0.689	0.689	0.688
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.324	0.378	-0.132
	95% CI	(0.096 , 1.097)	(0.129 , 1.11)	(-0.266 , 0.003)
	p-value	0.07	0.077	0.054
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	0.611	0.65	-0.054
	95% CI	(0.186 , 2.013)	(0.228 , 1.853)	(-0.182 , 0.075)
	p-value	0.418	0.42	0.412
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.667	0.693	-0.035
	95% CI	(0.176 , 2.52)	(0.208 , 2.312)	(-0.15 , 0.079)
	p-value	0.55	0.551	0.546
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.818	0.851	-0.032
	95% CI	(0.307 , 2.183)	(0.386 , 1.876)	(-0.185 , 0.122)
	p-value	0.689	0.689	0.688
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.75	0.78	-0.034

	Result	OR	RR	ARR
	95% CI	(0.24 , 2.34)	(0.291 , 2.088)	(-0.167 , 0.099)
	p-value	0.62	0.621	0.618
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.877	0.891	-0.015
	95% CI	(0.273 , 2.816)	(0.322 , 2.47)	(-0.144 , 0.115)
	p-value	0.825	0.825	0.825
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.044	1.04	0.004
	95% CI	(0.283 , 3.853)	(0.32 , 3.375)	(-0.112 , 0.119)
	p-value	0.948	0.948	0.948

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab42_44Related_PedsQLFatigueParent_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale (Parent)

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	10 (14.08)	7 (10.94)	17 (16.67)
	No	40 (56.34)	45 (70.31)	85 (83.33)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	8 (11.27)	6 (9.38)	14 (13.73)
	No	42 (59.15)	46 (71.88)	88 (86.27)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	5 (7.04)	6 (9.38)	11 (10.78)
	No	45 (63.38)	46 (71.88)	91 (89.22)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (1.41)	3 (4.69)	4 (3.92)
	No	49 (69.01)	49 (76.56)	98 (96.08)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	9 (12.68)	4 (6.25)	13 (12.75)
	No	41 (57.75)	48 (75.00)	89 (87.25)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	9 (12.68)	2 (3.12)	11 (10.78)
	No	41 (57.75)	50 (78.12)	91 (89.22)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	10 (14.08)	3 (4.69)	13 (12.75)
	No	40 (56.34)	49 (76.56)	89 (87.25)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	2 (2.82)	2 (3.12)	4 (3.92)
	No	48 (67.61)	50 (78.12)	98 (96.08)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	8 (11.27)	9 (14.06)	17 (16.67)
	No	42 (59.15)	43 (67.19)	85 (83.33)

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	7 (9.86)	4 (6.25)	11 (10.78)
	No	43 (60.56)	48 (75.00)	91 (89.22)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	5 (7.04)	6 (9.38)	11 (10.78)
	No	45 (63.38)	46 (71.88)	91 (89.22)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	4 (5.63)	4 (6.25)	8 (7.84)
	No	46 (64.79)	48 (75.00)	94 (92.16)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Yes	4 (5.63)	11 (17.19)	15 (14.71)
	No	46 (64.79)	41 (64.06)	87 (85.29)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Yes	3 (4.23)	8 (12.50)	11 (10.78)
	No	47 (66.20)	44 (68.75)	91 (89.22)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Yes	3 (4.23)	6 (9.38)	9 (8.82)
	No	47 (66.20)	46 (71.88)	93 (91.18)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (1.41)	7 (10.94)	8 (7.84)
	No	49 (69.01)	45 (70.31)	94 (92.16)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Yes	9 (12.68)	11 (17.19)	20 (19.61)
	No	41 (57.75)	41 (64.06)	82 (80.39)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	4 (5.63)	11 (17.19)	15 (14.71)
	No	46 (64.79)	41 (64.06)	87 (85.29)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	5 (7.04)	8 (12.50)	13 (12.75)
	No	45 (63.38)	44 (68.75)	89 (87.25)

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Missing	21 (29.58)	12 (18.75)	33 (24.44)
	Yes	4 (5.63)	6 (9.38)	10 (9.80)
	No	46 (64.79)	46 (71.88)	92 (90.20)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Missing	21 (29.58)	12 (18.75)	33 (24.44)
	Yes	9 (12.68)	11 (17.19)	20 (19.61)
	No	41 (57.75)	41 (64.06)	82 (80.39)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Missing	21 (29.58)	12 (18.75)	33 (24.44)
	Yes	6 (8.45)	8 (12.50)	14 (13.73)
	No	44 (61.97)	44 (68.75)	88 (86.27)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Missing	21 (29.58)	12 (18.75)	33 (24.44)
	Yes	6 (8.45)	7 (10.94)	13 (12.75)
	No	44 (61.97)	45 (70.31)	89 (87.25)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Missing	21 (29.58)	12 (18.75)	33 (24.44)
	Yes	5 (7.04)	5 (7.81)	10 (9.80)
	No	45 (63.38)	47 (73.44)	92 (90.20)
	Missing	21 (29.58)	12 (18.75)	33 (24.44)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab42_44Related_PedsQLFatigueParent_responsRate

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)	**Response (n (%))**	**DMF (N=71)**	**IFN B-1a (N=64)**	**Total (N=135)**
COGNITIVE FATIGUE-Baseline	Yes	50 (70.42)	52 (81.25)	102 (75.56)
	No	21 (29.58)	12 (18.75)	33 (24.44)
COGNITIVE FATIGUE-Week 24	Yes	56 (78.87)	58 (90.62)	114 (84.44)
	No	15 (21.13)	6 (9.38)	21 (15.56)
COGNITIVE FATIGUE-Week 48	Yes	51 (71.83)	43 (67.19)	94 (69.63)
	No	20 (28.17)	21 (32.81)	41 (30.37)
COGNITIVE FATIGUE-Week 72	Yes	43 (60.56)	29 (45.31)	72 (53.33)
	No	28 (39.44)	35 (54.69)	63 (46.67)
COGNITIVE FATIGUE-Week 96	Yes	28 (39.44)	22 (34.38)	50 (37.04)
	No	43 (60.56)	42 (65.62)	85 (62.96)
GENERAL FATIGUE-Baseline	Yes	50 (70.42)	52 (81.25)	102 (75.56)
	No	21 (29.58)	12 (18.75)	33 (24.44)
GENERAL FATIGUE-Week 24	Yes	56 (78.87)	58 (90.62)	114 (84.44)
	No	15 (21.13)	6 (9.38)	21 (15.56)
GENERAL FATIGUE-Week 48	Yes	51 (71.83)	43 (67.19)	94 (69.63)
	No	20 (28.17)	21 (32.81)	41 (30.37)
GENERAL FATIGUE-Week 72	Yes	43 (60.56)	29 (45.31)	72 (53.33)
	No	28 (39.44)	35 (54.69)	63 (46.67)
GENERAL FATIGUE-Week 96	Yes	28 (39.44)	22 (34.38)	50 (37.04)
	No	43 (60.56)	42 (65.62)	85 (62.96)
SLEEP/REST FATIGUE-Baseline	Yes	50 (70.42)	52 (81.25)	102 (75.56)
	No	21 (29.58)	12 (18.75)	33 (24.44)
SLEEP/REST FATIGUE-Week 24	Yes	56 (78.87)	58 (90.62)	114 (84.44)
	No	15 (21.13)	6 (9.38)	21 (15.56)
SLEEP/REST FATIGUE-Week 48	Yes	51 (71.83)	43 (67.19)	94 (69.63)
	No	20 (28.17)	21 (32.81)	41 (30.37)
SLEEP/REST FATIGUE-Week 72	Yes	42 (59.15)	29 (45.31)	71 (52.59)
	No	29 (40.85)	35 (54.69)	64 (47.41)

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)	**Response (n (%))**	**DMF (N=71)**	**IFN B-1a (N=64)**	**Total (N=135)**
SLEEP/REST FATIGUE-Week 96	Yes	28 (39.44)	22 (34.38)	50 (37.04)
	No	43 (60.56)	42 (65.62)	85 (62.96)

NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
General Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	40 (56)	49 (77)	89 (66)
Mean (SD)	-1.8 (16.18)	-4.5 (17.39)	-3.3 (16.81)
Median	-4.2	-4.2	-4.2
Q1,Q3	-12.5, 6.3	-12.5, 4.2	-12.5, 4.2
Min, Max	-38, 29	-50, 38	-50, 38
Week 48			
n (%)	35 (49)	36 (56)	71 (53)
Mean (SD)	4.5 (16.32)	-10.3 (21.47)	-3.0 (20.37)
Median	4.2	-4.2	0.0
Q1,Q3	-4.2, 16.7	-20.8, 4.2	-12.5, 8.3
Min, Max	-29, 38	-71, 29	-71, 38

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
General Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	1.3 (19.29)	-6.0 (19.44)	-1.9 (19.53)
Median	0.0	-8.3	-4.2
Q1,Q3	-12.5, 20.8	-16.7, 0.0	-12.5, 10.4
Min, Max	-38, 33	-42, 54	-42, 54
Week 96			
n (%)	20 (28)	19 (30)	39 (29)
Mean (SD)	-3.3 (14.47)	-4.2 (21.29)	-3.7 (17.88)
Median	-4.2	0.0	-4.2
Q1,Q3	-12.5, 0.0	-20.8, 8.3	-16.7, 4.2
Min, Max	-29, 38	-46, 38	-46, 38

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
Sleep/Rest Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 24			
n (%)	40 (56)	49 (77)	89 (66)
Mean (SD)	0.8 (18.47)	0.8 (19.39)	0.8 (18.87)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 6.3	-12.5, 12.5	-12.5, 8.3
Min, Max	-29, 46	-38, 46	-38, 46
Week 48			
n (%)	35 (49)	36 (56)	71 (53)
Mean (SD)	1.8 (19.39)	-2.5 (21.48)	-0.4 (20.45)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-12.5, 8.3	-8.3, 8.3
Min, Max	-33, 50	-63, 50	-63, 50

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
Sleep/Rest Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 72			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	-0.8 (18.08)	-3.2 (18.88)	-1.9 (18.31)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 12.5	-16.7, 12.5	-12.5, 12.5
Min, Max	-42, 38	-33, 25	-42, 38
Week 96			
n (%)	20 (28)	19 (30)	39 (29)
Mean (SD)	-0.2 (21.65)	-2.6 (22.58)	-1.4 (21.85)
Median	0.0	0.0	0.0
Q1,Q3	-14.6, 8.3	-20.8, 12.5	-16.7, 12.5
Min, Max	-29, 46	-42, 46	-42, 46

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
Cognitive Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	40 (56)	49 (77)	89 (66)
Mean (SD)	2.8 (19.21)	-2.9 (18.09)	-0.3 (18.71)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 12.5	-12.5, 4.2	-8.3, 4.2
Min, Max	-42, 54	-50, 46	-50, 54
Week 48			
n (%)	35 (49)	36 (56)	71 (53)
Mean (SD)	4.3 (15.28)	-1.5 (19.56)	1.4 (17.69)
Median	0.0	2.1	0.0
Q1,Q3	-4.2, 12.5	-12.5, 8.3	-4.2, 8.3
Min, Max	-21, 46	-50, 46	-50, 46

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135), Change from Baseline
Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	31 (44)	25 (39)	56 (41)
Mean (SD)	0.3 (16.52)	-1.0 (25.27)	-0.3 (20.69)
Median	0.0	-4.2	0.0
Q1,Q3	-4.2, 4.2	-12.5, 8.3	-8.3, 6.3
Min, Max	-46, 38	-46, 58	-46, 58
Week 96			
n (%)	20 (28)	19 (30)	39 (29)
Mean (SD)	1.3 (11.48)	-5.3 (22.60)	-1.9 (17.85)
Median	0.0	-4.2	0.0
Q1,Q3	-4.2, 6.3	-20.8, 12.5	-8.3, 8.3
Min, Max	-25, 33	-50, 33	-50, 33

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

109MS306_table42_44_CHG_DESCRIBE

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)
General Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total(N= 135)
Baseline			
n (%)	50 (70)	52 (81)	102 (76)
Mean (SD)	69.0 (24.67)	72.3 (22.50)	70.7 (23.53)
Median	70.8	79.2	70.8
Q1,Q3	54.2, 91.7	58.3, 91.7	58.3, 91.7
Min, Max	0, 100	13, 100	0, 100
Week 24			
n (%)	56 (79)	58 (91)	114 (84)
Mean (SD)	70.1 (21.50)	66.8 (23.93)	68.4 (22.73)
Median	70.8	68.8	70.8
Q1,Q3	58.3, 87.5	50.0, 87.5	50.0, 87.5
Min, Max	21, 100	13, 100	13, 100
Week 48			
n (%)	51 (72)	43 (67)	94 (70)
Mean (SD)	72.2 (23.29)	67.2 (23.10)	69.9 (23.21)
Median	79.2	70.8	75.0
Q1,Q3	54.2, 91.7	54.2, 79.2	54.2, 91.7
Min, Max	25, 100	8, 100	8, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total(N= 135)**
Week 72			
n (%)	43 (61)	29 (45)	72 (53)
Mean (SD)	72.3 (21.55)	71.6 (24.90)	72.0 (22.79)
Median	79.2	75.0	77.1
Q1,Q3	54.2, 87.5	62.5, 87.5	54.2, 87.5
Min, Max	25, 100	8, 100	8, 100
Week 96			
n (%)	28 (39)	22 (34)	50 (37)
Mean (SD)	69.6 (23.35)	74.4 (19.64)	71.8 (21.71)
Median	70.8	75.0	70.8
Q1,Q3	52.1, 87.5	62.5, 91.7	54.2, 91.7
Min, Max	25, 100	29, 100	25, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)
Sleep/Rest Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total(N= 135)
Baseline			
n (%)	50 (70)	52 (81)	102 (76)
Mean (SD)	67.2 (24.20)	66.8 (24.50)	67.0 (24.24)
Median	66.7	66.7	66.7
Q1,Q3	50.0, 87.5	45.8, 91.7	50.0, 87.5
Min, Max	0, 100	13, 100	0, 100
Week 24			
n (%)	56 (79)	58 (91)	114 (84)
Mean (SD)	67.6 (22.59)	67.8 (25.17)	67.7 (23.83)
Median	70.8	68.8	70.8
Q1,Q3	56.3, 82.3	50.0, 91.7	50.0, 87.5
Min, Max	8, 100	21, 100	8, 100
Week 48			
n (%)	51 (72)	43 (67)	94 (70)
Mean (SD)	68.9 (24.20)	68.8 (21.47)	68.8 (22.87)
Median	75.0	70.8	72.9
Q1,Q3	54.2, 91.7	54.2, 87.5	54.2, 87.5
Min, Max	13, 100	25, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total(N= 135)**
Week 72			
n (%)	42 (59)	29 (45)	71 (53)
Mean (SD)	67.2 (23.77)	71.8 (21.84)	69.1 (22.96)
Median	70.8	70.8	70.8
Q1,Q3	54.2, 83.3	58.3, 87.5	58.3, 87.5
Min, Max	13, 100	17, 100	13, 100
Week 96			
n (%)	28 (39)	22 (34)	50 (37)
Mean (SD)	70.4 (21.47)	68.8 (22.26)	69.7 (21.61)
Median	75.0	66.7	70.8
Q1,Q3	58.3, 85.4	54.2, 87.5	58.3, 87.5
Min, Max	29, 100	25, 100	25, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)
Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total(N= 135)**
Baseline			
n (%)	50 (70)	52 (81)	102 (76)
Mean (SD)	70.9 (28.19)	76.7 (21.41)	73.9 (25.01)
Median	79.2	77.1	77.1
Q1,Q3	50.0, 95.8	60.4, 95.8	54.2, 95.8
Min, Max	0, 100	0, 100	0, 100
Week 24			
n (%)	56 (79)	58 (91)	114 (84)
Mean (SD)	74.5 (23.83)	74.0 (23.60)	74.2 (23.61)
Median	79.2	79.2	79.2
Q1,Q3	56.3, 100.0	54.2, 95.8	54.2, 100.0
Min, Max	21, 100	4, 100	4, 100
Week 48			
n (%)	51 (72)	43 (67)	94 (70)
Mean (SD)	73.4 (23.60)	76.5 (21.46)	74.8 (22.58)
Median	79.2	79.2	79.2
Q1,Q3	58.3, 95.8	58.3, 100.0	58.3, 95.8
Min, Max	4, 100	29, 100	4, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total(N= 135)**
Week 72			
n (%)	43 (61)	29 (45)	72 (53)
Mean (SD)	72.1 (22.19)	77.2 (19.50)	74.1 (21.15)
Median	75.0	83.3	75.0
Q1,Q3	50.0, 91.7	58.3, 95.8	58.3, 93.8
Min, Max	33, 100	42, 100	33, 100
Week 96			
n (%)	28 (39)	22 (34)	50 (37)
Mean (SD)	69.6 (27.98)	74.6 (21.13)	71.8 (25.08)
Median	70.8	77.1	75.0
Q1,Q3	56.3, 95.8	62.5, 95.8	58.3, 95.8
Min, Max	13, 100	33, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

109MS306_table42_44_CHG_HEDGESCI

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.307	-0.113	0.727
	48	0.327	-0.142	0.795
	72	0.061	-0.466	0.588
	96	0.366	-0.267	1.000
GENERAL FATIGUE	24	0.162	-0.256	0.581
	48	0.774	0.291	1.256
	72	0.379	-0.152	0.911
	96	0.046	-0.582	0.674
SLEEP/REST FATIGUE	24	0.004	-0.414	0.421
	48	0.212	-0.255	0.678
	72	0.128	-0.399	0.655
	96	0.11	-0.519	0.738

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T42_44/109MS306_table42_44_CHG_HEDGESCI.sas date: 16FEB2022

109MS306_table42_44_CHG_LSMEANS

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

General Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	40 (56)	49 (77)
Lsmean (SE)	-4.08 (2.786)	-6.73 (2.522)
Lsmean_95 % CI	(-9.617, 01.463)	(-11.75, -1.721)
Diffrence (95% CI)	2.66 (-4.002, 9.316)	
SE_Difference	3.3493	
p-value	0.4298	
Week 48		
n (%)	35 (49)	36 (56)
Lsmean (SE)	02.13 (3.522)	-10.8 (3.349)
Lsmean_95 % CI	(-4.898, 09.163)	(-17.49, -4.119)
Diffrence (95% CI)	12.94 (4.279, 21.595)	
SE_Difference	4.3377	
p-value	0.0040	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	31 (44)	25 (39)
Lsmean (SE)	02.12 (3.412)	-2.66 (3.779)
Lsmean_95 % CI	(-4.727, 08.965)	(-10.25, 04.919)
Diffrence (95% CI)	4.78 (-4.823, 14.391)	
SE_Difference	4.7876	
p-value	0.3223	
Week 96		
n (%)	20 (28)	19 (30)
Lsmean (SE)	-2.99 (3.732)	-2.58 (3.943)
Lsmean_95 % CI	(-10.56, 04.590)	(-10.58, 05.430)
Diffrence (95% CI)	-0.41 (-11.211, 10.389)	
SE_Difference	5.3197	
p-value	0.9389	

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Sleep/Rest Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	40 (56)	49 (77)
Lsmean (SE)	00.93 (3.105)	-0.26 (2.782)
Lsmean_95 % CI	(-5.240, 07.109)	(-5.786, 05.275)
Diffrence (95% CI)	1.19 (-6.200, 8.579)	
SE_Difference	3.7165	
p-value	0.7496	
Week 48		
n (%)	35 (49)	36 (56)
Lsmean (SE)	-0.09 (3.590)	-3.74 (3.359)
Lsmean_95 % CI	(-7.253, 07.077)	(-10.44, 02.969)
Diffrence (95% CI)	3.65 (-5.083, 12.378)	
SE_Difference	4.3740	
p-value	0.4073	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	31 (44)	25 (39)
Lsmean (SE)	00.45 (3.182)	-0.71 (3.488)
Lsmean_95 % CI	(-5.936, 06.836)	(-7.711, 06.287)
Diffrence (95% CI)	1.16 (-7.702, 10.026)	
SE_Difference	4.4174	
p-value	0.7936	
Week 96		
n (%)	20 (28)	19 (30)
Lsmean (SE)	01.87 (4.175)	-2.57 (4.358)
Lsmean_95 % CI	(-6.611, 10.341)	(-11.42, 06.279)
Diffrence (95% CI)	4.43 (-7.580, 16.448)	
SE_Difference	5.9180	
p-value	0.4587	

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	40 (56)	49 (77)
Lsmean (SE)	02.26 (3.009)	-2.52 (2.726)
Lsmean_95 % CI	(-3.722, 08.245)	(-7.940, 02.902)
Diffrence (95% CI)	4.78 (-2.467, 12.028)	
SE_Difference	3.6451	
p-value	0.1932	
Week 48		
n (%)	35 (49)	36 (56)
Lsmean (SE)	02.42 (3.099)	-1.02 (2.893)
Lsmean_95 % CI	(-3.762, 08.609)	(-6.798, 04.752)
Diffrence (95% CI)	3.45 (-4.173, 11.067)	
SE_Difference	3.8177	
p-value	0.3698	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	31 (44)	25 (39)
Lsmean (SE)	00.75 (3.257)	02.98 (3.535)
Lsmean_95 % CI	(-5.789, 07.284)	(-4.117, 10.069)
Diffrence (95% CI)	-2.23 (-11.346, 6.888)	
SE_Difference	4.5434	
p-value	0.6258	
Week 96		
n (%)	20 (28)	19 (30)
Lsmean (SE)	00.21 (3.814)	-3.42 (4.010)
Lsmean_95 % CI	(-7.530, 07.958)	(-11.57, 04.717)
Diffrence (95% CI)	3.64 (-7.483, 14.761)	
SE_Difference	5.4784	
p-value	0.5109	

Sub groups

Change

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_age13to14

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 13 TO 14. General Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	-6.3 (20.29)	-15.9 (19.62)	-11.8 (19.95)
Median	0.0	-12.5	-8.3
Q1,Q3	-22.9, 4.2	-29.2, 0.0	-29.2, 0.0
Min, Max	-38, 25	-50, 13	-50, 25
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	6.9 (14.59)	-23.1 (24.92)	-11.1 (25.77)
Median	2.1	-20.8	-4.2
Q1,Q3	0.0, 12.5	-41.7, -4.2	-25.0, 4.2
Min, Max	-8, 33	-71, 8	-71, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	2.6 (16.36)	-2.4 (21.23)	0.3 (18.26)
Median	0.0	0.0	0.0
Q1,Q3	-2.1, 8.3	-16.7, 16.7	-4.2, 12.5
Min, Max	-25, 33	-42, 21	-42, 33
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	1.6 (9.69)	-8.3 (21.41)	-2.7 (15.90)
Median	0.0	0.0	0.0
Q1,Q3	-2.1, 4.2	-20.8, 4.2	-4.2, 4.2
Min, Max	-13, 21	-46, 13	-46, 21

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	-1.0 (12.75)	-7.2 (14.32)	-4.6 (13.67)
Median	-2.1	-4.2	-4.2
Q1,Q3	-8.3, 6.3	-12.5, 4.2	-12.5, 4.2
Min, Max	-21, 21	-33, 13	-33, 21
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	2.8 (13.35)	-17.1 (26.06)	-9.2 (23.53)
Median	0.0	-20.8	-4.2
Q1,Q3	-4.2, 0.0	-29.2, 0.0	-25.0, 0.0
Min, Max	-8, 29	-63, 21	-63, 29

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	-2.1 (11.79)	1.8 (20.11)	-0.3 (15.71)
Median	0.0	8.3	0.0
Q1,Q3	-8.3, 0.0	-16.7, 16.7	-8.3, 16.7
Min, Max	-21, 21	-33, 21	-33, 21
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	1.0 (15.87)	-4.2 (22.67)	-1.2 (18.45)
Median	0.0	4.2	0.0
Q1,Q3	-2.1, 2.1	-20.8, 12.5	-4.2, 8.3
Min, Max	-25, 33	-42, 17	-42, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	0.5 (15.97)	-1.1 (21.09)	-0.4 (18.63)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 12.5	-12.5, 12.5	-12.5, 12.5
Min, Max	-29, 21	-50, 29	-50, 29
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	4.9 (12.75)	-4.0 (27.63)	-0.4 (22.68)
Median	0.0	4.2	0.0
Q1,Q3	-4.2, 8.3	-25.0, 8.3	-4.2, 8.3
Min, Max	-4, 29	-50, 33	-50, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	2.1 (9.71)	12.5 (34.27)	6.9 (24.07)
Median	0.0	20.8	0.0
Q1,Q3	-4.2, 6.3	-12.5, 37.5	-4.2, 20.8
Min, Max	-8, 21	-46, 58	-46, 58
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	2.1 (5.46)	-2.8 (28.95)	0.0 (18.56)
Median	0.0	4.2	0.0
Q1,Q3	0.0, 4.2	-20.8, 12.5	0.0, 8.3
Min, Max	-4, 13	-50, 33	-50, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_age15to17

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 15 TO 17. General Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	32 (60)	38 (76)	70 (68)
Mean (SD)	-0.7 (15.16)	-1.2 (15.44)	-1.0 (15.20)
Median	-4.2	0.0	-4.2
Q1,Q3	-12.5, 12.5	-8.3, 8.3	-8.3, 8.3
Min, Max	-25, 29	-38, 38	-38, 38
Week 48			
n (%)	29 (55)	27 (54)	56 (54)
Mean (SD)	4.0 (16.84)	-6.0 (18.79)	-0.8 (18.35)
Median	4.2	-4.2	0.0
Q1,Q3	-4.2, 16.7	-12.5, 4.2	-12.5, 8.3
Min, Max	-29, 38	-67, 29	-67, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	23 (43)	18 (36)	41 (40)
Mean (SD)	0.9 (20.53)	-7.4 (19.15)	-2.7 (20.13)
Median	-4.2	-8.3	-8.3
Q1,Q3	-12.5, 20.8	-16.7, 0.0	-12.5, 8.3
Min, Max	-38, 33	-38, 54	-38, 54
Week 96			
n (%)	12 (23)	13 (26)	25 (24)
Mean (SD)	-6.6 (16.52)	-2.2 (21.82)	-4.3 (19.19)
Median	-10.4	-4.2	-8.3
Q1,Q3	-16.7, -2.1	-16.7, 8.3	-16.7, 4.2
Min, Max	-29, 38	-38, 38	-38, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	32 (60)	38 (76)	70 (68)
Mean (SD)	1.3 (19.78)	3.1 (20.20)	2.3 (19.88)
Median	0.0	2.1	0.0
Q1,Q3	-14.6, 8.3	-12.5, 12.5	-12.5, 12.5
Min, Max	-29, 46	-38, 46	-38, 46
Week 48			
n (%)	29 (55)	27 (54)	56 (54)
Mean (SD)	1.6 (20.61)	2.3 (17.73)	1.9 (19.10)
Median	4.2	4.2	4.2
Q1,Q3	-8.3, 8.3	-8.3, 12.5	-8.3, 8.3
Min, Max	-33, 50	-33, 50	-33, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	23 (43)	18 (36)	41 (40)
Mean (SD)	-0.4 (20.02)	-5.1 (18.61)	-2.4 (19.32)
Median	0.0	-4.2	-4.2
Q1,Q3	-12.5, 12.5	-25.0, 8.3	-12.5, 12.5
Min, Max	-42, 38	-33, 25	-42, 38
Week 96			
n (%)	12 (23)	13 (26)	25 (24)
Mean (SD)	-1.0 (25.45)	-1.9 (23.42)	-1.5 (23.90)
Median	-12.5	-4.2	-8.3
Q1,Q3	-20.8, 18.8	-12.5, 12.5	-16.7, 12.5
Min, Max	-29, 46	-42, 46	-42, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	32 (60)	38 (76)	70 (68)
Mean (SD)	3.4 (20.12)	-3.4 (17.41)	-0.3 (18.87)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 12.5	-12.5, 4.2	-8.3, 4.2
Min, Max	-42, 54	-50, 46	-50, 54
Week 48			
n (%)	29 (55)	27 (54)	56 (54)
Mean (SD)	4.2 (15.94)	-0.6 (16.65)	1.9 (16.32)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 12.5	-12.5, 8.3	-6.3, 8.3
Min, Max	-21, 46	-38, 46	-38, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	23 (43)	18 (36)	41 (40)
Mean (SD)	-0.4 (18.46)	-6.3 (19.56)	-2.9 (18.94)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 4.2	-16.7, 0.0	-8.3, 4.2
Min, Max	-46, 38	-42, 42	-46, 42
Week 96			
n (%)	12 (23)	13 (26)	25 (24)
Mean (SD)	0.7 (14.42)	-6.4 (20.31)	-3.0 (17.74)
Median	0.0	-4.2	-4.2
Q1,Q3	-6.3, 6.3	-20.8, 4.2	-12.5, 4.2
Min, Max	-25, 33	-38, 33	-38, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_female

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for FEMALE SEX. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	25 (50)	35 (76)	60 (63)
Mean (SD)	-4.3 (14.95)	-5.5 (18.87)	-5.0 (17.22)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 4.2	-16.7, 4.2	-16.7, 4.2
Min, Max	-38, 29	-50, 38	-50, 38
Week 48			
n (%)	23 (46)	27 (59)	50 (52)
Mean (SD)	0.5 (15.66)	-11.6 (23.18)	-6.0 (20.79)
Median	0.0	-8.3	-4.2
Q1,Q3	-12.5, 12.5	-25.0, 4.2	-16.7, 8.3
Min, Max	-29, 38	-71, 29	-71, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	19 (38)	21 (46)	40 (42)
Mean (SD)	-1.8 (19.06)	-6.9 (21.14)	-4.5 (20.09)
Median	-8.3	-8.3	-8.3
Q1,Q3	-12.5, 20.8	-16.7, 4.2	-16.7, 4.2
Min, Max	-29, 33	-42, 54	-42, 54
Week 96			
n (%)	12 (24)	16 (35)	28 (29)
Mean (SD)	-2.4 (16.33)	-5.7 (22.82)	-4.3 (20.01)
Median	-6.3	-6.3	-6.3
Q1,Q3	-12.5, 0.0	-20.8, 8.3	-16.7, 6.3
Min, Max	-17, 38	-46, 38	-46, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	25 (50)	35 (76)	60 (63)
Mean (SD)	-0.2 (18.92)	-1.7 (18.22)	-1.0 (18.37)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 4.2	-12.5, 4.2	-12.5, 4.2
Min, Max	-29, 46	-38, 46	-38, 46
Week 48			
n (%)	23 (46)	27 (59)	50 (52)
Mean (SD)	1.8 (14.86)	-2.0 (19.45)	-0.3 (17.42)
Median	4.2	0.0	0.0
Q1,Q3	-4.2, 8.3	-12.5, 8.3	-8.3, 8.3
Min, Max	-29, 46	-42, 50	-42, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	19 (38)	21 (46)	40 (42)
Mean (SD)	-1.3 (14.03)	-4.6 (19.63)	-3.0 (17.06)
Median	0.0	-4.2	-2.1
Q1,Q3	-8.3, 12.5	-25.0, 12.5	-16.7, 12.5
Min, Max	-25, 25	-33, 25	-33, 25
Week 96			
n (%)	12 (24)	16 (35)	28 (29)
Mean (SD)	-0.3 (22.71)	-7.6 (19.91)	-4.5 (21.06)
Median	-6.3	-6.3	-6.3
Q1,Q3	-14.6, 8.3	-20.8, 10.4	-18.8, 10.4
Min, Max	-25, 46	-42, 21	-42, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	25 (50)	35 (76)	60 (63)
Mean (SD)	0.2 (21.02)	-4.3 (17.55)	-2.4 (19.03)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 4.2	-12.5, 4.2	-12.5, 4.2
Min, Max	-42, 54	-50, 46	-50, 54
Week 48			
n (%)	23 (46)	27 (59)	50 (52)
Mean (SD)	4.2 (14.32)	-2.9 (19.98)	0.3 (17.79)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 8.3	-16.7, 8.3	-8.3, 8.3
Min, Max	-21, 46	-50, 46	-50, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	19 (38)	21 (46)	40 (42)
Mean (SD)	-0.9 (15.93)	-5.0 (23.59)	-3.0 (20.17)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 4.2	-16.7, 4.2	-10.4, 4.2
Min, Max	-46, 38	-46, 42	-46, 42
Week 96			
n (%)	12 (24)	16 (35)	28 (29)
Mean (SD)	0.3 (14.37)	-9.6 (21.34)	-5.4 (19.04)
Median	-2.1	-6.3	-4.2
Q1,Q3	-6.3, 6.3	-25.0, 4.2	-18.8, 4.2
Min, Max	-25, 33	-50, 33	-50, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_male

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for MALE SEX. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	14 (78)	29 (74)
Mean (SD)	2.5 (17.73)	-2.1 (13.25)	0.3 (15.63)
Median	0.0	-2.1	0.0
Q1,Q3	-8.3, 16.7	-8.3, 4.2	-8.3, 12.5
Min, Max	-29, 29	-25, 25	-29, 29
Week 48			
n (%)	12 (57)	9 (50)	21 (54)
Mean (SD)	12.0 (15.44)	-6.5 (15.74)	4.1 (17.84)
Median	12.5	0.0	0.0
Q1,Q3	-2.1, 27.1	-8.3, 4.2	-4.2, 16.7
Min, Max	-10, 33	-42, 8	-42, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	4 (22)	16 (41)
Mean (SD)	6.3 (19.42)	-1.0 (2.08)	4.4 (16.97)
Median	6.3	0.0	0.0
Q1,Q3	-2.1, 20.8	-2.1, 0.0	-2.1, 18.8
Min, Max	-38, 33	-4, 0	-38, 33
Week 96			
n (%)	8 (38)	3 (17)	11 (28)
Mean (SD)	-4.7 (12.08)	4.2 (7.22)	-2.3 (11.39)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 0.0	0.0, 12.5	0.0, 0.0
Min, Max	-29, 8	0, 13	-29, 13

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	14 (78)	29 (74)
Mean (SD)	2.5 (18.22)	6.8 (21.53)	4.6 (19.65)
Median	-4.2	10.4	8.3
Q1,Q3	-12.5, 16.7	-4.2, 16.7	-8.3, 16.7
Min, Max	-17, 42	-29, 46	-29, 46
Week 48			
n (%)	12 (57)	9 (50)	21 (54)
Mean (SD)	1.7 (26.85)	-4.2 (28.03)	-0.8 (26.83)
Median	-4.2	-4.2	-4.2
Q1,Q3	-18.8, 27.1	-16.7, 12.5	-16.7, 12.5
Min, Max	-33, 50	-63, 38	-63, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	4 (22)	16 (41)
Mean (SD)	0.0 (23.84)	4.2 (14.03)	1.0 (21.44)
Median	0.0	4.2	0.0
Q1,Q3	-10.4, 16.7	-6.3, 14.6	-10.4, 16.7
Min, Max	-42, 38	-13, 21	-42, 38
Week 96			
n (%)	8 (38)	3 (17)	11 (28)
Mean (SD)	0.0 (21.48)	23.6 (19.69)	6.4 (22.85)
Median	0.0	16.7	0.0
Q1,Q3	-14.6, 12.5	8.3, 45.8	-4.2, 25.0
Min, Max	-29, 33	8, 46	-29, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for MALE SEX. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	14 (78)	29 (74)
Mean (SD)	7.2 (15.39)	0.6 (19.60)	4.0 (17.55)
Median	0.0	2.1	0.0
Q1,Q3	-4.2, 16.7	-12.5, 16.7	-4.2, 16.7
Min, Max	-13, 38	-42, 29	-42, 38
Week 48			
n (%)	12 (57)	9 (50)	21 (54)
Mean (SD)	4.5 (17.63)	3.0 (18.66)	3.8 (17.63)
Median	0.0	4.2	0.0
Q1,Q3	-6.3, 20.8	-4.2, 8.3	-4.2, 16.7
Min, Max	-21, 33	-36, 33	-36, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	4 (22)	16 (41)
Mean (SD)	2.1 (17.99)	19.8 (26.65)	6.5 (21.03)
Median	0.0	10.4	2.1
Q1,Q3	-4.2, 14.6	2.1, 37.5	-2.1, 18.8
Min, Max	-42, 25	0, 58	-42, 58
Week 96			
n (%)	8 (38)	3 (17)	11 (28)
Mean (SD)	2.6 (5.43)	18.1 (14.63)	6.8 (10.75)
Median	0.0	16.7	4.2
Q1,Q3	0.0, 6.3	4.2, 33.3	0.0, 12.5
Min, Max	-4, 13	4, 33	-4, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE_age13to14

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. General Fatigue

	IFN B-1a (N= 14)	DMF (N= 18)	Total (N= 32)
Baseline			
n (%)	11 (79)	10 (56)	21 (66)
Mean (SD)	83.3 (14.67)	84.2 (18.30)	83.7 (16.08)
Median	83.3	89.6	83.3
Q1,Q3	66.7, 95.8	66.7, 100.0	66.7, 100.0
Min, Max	58, 100	54, 100	54, 100
Week 24			
n (%)	13 (93)	15 (83)	28 (88)
Mean (SD)	66.7 (26.63)	68.6 (22.49)	67.7 (24.05)
Median	70.8	70.8	70.8
Q1,Q3	50.0, 91.7	50.0, 79.2	50.0, 85.4
Min, Max	25, 100	29, 100	25, 100
Week 48			
n (%)	10 (71)	12 (67)	22 (69)
Mean (SD)	65.8 (27.20)	77.8 (21.27)	72.3 (24.31)
Median	70.8	79.2	75.0
Q1,Q3	54.2, 79.2	66.7, 95.8	66.7, 91.7
Min, Max	8, 100	25, 100	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 14)	**DMF (N= 18)**	**Total (N= 32)**
Week 72			
n (%)	8 (57)	14 (78)	22 (69)
Mean (SD)	84.4 (16.33)	82.4 (15.69)	83.1 (15.56)
Median	87.5	83.3	87.5
Q1,Q3	75.0, 97.9	70.8, 95.8	70.8, 95.8
Min, Max	54, 100	46, 100	46, 100
Week 96			
n (%)	7 (50)	13 (72)	20 (63)
Mean (SD)	79.8 (17.25)	78.2 (21.32)	78.8 (19.54)
Median	79.2	87.5	85.4
Q1,Q3	66.7, 95.8	66.7, 91.7	66.7, 93.8
Min, Max	50, 100	29, 100	29, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	IFN B-1a (N= 14)	DMF (N= 18)	Total (N= 32)
Baseline			
n (%)	11 (79)	10 (56)	21 (66)
Mean (SD)	77.7 (18.28)	85.0 (15.49)	81.2 (17.01)
Median	87.5	87.5	87.5
Q1,Q3	62.5, 91.7	75.0, 100.0	70.8, 91.7
Min, Max	42, 96	58, 100	42, 100
Week 24			
n (%)	13 (93)	15 (83)	28 (88)
Mean (SD)	69.6 (23.41)	68.9 (25.51)	69.2 (24.10)
Median	62.5	75.0	72.9
Q1,Q3	58.3, 91.7	60.0, 83.3	58.3, 89.6
Min, Max	29, 100	8, 100	8, 100
Week 48			
n (%)	10 (71)	12 (67)	22 (69)
Mean (SD)	66.3 (26.09)	76.4 (19.33)	71.8 (22.67)
Median	66.7	77.1	72.9
Q1,Q3	41.7, 91.7	62.5, 93.8	58.3, 91.7
Min, Max	29, 100	38, 100	29, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 14)	**DMF (N= 18)**	**Total (N= 32)**
Week 72			
n (%)	8 (57)	14 (78)	22 (69)
Mean (SD)	82.8 (15.01)	77.1 (19.18)	79.2 (17.63)
Median	85.4	75.0	77.1
Q1,Q3	70.8, 95.8	66.7, 91.7	66.7, 91.7
Min, Max	58, 100	29, 100	29, 100
Week 96			
n (%)	7 (50)	13 (72)	20 (63)
Mean (SD)	76.2 (18.43)	77.9 (20.58)	77.3 (19.38)
Median	70.8	79.2	77.1
Q1,Q3	66.7, 100.0	70.8, 95.8	66.7, 97.9
Min, Max	50, 100	29, 100	29, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	IFN B-1a (N= 14)	DMF (N= 18)	Total (N= 32)
Baseline			
n (%)	11 (79)	10 (56)	21 (66)
Mean (SD)	74.2 (30.09)	79.2 (29.46)	76.6 (29.15)
Median	70.8	93.8	91.7
Q1,Q3	62.5, 100.0	70.8, 100.0	66.7, 100.0
Min, Max	0, 100	13, 100	0, 100
Week 24			
n (%)	13 (93)	15 (83)	28 (88)
Mean (SD)	72.8 (24.15)	69.3 (24.79)	70.9 (24.11)
Median	75.0	62.5	64.6
Q1,Q3	58.3, 100.0	58.3, 100.0	58.3, 100.0
Min, Max	29, 100	21, 100	21, 100
Week 48			
n (%)	10 (71)	12 (67)	22 (69)
Mean (SD)	70.6 (24.72)	72.2 (23.79)	71.5 (23.64)
Median	65.4	77.1	72.9
Q1,Q3	50.0, 95.8	56.3, 91.7	54.2, 95.8
Min, Max	33, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 14)	**DMF (N= 18)**	**Total (N= 32)**
Week 72			
n (%)	8 (57)	14 (78)	22 (69)
Mean (SD)	82.8 (17.17)	76.2 (23.48)	78.6 (21.22)
Median	89.6	87.5	87.5
Q1,Q3	70.8, 93.8	58.3, 95.8	58.3, 95.8
Min, Max	54, 100	33, 100	33, 100
Week 96			
n (%)	7 (50)	13 (72)	20 (63)
Mean (SD)	72.6 (24.75)	73.4 (31.34)	73.1 (28.53)
Median	79.2	83.3	81.3
Q1,Q3	50.0, 100.0	58.3, 100.0	56.3, 100.0
Min, Max	33, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE_age15to17

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. General Fatigue

	IFN B-1a (N= 50)	DMF (N= 53)	Total (N= 103)
Baseline			
n (%)	41 (82)	40 (75)	81 (79)
Mean (SD)	69.3 (23.44)	65.2 (24.78)	67.3 (24.05)
Median	70.8	66.7	70.8
Q1,Q3	50.0, 87.5	50.0, 87.5	50.0, 87.5
Min, Max	13, 100	0, 100	0, 100
Week 24			
n (%)	45 (90)	41 (77)	86 (83)
Mean (SD)	66.9 (23.42)	70.6 (21.39)	68.7 (22.42)
Median	66.7	75.0	70.8
Q1,Q3	50.0, 87.5	58.3, 87.5	54.2, 87.5
Min, Max	13, 100	21, 100	13, 100
Week 48			
n (%)	33 (66)	39 (74)	72 (70)
Mean (SD)	67.6 (22.16)	70.5 (23.87)	69.1 (22.99)
Median	70.8	75.0	72.9
Q1,Q3	58.3, 79.2	50.0, 91.7	54.2, 91.7
Min, Max	13, 100	25, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 50)	DMF (N= 53)	Total (N= 103)
Week 72			
n (%)	21 (42)	29 (55)	50 (49)
Mean (SD)	66.7 (26.15)	67.4 (22.50)	67.1 (23.84)
Median	70.8	75.0	75.0
Q1,Q3	58.3, 87.5	50.0, 87.5	54.2, 87.5
Min, Max	8, 100	25, 100	8, 100
Week 96			
n (%)	15 (30)	15 (28)	30 (29)
Mean (SD)	71.9 (20.74)	62.2 (23.12)	67.1 (22.14)
Median	70.8	66.7	68.8
Q1,Q3	54.2, 91.7	37.5, 87.5	50.0, 87.5
Min, Max	29, 100	25, 96	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	IFN B-1a (N= 50)	DMF (N= 53)	Total (N= 103)
Baseline			
n (%)	41 (82)	40 (75)	81 (79)
Mean (SD)	63.9 (25.32)	62.7 (24.06)	63.3 (24.56)
Median	62.5	66.7	66.7
Q1,Q3	41.7, 87.5	50.0, 81.3	45.8, 83.3
Min, Max	13, 100	0, 100	0, 100
Week 24			
n (%)	45 (90)	41 (77)	86 (83)
Mean (SD)	67.3 (25.88)	67.1 (21.75)	67.2 (23.86)
Median	70.8	66.7	68.8
Q1,Q3	45.8, 87.5	54.2, 79.2	50.0, 87.5
Min, Max	21, 100	8, 100	8, 100
Week 48			
n (%)	33 (66)	39 (74)	72 (70)
Mean (SD)	69.6 (20.27)	66.6 (25.28)	67.9 (23.01)
Median	75.0	66.7	72.9
Q1,Q3	58.3, 87.5	45.8, 91.7	54.2, 87.5
Min, Max	25, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 50)	DMF (N= 53)	Total (N= 103)
Week 72			
n (%)	21 (42)	28 (53)	49 (48)
Mean (SD)	67.7 (22.86)	62.2 (24.58)	64.5 (23.77)
Median	66.7	66.7	66.7
Q1,Q3	58.3, 87.5	41.7, 83.3	54.2, 83.3
Min, Max	17, 100	13, 100	13, 100
Week 96			
n (%)	15 (30)	15 (28)	30 (29)
Mean (SD)	65.3 (23.61)	63.9 (20.69)	64.6 (21.82)
Median	66.7	70.8	66.7
Q1,Q3	50.0, 87.5	45.8, 75.0	50.0, 79.2
Min, Max	25, 100	33, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	IFN B-1a (N= 50)	DMF (N= 53)	Total (N= 103)
Baseline			
n (%)	41 (82)	40 (75)	81 (79)
Mean (SD)	77.3 (18.87)	68.9 (27.86)	73.1 (23.97)
Median	79.2	66.7	75.0
Q1,Q3	58.3, 95.8	47.9, 95.8	54.2, 95.8
Min, Max	46, 100	0, 100	0, 100
Week 24			
n (%)	45 (90)	41 (77)	86 (83)
Mean (SD)	74.4 (23.70)	76.4 (23.49)	75.3 (23.49)
Median	79.2	83.3	79.2
Q1,Q3	54.2, 95.8	54.2, 100.0	54.2, 95.8
Min, Max	4, 100	25, 100	4, 100
Week 48			
n (%)	33 (66)	39 (74)	72 (70)
Mean (SD)	78.3 (20.46)	73.7 (23.84)	75.8 (22.32)
Median	83.3	79.2	81.3
Q1,Q3	62.5, 100.0	58.3, 95.8	58.3, 95.8
Min, Max	29, 100	4, 100	4, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 50)	**DMF (N= 53)**	**Total (N= 103)**
Week 72			
n (%)	21 (42)	29 (55)	50 (49)
Mean (SD)	75.0 (20.28)	70.1 (21.68)	72.2 (21.04)
Median	75.0	66.7	72.9
Q1,Q3	58.3, 95.8	50.0, 87.5	50.0, 91.7
Min, Max	42, 100	33, 100	33, 100
Week 96			
n (%)	15 (30)	15 (28)	30 (29)
Mean (SD)	75.6 (20.10)	66.4 (25.37)	71.0 (22.97)
Median	75.0	62.5	66.7
Q1,Q3	62.5, 95.8	50.0, 95.8	58.3, 95.8
Min, Max	42, 100	21, 100	21, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE_female

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. General Fatigue

	IFN B-1a (N= 46)	DMF (N= 50)	Total (N= 96)
Baseline			
n (%)	37 (80)	33 (66)	70 (73)
Mean (SD)	70.0 (23.05)	67.6 (24.91)	68.9 (23.80)
Median	79.2	66.7	70.8
Q1,Q3	58.3, 87.5	54.2, 87.5	54.2, 87.5
Min, Max	13, 100	0, 100	0, 100
Week 24			
n (%)	42 (91)	39 (78)	81 (84)
Mean (SD)	63.3 (23.54)	68.2 (21.30)	65.6 (22.48)
Median	62.5	70.8	66.7
Q1,Q3	50.0, 87.5	50.0, 87.5	50.0, 87.5
Min, Max	13, 100	21, 100	13, 100
Week 48			
n (%)	32 (70)	36 (72)	68 (71)
Mean (SD)	64.2 (22.37)	70.7 (22.10)	67.6 (22.31)
Median	68.8	72.9	70.8
Q1,Q3	54.2, 77.1	56.3, 91.7	54.2, 81.3
Min, Max	8, 100	25, 100	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 46)	**DMF (N= 50)**	**Total (N= 96)**
Week 72			
n (%)	22 (48)	29 (58)	51 (53)
Mean (SD)	70.8 (23.50)	69.7 (20.68)	70.2 (21.72)
Median	77.1	75.0	75.0
Q1,Q3	58.3, 87.5	54.2, 83.3	54.2, 87.5
Min, Max	8, 100	25, 100	8, 100
Week 96			
n (%)	17 (37)	19 (38)	36 (38)
Mean (SD)	71.6 (19.61)	66.4 (24.43)	68.9 (22.13)
Median	70.8	70.8	70.8
Q1,Q3	54.2, 87.5	37.5, 87.5	52.1, 87.5
Min, Max	29, 100	25, 96	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	IFN B-1a (N= 46)	DMF (N= 50)	Total (N= 96)
Baseline			
n (%)	37 (80)	33 (66)	70 (73)
Mean (SD)	67.1 (24.72)	64.6 (24.87)	66.0 (24.64)
Median	66.7	66.7	66.7
Q1,Q3	45.8, 91.7	50.0, 87.5	45.8, 87.5
Min, Max	17, 100	0, 100	0, 100
Week 24			
n (%)	42 (91)	39 (78)	81 (84)
Mean (SD)	65.6 (25.77)	64.8 (24.00)	65.2 (24.78)
Median	62.5	66.7	66.7
Q1,Q3	45.8, 91.7	50.0, 79.2	50.0, 87.5
Min, Max	25, 100	8, 100	8, 100
Week 48			
n (%)	32 (70)	36 (72)	68 (71)
Mean (SD)	68.2 (19.54)	67.8 (24.35)	68.0 (22.05)
Median	66.7	72.9	68.8
Q1,Q3	56.3, 87.5	47.9, 89.6	54.2, 87.5
Min, Max	29, 100	17, 100	17, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 46)	**DMF (N= 50)**	**Total (N= 96)**
Week 72			
n (%)	22 (48)	28 (56)	50 (52)
Mean (SD)	68.4 (22.22)	64.0 (23.93)	65.9 (23.06)
Median	68.8	66.7	66.7
Q1,Q3	58.3, 87.5	41.7, 83.3	54.2, 83.3
Min, Max	17, 100	13, 100	13, 100
Week 96			
n (%)	17 (37)	19 (38)	36 (38)
Mean (SD)	66.4 (23.22)	65.1 (21.53)	65.7 (22.03)
Median	66.7	70.8	66.7
Q1,Q3	50.0, 79.2	50.0, 79.2	50.0, 79.2
Min, Max	25, 100	29, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	IFN B-1a (N= 46)	DMF (N= 50)	Total (N= 96)
Baseline			
n (%)	37 (80)	33 (66)	70 (73)
Mean (SD)	77.7 (19.28)	71.0 (28.44)	74.5 (24.09)
Median	75.0	87.5	77.1
Q1,Q3	58.3, 95.8	45.8, 95.8	54.2, 95.8
Min, Max	46, 100	0, 100	0, 100
Week 24			
n (%)	42 (91)	39 (78)	81 (84)
Mean (SD)	73.7 (22.94)	72.8 (23.15)	73.3 (22.90)
Median	75.0	75.0	75.0
Q1,Q3	50.0, 100.0	54.2, 95.8	54.2, 95.8
Min, Max	25, 100	21, 100	21, 100
Week 48			
n (%)	32 (70)	36 (72)	68 (71)
Mean (SD)	77.0 (20.85)	73.6 (21.96)	75.2 (21.35)
Median	79.2	77.1	79.2
Q1,Q3	60.4, 100.0	58.3, 93.8	58.3, 95.8
Min, Max	29, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 46)	**DMF (N= 50)**	**Total (N= 96)**
Week 72			
n (%)	22 (48)	29 (58)	51 (53)
Mean (SD)	76.5 (19.94)	73.3 (20.97)	74.7 (20.39)
Median	81.3	75.0	75.0
Q1,Q3	58.3, 95.8	58.3, 87.5	58.3, 91.7
Min, Max	42, 100	38, 100	38, 100
Week 96			
n (%)	17 (37)	19 (38)	36 (38)
Mean (SD)	74.5 (19.70)	68.9 (28.48)	71.5 (24.55)
Median	75.0	75.0	75.0
Q1,Q3	62.5, 91.7	50.0, 95.8	56.3, 95.8
Min, Max	42, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_DESCRIBE_male

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. General Fatigue

	IFN B-1a (N= 18)	DMF (N= 21)	Total (N= 39)
Baseline			
n (%)	15 (83)	17 (81)	32 (82)
Mean (SD)	77.8 (20.81)	71.8 (24.72)	74.6 (22.81)
Median	83.3	70.8	75.0
Q1,Q3	62.5, 95.8	58.3, 91.7	60.4, 95.8
Min, Max	38, 100	8, 100	8, 100
Week 24			
n (%)	16 (89)	17 (81)	33 (85)
Mean (SD)	76.0 (23.15)	74.5 (21.94)	75.3 (22.19)
Median	85.4	79.2	83.3
Q1,Q3	64.6, 91.7	62.5, 91.7	62.5, 91.7
Min, Max	17, 100	29, 100	17, 100
Week 48			
n (%)	11 (61)	15 (71)	26 (67)
Mean (SD)	75.8 (24.07)	75.7 (26.39)	75.7 (24.93)
Median	91.7	87.5	88.8
Q1,Q3	54.2, 95.8	54.2, 100.0	54.2, 95.8
Min, Max	38, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 18)	**DMF (N= 21)**	**Total (N= 39)**
Week 72			
n (%)	7 (39)	14 (67)	21 (54)
Mean (SD)	73.8 (30.87)	77.7 (23.09)	76.4 (25.22)
Median	75.0	87.5	87.5
Q1,Q3	66.7, 100.0	54.2, 100.0	66.7, 100.0
Min, Max	13, 100	29, 100	13, 100
Week 96			
n (%)	5 (28)	9 (43)	14 (36)
Mean (SD)	84.2 (18.26)	76.4 (20.52)	79.2 (19.41)
Median	91.7	70.8	77.1
Q1,Q3	66.7, 100.0	66.7, 100.0	66.7, 100.0
Min, Max	63, 100	46, 100	46, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	IFN B-1a (N= 18)	DMF (N= 21)	Total (N= 39)
Baseline			
n (%)	15 (83)	17 (81)	32 (82)
Mean (SD)	66.1 (24.79)	72.1 (22.76)	69.3 (23.54)
Median	62.5	70.8	66.7
Q1,Q3	50.0, 91.7	58.3, 95.8	54.2, 91.7
Min, Max	13, 100	21, 100	13, 100
Week 24			
n (%)	16 (89)	17 (81)	33 (85)
Mean (SD)	73.7 (23.26)	73.9 (18.01)	73.8 (20.39)
Median	77.1	79.2	79.2
Q1,Q3	62.5, 91.7	62.5, 83.3	62.5, 87.5
Min, Max	21, 100	38, 100	21, 100
Week 48			
n (%)	11 (61)	15 (71)	26 (67)
Mean (SD)	70.5 (27.35)	71.4 (24.49)	71.0 (25.21)
Median	79.2	75.0	75.0
Q1,Q3	41.7, 95.8	62.5, 91.7	62.5, 91.7
Min, Max	25, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
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	IFN B-1a (N= 18)	DMF (N= 21)	Total (N= 39)
Week 72			
n (%)	7 (39)	14 (67)	21 (54)
Mean (SD)	82.7 (17.75)	73.5 (22.97)	76.6 (21.39)
Median	87.5	75.0	79.2
Q1,Q3	58.3, 100.0	66.7, 87.5	66.7, 91.7
Min, Max	58, 100	13, 100	13, 100
Week 96			
n (%)	5 (28)	9 (43)	14 (36)
Mean (SD)	76.7 (18.54)	81.5 (17.57)	79.8 (17.36)
Median	79.2	79.2	79.2
Q1,Q3	62.5, 87.5	75.0, 95.8	70.8, 95.8
Min, Max	54, 100	46, 100	46, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Cognitive Fatigue

	IFN B-1a (N= 18)	DMF (N= 21)	Total (N= 39)
Baseline			
n (%)	15 (83)	17 (81)	32 (82)
Mean (SD)	74.2 (26.55)	70.8 (28.57)	72.4 (27.25)
Median	79.2	66.7	75.0
Q1,Q3	62.5, 95.8	50.0, 100.0	56.3, 95.8
Min, Max	0, 100	13, 100	0, 100
Week 24			
n (%)	16 (89)	17 (81)	33 (85)
Mean (SD)	74.7 (26.02)	78.4 (25.61)	76.6 (25.47)
Median	79.2	91.7	79.2
Q1,Q3	70.8, 93.8	62.5, 100.0	66.7, 100.0
Min, Max	4, 100	25, 100	4, 100
Week 48			
n (%)	11 (61)	15 (71)	26 (67)
Mean (SD)	75.2 (24.19)	72.8 (27.99)	73.8 (25.96)
Median	87.5	79.2	81.3
Q1,Q3	54.2, 95.8	54.2, 100.0	54.2, 100.0
Min, Max	33, 100	4, 100	4, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

	IFN B-1a (N= 18)	DMF (N= 21)	Total (N= 39)
Week 72			
n (%)	7 (39)	14 (67)	21 (54)
Mean (SD)	79.2 (19.39)	69.6 (25.18)	72.8 (23.37)
Median	83.3	64.6	75.0
Q1,Q3	58.3, 100.0	50.0, 95.8	58.3, 95.8
Min, Max	50, 100	33, 100	33, 100
Week 96			
n (%)	5 (28)	9 (43)	14 (36)
Mean (SD)	75.0 (28.11)	71.3 (28.52)	72.6 (27.33)
Median	79.2	66.7	72.9
Q1,Q3	62.5, 100.0	58.3, 100.0	58.3, 100.0
Min, Max	33, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_HEDGESCI_age13to14

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.087	-0.825	0.998
	48	0.383	-0.660	1.427
	72	-0.428	-1.455	0.600
	96	0.254	-0.809	1.317
GENERAL FATIGUE	24	0.485	-0.440	1.411
	48	1.397	0.233	2.561
	72	0.266	-0.754	1.285
	96	0.631	-0.457	1.719
SLEEP/REST FATIGUE	24	0.449	-0.474	1.373
	48	0.903	-0.187	1.992
	72	-0.239	-1.258	0.779
	96	0.274	-0.790	1.338

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source:
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109MS306_table42_44_CHG_HEDGESCI_age15to17

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.363	-0.111	0.837
	48	0.294	-0.233	0.821
	72	0.311	-0.310	0.931
	96	0.401	-0.393	1.194
GENERAL FATIGUE	24	0.036	-0.434	0.507
	48	0.561	0.026	1.095
	72	0.417	-0.207	1.041
	96	-0.224	-1.011	0.564
SLEEP/REST FATIGUE	24	-0.088	-0.559	0.382
	48	-0.038	-0.562	0.486
	72	0.244	-0.376	0.863
	96	0.036	-0.749	0.821

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_HEDGESCI_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_HEDGESCI_female

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.234	-0.281	0.749
	48	0.403	-0.159	0.965
	72	0.201	-0.421	0.823
	96	0.533	-0.229	1.296
GENERAL FATIGUE	24	0.066	-0.448	0.579
	48	0.603	0.034	1.172
	72	0.257	-0.366	0.880
	96	0.162	-0.587	0.912
SLEEP/REST FATIGUE	24	0.081	-0.432	0.594
	48	0.218	-0.340	0.776
	72	0.189	-0.433	0.811
	96	0.341	-0.413	1.095

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_HEDGESCI_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_HEDGESCI_male

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.378	-0.358	1.113
	48	0.086	-0.779	0.951
	72	-0.878	-2.056	0.299
	96	-1.84	-3.416	-0.264
GENERAL FATIGUE	24	0.291	-0.441	1.024
	48	1.188	0.245	2.131
	72	0.423	-0.719	1.565
	96	-0.791	-2.168	0.585
SLEEP/REST FATIGUE	24	-0.219	-0.949	0.512
	48	0.216	-0.651	1.083
	72	-0.189	-1.322	0.945
	96	-1.119	-2.543	0.305

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source:
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109MS306_table42_44_CHG_LSMEANS_age13to14

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. General Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	-6.36 (7.170)	-15.8 (6.114)
Lsmean_95 % CI	(-21.56, 08.842)	(-28.79, -2.871)
Diffrence (95% CI)	9.47 (-10.506, 29.454)	
SE_Difference	9.4247	
p-value	0.3297	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	07.25 (8.337)	-23.3 (6.807)
Lsmean_95 % CI	(-10.92, 25.412)	(-38.18, -8.518)
Diffrence (95% CI)	30.60 (7.139, 54.052)	
SE_Difference	0.7654	
p-value	0.0148	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	02.55 (4.996)	-2.32 (5.340)
Lsmean_95 % CI	(-8.330, 13.439)	(-13.96, 09.311)
Diffrence (95% CI)	4.88 (-11.054, 20.812)	
SE_Difference	7.3127	
p-value	0.5173	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	01.37 (4.934)	-8.07 (5.698)
Lsmean_95 % CI	(-9.492, 12.228)	(-20.62, 04.467)
Diffrence (95% CI)	9.44 (-7.152, 26.036)	
SE_Difference	7.5391	
p-value	0.2364	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	00.18 (4.630)	-8.08 (3.936)
Lsmean_95 % CI	(-9.636, 09.993)	(-16.43, 00.259)
Diffrence (95% CI)	8.26 (-4.743, 21.268)	
SE_Difference	6.1349	
p-value	0.1968	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	04.58 (8.756)	-18.3 (7.125)
Lsmean_95 % CI	(-14.50, 23.657)	(-33.85, -2.807)
Diffrence (95% CI)	22.91 (-1.890, 47.710)	
SE_Difference	1.3822	
p-value	0.0671	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
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	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	-0.17 (4.953)	-0.40 (5.305)
Lsmean_95 % CI	(-10.96, 10.624)	(-11.96, 11.156)
Diffrence (95% CI)	0.24 (-15.796, 16.266)	
SE_Difference	7.3575	
p-value	0.9750	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	03.91 (5.636)	-7.99 (6.549)
Lsmean_95 % CI	(-8.498, 16.311)	(-22.40, 06.429)
Diffrence (95% CI)	11.89 (-7.535, 31.320)	
SE_Difference	8.8268	
p-value	0.2050	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	00.70 (5.344)	-1.26 (4.558)
Lsmean_95 % CI	(-10.63, 12.026)	(-10.93, 08.398)
Diffrence (95% CI)	1.96 (-12.931, 16.851)	
SE_Difference	7.0241	
p-value	0.7838	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	06.19 (7.152)	-4.87 (5.836)
Lsmean_95 % CI	(-9.389, 21.777)	(-17.59, 07.847)
Diffrence (95% CI)	11.06 (-9.076, 31.204)	
SE_Difference	9.2433	
p-value	0.2544	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	03.78 (6.275)	10.56 (6.711)
Lsmean_95 % CI	(-9.893, 17.452)	(-4.061, 25.184)
Diffrence (95% CI)	-6.78 (-26.863, 13.298)	
SE_Difference	9.2161	
p-value	0.4759	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	02.73 (5.701)	-3.65 (6.585)
Lsmean_95 % CI	(-9.812, 15.281)	(-18.14, 10.847)
Diffrence (95% CI)	6.38 (-12.814, 25.575)	
SE_Difference	8.7205	
p-value	0.4797	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table42_44_CHG_LSMEANS_age15to17

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. General Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	32 (60)	38 (76)
Lsmean (SE)	-0.49 (2.566)	-1.35 (2.355)
Lsmean_95 % CI	(-5.608, 04.637)	(-6.046, 03.355)
Diffrence (95% CI)	0.86 (-6.094, 7.814)	
SE_Difference	3.4840	
p-value	0.8058	
Week 48		
n (%)	29 (55)	27 (54)
Lsmean (SE)	03.28 (3.169)	-5.28 (3.285)
Lsmean_95 % CI	(-3.077, 09.635)	(-11.87, 01.308)
Diffrence (95% CI)	8.56 (-0.631, 17.751)	
SE_Difference	4.5823	
p-value	0.0673	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	23 (43)	18 (36)
Lsmean (SE)	-0.41 (3.917)	-5.72 (4.439)
Lsmean_95 % CI	(-8.342, 07.519)	(-14.71, 03.261)
Diffrence (95% CI)	5.31 (-6.785, 17.411)	
SE_Difference	5.9759	
p-value	0.3796	
Week 96		
n (%)	12 (23)	13 (26)
Lsmean (SE)	-7.36 (5.105)	-1.54 (4.904)
Lsmean_95 % CI	(-17.95, 03.229)	(-11.71, 08.629)
Diffrence (95% CI)	-5.82 (-20.524, 8.891)	
SE_Difference	7.0915	
p-value	0.4209	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
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Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	32 (60)	38 (76)
Lsmean (SE)	01.87 (3.254)	02.59 (2.985)
Lsmean_95 % CI	(-4.627, 08.362)	(-3.365, 08.553)
Diffrence (95% CI)	-0.73 (-9.549, 8.096)	
SE_Difference	4.4202	
p-value	0.8700	
Week 48		
n (%)	29 (55)	27 (54)
Lsmean (SE)	01.40 (3.178)	02.51 (3.294)
Lsmean_95 % CI	(-4.974, 07.775)	(-4.098, 09.115)
Diffrence (95% CI)	-1.11 (-10.290, 8.073)	
SE_Difference	4.5776	
p-value	0.8097	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	23 (43)	18 (36)
Lsmean (SE)	-1.49 (3.649)	-3.65 (4.131)
Lsmean_95 % CI	(-8.881, 05.894)	(-12.01, 04.715)
Diffrence (95% CI)	2.15 (-9.062, 13.369)	
SE_Difference	5.5401	
p-value	0.6997	
Week 96		
n (%)	12 (23)	13 (26)
Lsmean (SE)	-1.00 (5.783)	-1.96 (5.556)
Lsmean_95 % CI	(-12.99, 10.990)	(-13.48, 09.562)
Diffrence (95% CI)	0.96 (-15.673, 17.588)	
SE_Difference	8.0190	
p-value	0.9061	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	32 (60)	38 (76)
Lsmean (SE)	02.79 (3.130)	-2.90 (2.871)
Lsmean_95 % CI	(-3.456, 09.038)	(-8.630, 02.832)
Diffrence (95% CI)	5.69 (-2.803, 14.183)	
SE_Difference	4.2549	
p-value	0.1856	
Week 48		
n (%)	29 (55)	27 (54)
Lsmean (SE)	02.98 (2.882)	00.66 (2.989)
Lsmean_95 % CI	(-2.802, 08.758)	(-5.336, 06.654)
Diffrence (95% CI)	2.32 (-6.102, 10.740)	
SE_Difference	4.1983	
p-value	0.5830	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	23 (43)	18 (36)
Lsmean (SE)	-2.79 (3.533)	-3.15 (4.014)
Lsmean_95 % CI	(-9.938, 04.365)	(-11.28, 04.974)
Diffrence (95% CI)	0.37 (-10.682, 11.412)	
SE_Difference	5.4570	
p-value	0.9470	
Week 96		
n (%)	12 (23)	13 (26)
Lsmean (SE)	-1.18 (5.315)	-4.68 (5.089)
Lsmean_95 % CI	(-12.21, 09.838)	(-15.23, 05.877)
Diffrence (95% CI)	3.49 (-12.403, 19.387)	
SE_Difference	7.6642	
p-value	0.6531	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
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109MS306_table42_44_CHG_LSMEANS_female

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	25 (50)	35 (76)
Lsmean (SE)	-7.16 (3.718)	-8.61 (3.046)
Lsmean_95 % CI	(-14.60, 00.293)	(-14.71, -2.507)
Diffrence (95% CI)	1.45 (-7.001, 9.909)	
SE_Difference	4.2206	
p-value	0.7317	
Week 48		
n (%)	23 (46)	27 (59)
Lsmean (SE)	-1.48 (4.718)	-12.6 (4.146)
Lsmean_95 % CI	(-10.97, 08.021)	(-20.90, -4.212)
Diffrence (95% CI)	11.08 (0.281, 21.880)	
SE_Difference	5.3650	
p-value	0.0446	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
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	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	19 (38)	21 (46)
Lsmean (SE)	-0.72 (4.937)	-3.90 (4.571)
Lsmean_95 % CI	(-10.73, 09.294)	(-13.17, 05.366)
Diffrence (95% CI)	3.18 (-8.821, 15.190)	
SE_Difference	5.9196	
p-value	0.5939	
Week 96		
n (%)	12 (24)	16 (35)
Lsmean (SE)	-2.21 (5.656)	-3.94 (5.070)
Lsmean_95 % CI	(-13.89, 09.459)	(-14.41, 06.518)
Diffrence (95% CI)	1.73 (-12.732, 16.195)	
SE_Difference	7.0077	
p-value	0.8070	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
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Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	25 (50)	35 (76)
Lsmean (SE)	-1.72 (4.036)	-3.60 (3.333)
Lsmean_95 % CI	(-9.801, 06.368)	(-10.28, 03.074)
Diffrence (95% CI)	1.89 (-7.333, 11.105)	
SE_Difference	4.6022	
p-value	0.6835	
Week 48		
n (%)	23 (46)	27 (59)
Lsmean (SE)	-1.08 (3.952)	-4.13 (3.453)
Lsmean_95 % CI	(-9.039, 06.870)	(-11.08, 02.818)
Diffrence (95% CI)	3.05 (-6.003, 12.098)	
SE_Difference	4.4961	
p-value	0.5013	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	19 (38)	21 (46)
Lsmean (SE)	-1.15 (4.187)	-3.71 (3.817)
Lsmean_95 % CI	(-9.641, 07.344)	(-11.45, 04.034)
Diffrence (95% CI)	2.56 (-7.537, 12.656)	
SE_Difference	4.9784	
p-value	0.6103	
Week 96		
n (%)	12 (24)	16 (35)
Lsmean (SE)	-1.10 (5.608)	-7.97 (4.968)
Lsmean_95 % CI	(-12.68, 10.470)	(-18.22, 02.281)
Diffrence (95% CI)	6.87 (-7.427, 21.164)	
SE_Difference	6.9263	
p-value	0.3313	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	25 (50)	35 (76)
Lsmean (SE)	-0.51 (3.991)	-4.20 (3.338)
Lsmean_95 % CI	(-8.503, 07.487)	(-10.88, 02.490)
Diffrence (95% CI)	3.69 (-5.520, 12.895)	
SE_Difference	4.5964	
p-value	0.4258	
Week 48		
n (%)	23 (46)	27 (59)
Lsmean (SE)	01.64 (3.916)	-3.16 (3.430)
Lsmean_95 % CI	(-6.244, 09.522)	(-10.06, 03.748)
Diffrence (95% CI)	4.80 (-4.274, 13.866)	
SE_Difference	4.5060	
p-value	0.2927	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
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	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	19 (38)	21 (46)
Lsmean (SE)	00.10 (4.585)	-0.16 (4.176)
Lsmean_95 % CI	(-9.199, 09.400)	(-8.629, 08.309)
Diffrence (95% CI)	0.26 (-11.003, 11.524)	
SE_Difference	5.5537	
p-value	0.9628	
Week 96		
n (%)	12 (24)	16 (35)
Lsmean (SE)	-1.74 (5.744)	-8.32 (5.143)
Lsmean_95 % CI	(-13.60, 10.111)	(-18.93, 02.293)
Diffrence (95% CI)	6.58 (-8.506, 21.660)	
SE_Difference	7.3078	
p-value	0.3771	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

109MS306_table42_44_CHG_LSMEANS_male

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)
Week 24		
n (%)	15 (71)	14 (78)
Lsmean (SE)	00.61 (4.257)	-2.75 (4.603)
Lsmean_95 % CI	(-8.158, 09.376)	(-12.23, 06.735)
Diffrence (95% CI)	3.35 (-8.598, 15.307)	
SE_Difference	5.8035	
p-value	0.5684	
Week 48		
n (%)	12 (57)	9 (50)
Lsmean (SE)	08.76 (4.749)	-6.65 (5.395)
Lsmean_95 % CI	(-1.260, 18.778)	(-18.03, 04.733)
Diffrence (95% CI)	15.41 (0.660, 30.158)	
SE_Difference	6.9903	
p-value	0.0416	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	4 (22)
Lsmean (SE)	05.13 (4.658)	03.70 (8.215)
Lsmean_95 % CI	(-5.015, 15.284)	(-14.20, 21.595)
Diffrence (95% CI)	1.44 (-19.472, 22.350)	
SE_Difference	9.5974	
p-value	0.8833	
Week 96		
n (%)	8 (38)	3 (17)
Lsmean (SE)	-6.07 (3.981)	03.00 (6.450)
Lsmean_95 % CI	(-15.48, 03.348)	(-12.25, 18.249)
Diffrence (95% CI)	-9.06 (-26.720, 8.595)	
SE_Difference	7.4673	
p-value	0.2642	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	14 (78)
Lsmean (SE)	04.98 (4.722)	07.54 (4.949)
Lsmean_95 % CI	(-4.749, 14.700)	(-2.653, 17.732)
Diffrence (95% CI)	-2.56 (-15.432, 10.305)	
SE_Difference	6.2483	
p-value	0.6851	
Week 48		
n (%)	12 (57)	9 (50)
Lsmean (SE)	01.24 (7.962)	-3.63 (8.727)
Lsmean_95 % CI	(-15.56, 18.035)	(-22.05, 14.780)
Diffrence (95% CI)	4.87 (-18.764, 28.503)	
SE_Difference	1.2014	
p-value	0.6692	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	4 (22)
Lsmean (SE)	-0.91 (5.354)	10.61 (9.411)
Lsmean_95 % CI	(-12.58, 10.754)	(-9.897, 31.115)
Diffrence (95% CI)	-11.52 (-35.383, 12.343)	
SE_Difference	0.9520	
p-value	0.3136	
Week 96		
n (%)	8 (38)	3 (17)
Lsmean (SE)	01.51 (5.203)	10.03 (9.172)
Lsmean_95 % CI	(-10.80, 13.810)	(-11.65, 31.721)
Diffrence (95% CI)	-8.53 (-33.521, 16.467)	
SE_Difference	0.5699	
p-value	0.4464	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Cognitive Fatigue

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	14 (78)
Lsmean (SE)	07.11 (4.672)	01.40 (4.940)
Lsmean_95 % CI	(-2.515, 16.730)	(-8.779, 11.571)
Diffrence (95% CI)	5.71 (-7.158, 18.582)	
SE_Difference	6.2490	
p-value	0.3694	
Week 48		
n (%)	12 (57)	9 (50)
Lsmean (SE)	03.66 (5.483)	04.22 (5.975)
Lsmean_95 % CI	(-7.910, 15.226)	(-8.385, 16.827)
Diffrence (95% CI)	-0.56 (-16.982, 15.857)	
SE_Difference	7.7822	
p-value	0.9432	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	4 (22)
Lsmean (SE)	02.65 (4.545)	19.08 (7.792)
Lsmean_95 % CI	(-7.254, 12.550)	(02.099, 36.055)
Diffrence (95% CI)	-16.43 (-36.084, 3.227)	
SE_Difference	9.0210	
p-value	0.0936	
Week 96		
n (%)	8 (38)	3 (17)
Lsmean (SE)	02.87 (2.633)	17.21 (4.275)
Lsmean_95 % CI	(-3.357, 09.095)	(07.105, 27.321)
Diffrence (95% CI)	-14.34 (-26.033, -2.654)	
SE_Difference	4.9434	
p-value	0.0229	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 08MAR2022

MCID

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1314_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale (Parent)

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.125	1.1	0.018
	95% CI	(0.127 , 9.944)	(0.189 , 6.413)	(-0.319 , 0.355)
	p-value	0.916	0.916	0.916
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.194	0.275	-0.264
	95% CI	(0.018 , 2.151)	(0.037 , 2.067)	(-0.603 , 0.076)
	p-value	0.182	0.21	0.128
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.333	0.365	-0.091
	95% CI	(0.012 , 9.156)	(0.017 , 8.019)	(-0.356 , 0.174)
	p-value	0.516	0.523	0.958
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	3.632	3.286	0.1
	95% CI	(0.132 , 99.851)	(0.15 , 72.167)	(-0.181 , 0.381)
	p-value	0.446	0.45	0.962
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	3.632	3.286	0.1
	95% CI	(0.132 , 99.851)	(0.15 , 72.167)	(-0.181 , 0.381)
	p-value	0.446	0.45	0.962
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)

	Result	OR	RR	ARR
	p-value	0.597	0.601	0.586
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	3.632	3.286	0.1
	95% CI	(0.132 , 99.851)	(0.15 , 72.167)	(-0.181 , 0.381)
	p-value	0.446	0.45	0.962
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	3.632	3.286	0.1
	95% CI	(0.132 , 99.851)	(0.15 , 72.167)	(-0.181 , 0.381)
	p-value	0.446	0.45	0.962
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	1.111	1.1	0.009
	95% CI	(0.06 , 20.488)	(0.079 , 15.357)	(-0.243 , 0.261)
	p-value	0.944	0.944	0.944
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.296	0.367	-0.173
	95% CI	(0.025 , 3.452)	(0.045 , 2.979)	(-0.495 , 0.15)
	p-value	0.332	0.348	0.293
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.111	1.1	0.009
	95% CI	(0.06 , 20.488)	(0.079 , 15.357)	(-0.243 , 0.261)
	p-value	0.944	0.944	0.944
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.116	0.156	-0.273
	95% CI	(0.005 , 2.562)	(0.009 , 2.685)	(-0.631 , 0.086)
	p-value	0.172	0.201	0.187
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.333	0.365	-0.091

	Result	OR	RR	ARR
	95% CI	(0.012 , 9.156)	(0.017 , 8.019)	(-0.356 , 0.174)
	p-value	0.516	0.523	0.958
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.181	0.219	-0.182
	95% CI	(0.008 , 4.268)	(0.012 , 4.057)	(-0.505 , 0.142)
	p-value	0.289	0.308	0.458
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	0.75	0.825	-0.064
	95% CI	(0.121 , 4.662)	(0.242 , 2.816)	(-0.465 , 0.338)
	p-value	0.758	0.759	0.756
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.056	0.1	-0.455
	95% CI	(0.003 , 1.195)	(0.006 , 1.591)	(-0.844 , -0.065)
	p-value	0.065	0.103	0.017
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.181	0.219	-0.182
	95% CI	(0.008 , 4.268)	(0.012 , 4.057)	(-0.505 , 0.142)
	p-value	0.289	0.308	0.458
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.056	0.1	-0.455
	95% CI	(0.003 , 1.195)	(0.006 , 1.591)	(-0.844 , -0.065)
	p-value	0.065	0.103	0.017

	Result	OR	RR	ARR
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	0.5	0.55	-0.082
	95% CI	(0.038 , 6.547)	(0.058 , 5.179)	(-0.376 , 0.212)
	p-value	0.597	0.601	0.586

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1314_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale (Parent)

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	2 (11.11)	2 (14.29)	4 (19.05)
	No	8 (44.44)	9 (64.29)	17 (80.95)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	1 (5.56)	4 (28.57)	5 (23.81)
	No	9 (50.00)	7 (50.00)	16 (76.19)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	0 (0.00)	1 (7.14)	1 (4.76)
	No	10 (55.56)	10 (71.43)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	1 (5.56)	0 (0.00)	1 (4.76)
	No	9 (50.00)	11 (78.57)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	1 (5.56)	0 (0.00)	1 (4.76)
	No	9 (50.00)	11 (78.57)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	1 (5.56)	0 (0.00)	1 (4.76)
	No	9 (50.00)	11 (78.57)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	1 (5.56)	0 (0.00)	1 (4.76)
	No	9 (50.00)	11 (78.57)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	1 (5.56)	1 (7.14)	2 (9.52)
	No	9 (50.00)	10 (71.43)	19 (90.48)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	1 (5.56)	3 (21.43)	4 (19.05)
	No	9 (50.00)	8 (57.14)	17 (80.95)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	1 (5.56)	1 (7.14)	2 (9.52)
	No	9 (50.00)	10 (71.43)	19 (90.48)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Yes	0 (0.00)	3 (21.43)	3 (14.29)
	No	10 (55.56)	8 (57.14)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Yes	0 (0.00)	1 (7.14)	1 (4.76)
	No	10 (55.56)	10 (71.43)	20 (95.24)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	0 (0.00)	2 (14.29)	2 (9.52)
	No	10 (55.56)	9 (64.29)	19 (90.48)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Yes	3 (16.67)	4 (28.57)	7 (33.33)
	No	7 (38.89)	7 (50.00)	14 (66.67)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	0 (0.00)	5 (35.71)	5 (23.81)
	No	10 (55.56)	6 (42.86)	16 (76.19)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	0 (0.00)	2 (14.29)	2 (9.52)
	No	10 (55.56)	9 (64.29)	19 (90.48)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	0 (0.00)	5 (35.71)	5 (23.81)
	No	10 (55.56)	6 (42.86)	16 (76.19)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	1 (5.56)	2 (14.29)	3 (14.29)
	No	9 (50.00)	9 (64.29)	18 (85.71)
	Missing	8 (44.44)	3 (21.43)	11 (34.38)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1314_respons Rate

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
COGNITIVE FATIGUE-Baseline	Yes	10 (55.56)	11 (78.57)	21 (65.62)
	No	8 (44.44)	3 (21.43)	11 (34.38)
COGNITIVE FATIGUE-Week 24	Yes	15 (83.33)	13 (92.86)	28 (87.50)
	No	3 (16.67)	1 (7.14)	4 (12.50)
COGNITIVE FATIGUE-Week 48	Yes	12 (66.67)	10 (71.43)	22 (68.75)
	No	6 (33.33)	4 (28.57)	10 (31.25)
COGNITIVE FATIGUE-Week 72	Yes	14 (77.78)	8 (57.14)	22 (68.75)
	No	4 (22.22)	6 (42.86)	10 (31.25)
COGNITIVE FATIGUE-Week 96	Yes	13 (72.22)	7 (50.00)	20 (62.50)
	No	5 (27.78)	7 (50.00)	12 (37.50)
GENERAL FATIGUE-Baseline	Yes	10 (55.56)	11 (78.57)	21 (65.62)
	No	8 (44.44)	3 (21.43)	11 (34.38)
GENERAL FATIGUE-Week 24	Yes	15 (83.33)	13 (92.86)	28 (87.50)
	No	3 (16.67)	1 (7.14)	4 (12.50)
GENERAL FATIGUE-Week 48	Yes	12 (66.67)	10 (71.43)	22 (68.75)
	No	6 (33.33)	4 (28.57)	10 (31.25)
GENERAL FATIGUE-Week 72	Yes	14 (77.78)	8 (57.14)	22 (68.75)
	No	4 (22.22)	6 (42.86)	10 (31.25)
GENERAL FATIGUE-Week 96	Yes	13 (72.22)	7 (50.00)	20 (62.50)
	No	5 (27.78)	7 (50.00)	12 (37.50)
SLEEP/REST FATIGUE-Baseline	Yes	10 (55.56)	11 (78.57)	21 (65.62)
	No	8 (44.44)	3 (21.43)	11 (34.38)
SLEEP/REST FATIGUE-Week 24	Yes	15 (83.33)	13 (92.86)	28 (87.50)
	No	3 (16.67)	1 (7.14)	4 (12.50)
SLEEP/REST FATIGUE-Week 48	Yes	12 (66.67)	10 (71.43)	22 (68.75)
	No	6 (33.33)	4 (28.57)	10 (31.25)
SLEEP/REST FATIGUE-Week 72	Yes	14 (77.78)	8 (57.14)	22 (68.75)
	No	4 (22.22)	6 (42.86)	10 (31.25)
SLEEP/REST FATIGUE-Week 96	Yes	13 (72.22)	7 (50.00)	20 (62.50)
	No	5 (27.78)	7 (50.00)	12 (37.50)

NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1517_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale (Parent)

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.8	1.64	0.078
	95% CI	(0.534 , 6.064)	(0.586 , 4.589)	(-0.081 , 0.237)
	p-value	0.343	0.346	0.337
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	1.962	1.794	0.077
	95% CI	(0.527 , 7.309)	(0.569 , 5.658)	(-0.071 , 0.226)
	p-value	0.315	0.319	0.307
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	2.167	2.05	0.051
	95% CI	(0.374 , 12.554)	(0.397 , 10.574)	(-0.063 , 0.165)
	p-value	0.388	0.391	0.378
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.5	0.512	-0.024
	95% CI	(0.044 , 5.743)	(0.048 , 5.431)	(-0.106 , 0.058)
	p-value	0.578	0.579	0.569
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	2.312	2.05	0.102
	95% CI	(0.636 , 8.402)	(0.67 , 6.273)	(-0.051 , 0.256)
	p-value	0.203	0.208	0.191
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	4.875	4.1	0.151
	95% CI	(0.966 , 24.597)	(0.927 , 18.138)	(0.011 , 0.292)
	p-value	0.055	0.063	0.035
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	11.613	9.225	0.201
	95% CI	(1.396 , 96.612)	(1.224 , 69.512)	(0.063 , 0.338)
	p-value	0.023	0.031	0.004

	Result	OR	RR	ARR
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.5	0.512	-0.024
	95% CI	(0.044 , 5.743)	(0.048 , 5.431)	(-0.106 , 0.058)
	p-value	0.578	0.579	0.569
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.754	0.797	-0.045
	95% CI	(0.251 , 2.268)	(0.329 , 1.935)	(-0.217 , 0.128)
	p-value	0.616	0.616	0.614
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	2.235	2.05	0.077
	95% CI	(0.519 , 9.636)	(0.55 , 7.641)	(-0.06 , 0.213)
	p-value	0.281	0.285	0.27
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	1.407	1.367	0.027
	95% CI	(0.294 , 6.73)	(0.326 , 5.723)	(-0.096 , 0.149)
	p-value	0.669	0.669	0.668
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.027	1.025	0.002
	95% CI	(0.195 , 5.418)	(0.22 , 4.781)	(-0.112 , 0.116)
	p-value	0.975	0.975	0.975
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.288	0.342	-0.145
	95% CI	(0.072 , 1.157)	(0.1 , 1.171)	(-0.295 , 0.006)
	p-value	0.079	0.088	0.06
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.584	0.615	-0.047
	95% CI	(0.13 , 2.625)	(0.157 , 2.405)	(-0.176 , 0.082)
	p-value	0.483	0.485	0.476
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.584	0.615	-0.047
	95% CI	(0.13 , 2.625)	(0.157 , 2.405)	(-0.176 , 0.082)

	Result	OR	RR	ARR
	p-value	0.483	0.485	0.476
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.185	0.205	-0.097
	95% CI	(0.021 , 1.657)	(0.025 , 1.678)	(-0.208 , 0.014)
	p-value	0.131	0.14	0.088
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	0.857	0.879	-0.021
	95% CI	(0.261 , 2.816)	(0.323 , 2.387)	(-0.18 , 0.139)
	p-value	0.8	0.8	0.799
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.648	0.683	-0.046
	95% CI	(0.168 , 2.495)	(0.208 , 2.241)	(-0.189 , 0.096)
	p-value	0.528	0.53	0.524
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	0.648	0.683	-0.046
	95% CI	(0.168 , 2.495)	(0.208 , 2.241)	(-0.189 , 0.096)
	p-value	0.528	0.53	0.524
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.028	1.025	0.002
	95% CI	(0.239 , 4.425)	(0.275 , 3.821)	(-0.128 , 0.132)
	p-value	0.971	0.971	0.971
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.889	0.911	-0.02
	95% CI	(0.305 , 2.594)	(0.391 , 2.125)	(-0.197 , 0.158)
	p-value	0.829	0.829	0.829
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	2.235	2.05	0.077
	95% CI	(0.519 , 9.636)	(0.55 , 7.641)	(-0.06 , 0.213)
	p-value	0.281	0.285	0.27
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	1.029	1.025	0.003

	Result	OR	RR	ARR
	95% CI	(0.274 , 3.866)	(0.321 , 3.272)	(-0.14 , 0.146)
	p-value	0.967	0.967	0.967
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.407	1.367	0.027
	95% CI	(0.294 , 6.73)	(0.326 , 5.723)	(-0.096 , 0.149)
	p-value	0.669	0.669	0.668

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1517_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale (Parent)

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	8 (15.09)	5 (10.00)	13 (16.05)
	No	32 (60.38)	36 (72.00)	68 (83.95)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	7 (13.21)	4 (8.00)	11 (13.58)
	No	33 (62.26)	37 (74.00)	70 (86.42)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	4 (7.55)	2 (4.00)	6 (7.41)
	No	36 (67.92)	39 (78.00)	75 (92.59)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (1.89)	2 (4.00)	3 (3.70)
	No	39 (73.58)	39 (78.00)	78 (96.30)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	8 (15.09)	4 (8.00)	12 (14.81)
	No	32 (60.38)	37 (74.00)	69 (85.19)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	8 (15.09)	2 (4.00)	10 (12.35)
	No	32 (60.38)	39 (78.00)	71 (87.65)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	9 (16.98)	1 (2.00)	10 (12.35)
	No	31 (58.49)	40 (80.00)	71 (87.65)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	1 (1.89)	2 (4.00)	3 (3.70)
	No	39 (73.58)	39 (78.00)	78 (96.30)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	7 (13.21)	9 (18.00)	16 (19.75)
	No	33 (62.26)	32 (64.00)	65 (80.25)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	6 (11.32)	3 (6.00)	9 (11.11)
	No	34 (64.15)	38 (76.00)	72 (88.89)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	4 (7.55)	3 (6.00)	7 (8.64)
	No	36 (67.92)	38 (76.00)	74 (91.36)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	3 (5.66)	3 (6.00)	6 (7.41)
	No	37 (69.81)	38 (76.00)	75 (92.59)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Yes	3 (5.66)	9 (18.00)	12 (14.81)
	No	37 (69.81)	32 (64.00)	69 (85.19)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Yes	3 (5.66)	5 (10.00)	8 (9.88)
	No	37 (69.81)	36 (72.00)	73 (90.12)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Yes	3 (5.66)	5 (10.00)	8 (9.88)
	No	37 (69.81)	36 (72.00)	73 (90.12)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (1.89)	5 (10.00)	6 (7.41)
	No	39 (73.58)	36 (72.00)	75 (92.59)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Yes	6 (11.32)	7 (14.00)	13 (16.05)
	No	34 (64.15)	34 (68.00)	68 (83.95)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	4 (7.55)	6 (12.00)	10 (12.35)
	No	36 (67.92)	35 (70.00)	71 (87.65)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	4 (7.55)	6 (12.00)	10 (12.35)
	No	36 (67.92)	35 (70.00)	71 (87.65)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	4 (7.55)	4 (8.00)	8 (9.88)
	No	36 (67.92)	37 (74.00)	73 (90.12)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	8 (15.09)	9 (18.00)	17 (20.99)
	No	32 (60.38)	32 (64.00)	64 (79.01)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	6 (11.32)	3 (6.00)	9 (11.11)
	No	34 (64.15)	38 (76.00)	72 (88.89)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	5 (9.43)	5 (10.00)	10 (12.35)
	No	35 (66.04)	36 (72.00)	71 (87.65)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	4 (7.55)	3 (6.00)	7 (8.64)
	No	36 (67.92)	38 (76.00)	74 (91.36)
	Missing	13 (24.53)	9 (18.00)	22 (21.36)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab42_44Related_PedsQLFatigueParent_AGEGRN_Age1517_respons Rate

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
COGNITIVE FATIGUE-Baseline	Yes	40 (75.47)	41 (82.00)	81 (78.64)
	No	13 (24.53)	9 (18.00)	22 (21.36)
COGNITIVE FATIGUE-Week 24	Yes	41 (77.36)	45 (90.00)	86 (83.50)
	No	12 (22.64)	5 (10.00)	17 (16.50)
COGNITIVE FATIGUE-Week 48	Yes	39 (73.58)	33 (66.00)	72 (69.90)
	No	14 (26.42)	17 (34.00)	31 (30.10)
COGNITIVE FATIGUE-Week 72	Yes	29 (54.72)	21 (42.00)	50 (48.54)
	No	24 (45.28)	29 (58.00)	53 (51.46)
COGNITIVE FATIGUE-Week 96	Yes	15 (28.30)	15 (30.00)	30 (29.13)
	No	38 (71.70)	35 (70.00)	73 (70.87)
GENERAL FATIGUE-Baseline	Yes	40 (75.47)	41 (82.00)	81 (78.64)
	No	13 (24.53)	9 (18.00)	22 (21.36)
GENERAL FATIGUE-Week 24	Yes	41 (77.36)	45 (90.00)	86 (83.50)
	No	12 (22.64)	5 (10.00)	17 (16.50)
GENERAL FATIGUE-Week 48	Yes	39 (73.58)	33 (66.00)	72 (69.90)
	No	14 (26.42)	17 (34.00)	31 (30.10)
GENERAL FATIGUE-Week 72	Yes	29 (54.72)	21 (42.00)	50 (48.54)
	No	24 (45.28)	29 (58.00)	53 (51.46)
GENERAL FATIGUE-Week 96	Yes	15 (28.30)	15 (30.00)	30 (29.13)
	No	38 (71.70)	35 (70.00)	73 (70.87)
SLEEP/REST FATIGUE-Baseline	Yes	40 (75.47)	41 (82.00)	81 (78.64)
	No	13 (24.53)	9 (18.00)	22 (21.36)
SLEEP/REST FATIGUE-Week 24	Yes	41 (77.36)	45 (90.00)	86 (83.50)
	No	12 (22.64)	5 (10.00)	17 (16.50)
SLEEP/REST FATIGUE-Week 48	Yes	39 (73.58)	33 (66.00)	72 (69.90)
	No	14 (26.42)	17 (34.00)	31 (30.10)
SLEEP/REST FATIGUE-Week 72	Yes	28 (52.83)	21 (42.00)	49 (47.57)
	No	25 (47.17)	29 (58.00)	54 (52.43)
SLEEP/REST FATIGUE-Week 96	Yes	15 (28.30)	15 (30.00)	30 (29.13)
	No	38 (71.70)	35 (70.00)	73 (70.87)

NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Female_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale (Parent)

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.563	1.495	0.04
	95% CI	(0.323 , 7.565)	(0.361 , 6.194)	(-0.102 , 0.182)
	p-value	0.579	0.579	0.579
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	1.138	1.121	0.013
	95% CI	(0.261 , 4.964)	(0.304 , 4.131)	(-0.137 , 0.163)
	p-value	0.863	0.863	0.864
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.532	0.561	-0.048
	95% CI	(0.091 , 3.115)	(0.11 , 2.865)	(-0.176 , 0.081)
	p-value	0.484	0.487	0.47
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	1.125	1.121	0.003
	95% CI	(0.068 , 18.732)	(0.073 , 17.223)	(-0.075 , 0.082)
	p-value	0.935	0.935	0.935
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	1.133	1.121	0.01
	95% CI	(0.213 , 6.044)	(0.243 , 5.178)	(-0.122 , 0.142)
	p-value	0.883	0.883	0.884
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	1.75	1.682	0.037
	95% CI	(0.274 , 11.18)	(0.299 , 9.454)	(-0.085 , 0.159)
	p-value	0.554	0.555	0.554
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	2.024	1.869	0.07
	95% CI	(0.444 , 9.219)	(0.483 , 7.225)	(-0.08 , 0.221)
	p-value	0.362	0.365	0.36

	Result	OR	RR	ARR
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.129	1.121	0.007
	95% CI	(0.15 , 8.5)	(0.167 , 7.519)	(-0.103 , 0.116)
	p-value	0.906	0.906	0.906
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.883	0.897	-0.014
	95% CI	(0.216 , 3.607)	(0.263 , 3.063)	(-0.171 , 0.143)
	p-value	0.862	0.862	0.862
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	1.133	1.121	0.01
	95% CI	(0.213 , 6.044)	(0.243 , 5.178)	(-0.122 , 0.142)
	p-value	0.883	0.883	0.884
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.413	0.448	-0.075
	95% CI	(0.074 , 2.289)	(0.093 , 2.158)	(-0.212 , 0.062)
	p-value	0.311	0.317	0.286
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.129	1.121	0.007
	95% CI	(0.15 , 8.5)	(0.167 , 7.519)	(-0.103 , 0.116)
	p-value	0.906	0.906	0.906
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.5	0.561	-0.095
	95% CI	(0.135 , 1.846)	(0.186 , 1.692)	(-0.268 , 0.078)
	p-value	0.298	0.305	0.282
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.134	0.16	-0.159
	95% CI	(0.016 , 1.154)	(0.021 , 1.234)	(-0.298 , -0.02)
	p-value	0.067	0.079	0.025
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.333	0.374	-0.102
	95% CI	(0.062 , 1.781)	(0.081 , 1.726)	(-0.246 , 0.042)

	Result	OR	RR	ARR
	p-value	0.199	0.207	0.167
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.134	0.16	-0.159
	95% CI	(0.016 , 1.154)	(0.021 , 1.234)	(-0.298 , -0.02)
	p-value	0.067	0.079	0.025
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	0.838	0.872	-0.031
	95% CI	(0.273 , 2.574)	(0.366 , 2.08)	(-0.228 , 0.165)
	p-value	0.757	0.758	0.756
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.429	0.498	-0.122
	95% CI	(0.118 , 1.555)	(0.169 , 1.468)	(-0.3 , 0.055)
	p-value	0.198	0.206	0.178
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	0.5	0.561	-0.095
	95% CI	(0.135 , 1.846)	(0.186 , 1.692)	(-0.268 , 0.078)
	p-value	0.298	0.305	0.282
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.333	0.374	-0.102
	95% CI	(0.062 , 1.781)	(0.081 , 1.726)	(-0.246 , 0.042)
	p-value	0.199	0.207	0.167
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.806	0.841	-0.034
	95% CI	(0.247 , 2.625)	(0.326 , 2.172)	(-0.221 , 0.152)
	p-value	0.72	0.72	0.718
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.64	0.673	-0.044
	95% CI	(0.141 , 2.913)	(0.174 , 2.601)	(-0.192 , 0.103)
	p-value	0.564	0.566	0.557
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.591	0.641	-0.068

	Result	OR	RR	ARR
	95% CI	(0.156 , 2.236)	(0.206 , 1.994)	(-0.236 , 0.1)
	p-value	0.439	0.442	0.429
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	0.64	0.673	-0.044
	95% CI	(0.141 , 2.913)	(0.174 , 2.601)	(-0.192 , 0.103)
	p-value	0.564	0.566	0.557

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Female_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale (Parent)

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	4 (8.00)	3 (6.52)	7 (10.00)
	No	29 (58.00)	34 (73.91)	63 (90.00)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	4 (8.00)	4 (8.70)	8 (11.43)
	No	29 (58.00)	33 (71.74)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	2 (4.00)	4 (8.70)	6 (8.57)
	No	31 (62.00)	33 (71.74)	64 (91.43)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (2.00)	1 (2.17)	2 (2.86)
	No	32 (64.00)	36 (78.26)	68 (97.14)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	3 (6.00)	3 (6.52)	6 (8.57)
	No	30 (60.00)	34 (73.91)	64 (91.43)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	3 (6.00)	2 (4.35)	5 (7.14)
	No	30 (60.00)	35 (76.09)	65 (92.86)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	5 (10.00)	3 (6.52)	8 (11.43)
	No	28 (56.00)	34 (73.91)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	2 (4.00)	2 (4.35)	4 (5.71)
	No	31 (62.00)	35 (76.09)	66 (94.29)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	4 (8.00)	5 (10.87)	9 (12.86)
	No	29 (58.00)	32 (69.57)	61 (87.14)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	3 (6.00)	3 (6.52)	6 (8.57)
	No	30 (60.00)	34 (73.91)	64 (91.43)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	2 (4.00)	5 (10.87)	7 (10.00)
	No	31 (62.00)	32 (69.57)	63 (90.00)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	2 (4.00)	2 (4.35)	4 (5.71)
	No	31 (62.00)	35 (76.09)	66 (94.29)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Yes	4 (8.00)	8 (17.39)	12 (17.14)
	No	29 (58.00)	29 (63.04)	58 (82.86)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Yes	1 (2.00)	7 (15.22)	8 (11.43)
	No	32 (64.00)	30 (65.22)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Yes	2 (4.00)	6 (13.04)	8 (11.43)
	No	31 (62.00)	31 (67.39)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (2.00)	7 (15.22)	8 (11.43)
	No	32 (64.00)	30 (65.22)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Yes	7 (14.00)	9 (19.57)	16 (22.86)
	No	26 (52.00)	28 (60.87)	54 (77.14)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	4 (8.00)	9 (19.57)	13 (18.57)
	No	29 (58.00)	28 (60.87)	57 (81.43)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	4 (8.00)	8 (17.39)	12 (17.14)
	No	29 (58.00)	29 (63.04)	58 (82.86)

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Missing	17 (34.00)	9 (19.57)	26 (27.08)
	Yes	2 (4.00)	6 (13.04)	8 (11.43)
	No	31 (62.00)	31 (67.39)	62 (88.57)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Missing	17 (34.00)	9 (19.57)	26 (27.08)
	Yes	6 (12.00)	8 (17.39)	14 (20.00)
	No	27 (54.00)	29 (63.04)	56 (80.00)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Missing	17 (34.00)	9 (19.57)	26 (27.08)
	Yes	3 (6.00)	5 (10.87)	8 (11.43)
	No	30 (60.00)	32 (69.57)	62 (88.57)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Missing	17 (34.00)	9 (19.57)	26 (27.08)
	Yes	4 (8.00)	7 (15.22)	11 (15.71)
	No	29 (58.00)	30 (65.22)	59 (84.29)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Missing	17 (34.00)	9 (19.57)	26 (27.08)
	Yes	3 (6.00)	5 (10.87)	8 (11.43)
	No	30 (60.00)	32 (69.57)	62 (88.57)
	Missing	17 (34.00)	9 (19.57)	26 (27.08)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Female_responsRate

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
COGNITIVE FATIGUE-Baseline	Yes	33 (66.00)	37 (80.43)	70 (72.92)
	No	17 (34.00)	9 (19.57)	26 (27.08)
COGNITIVE FATIGUE-Week 24	Yes	39 (78.00)	42 (91.30)	81 (84.38)
	No	11 (22.00)	4 (8.70)	15 (15.62)
COGNITIVE FATIGUE-Week 48	Yes	36 (72.00)	32 (69.57)	68 (70.83)
	No	14 (28.00)	14 (30.43)	28 (29.17)
COGNITIVE FATIGUE-Week 72	Yes	29 (58.00)	22 (47.83)	51 (53.12)
	No	21 (42.00)	24 (52.17)	45 (46.88)
COGNITIVE FATIGUE-Week 96	Yes	19 (38.00)	17 (36.96)	36 (37.50)
	No	31 (62.00)	29 (63.04)	60 (62.50)
GENERAL FATIGUE-Baseline	Yes	33 (66.00)	37 (80.43)	70 (72.92)
	No	17 (34.00)	9 (19.57)	26 (27.08)
GENERAL FATIGUE-Week 24	Yes	39 (78.00)	42 (91.30)	81 (84.38)
	No	11 (22.00)	4 (8.70)	15 (15.62)
GENERAL FATIGUE-Week 48	Yes	36 (72.00)	32 (69.57)	68 (70.83)
	No	14 (28.00)	14 (30.43)	28 (29.17)
GENERAL FATIGUE-Week 72	Yes	29 (58.00)	22 (47.83)	51 (53.12)
	No	21 (42.00)	24 (52.17)	45 (46.88)
GENERAL FATIGUE-Week 96	Yes	19 (38.00)	17 (36.96)	36 (37.50)
	No	31 (62.00)	29 (63.04)	60 (62.50)
SLEEP/REST FATIGUE-Baseline	Yes	33 (66.00)	37 (80.43)	70 (72.92)
	No	17 (34.00)	9 (19.57)	26 (27.08)
SLEEP/REST FATIGUE-Week 24	Yes	39 (78.00)	42 (91.30)	81 (84.38)
	No	11 (22.00)	4 (8.70)	15 (15.62)
SLEEP/REST FATIGUE-Week 48	Yes	36 (72.00)	32 (69.57)	68 (70.83)
	No	14 (28.00)	14 (30.43)	28 (29.17)
SLEEP/REST FATIGUE-Week 72	Yes	28 (56.00)	22 (47.83)	50 (52.08)
	No	22 (44.00)	24 (52.17)	46 (47.92)
SLEEP/REST FATIGUE-Week 96	Yes	19 (38.00)	17 (36.96)	36 (37.50)
	No	31 (62.00)	29 (63.04)	60 (62.50)

NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Male_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale (Parent)

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.5	1.324	0.086
	95% CI	(0.329 , 6.833)	(0.46 , 3.811)	(-0.233 , 0.405)
	p-value	0.6	0.603	0.596
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	2	1.765	0.102
	95% CI	(0.31 , 12.891)	(0.375 , 8.305)	(-0.163 , 0.367)
	p-value	0.466	0.472	0.451
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	1.393	1.324	0.043
	95% CI	(0.2 , 9.712)	(0.254 , 6.885)	(-0.207 , 0.293)
	p-value	0.738	0.739	0.735
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.154	0.177	-0.133
	95% CI	(0.007 , 3.488)	(0.009 , 3.413)	(-0.368 , 0.101)
	p-value	0.24	0.252	0.421
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	7.636	5.294	0.286
	95% CI	(0.797 , 73.146)	(0.717 , 39.116)	(0.026 , 0.546)
	p-value	0.078	0.102	0.031
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	17.522	11.514	0.353
	95% CI	(0.894 , 343.561)	(0.704 , 188.23)	(0.063 , 0.643)
	p-value	0.059	0.087	0.012
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	13.64	9.743	0.294
	95% CI	(0.686 , 271.093)	(0.585 , 162.353)	(0.015 , 0.573)
	p-value	0.087	0.113	0.036
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A

	Result	OR	RR	ARR
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.846	0.882	-0.031
	95% CI	(0.171 , 4.198)	(0.266 , 2.928)	(-0.333 , 0.27)
	p-value	0.838	0.838	0.838
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	4.308	3.529	0.169
	95% CI	(0.424 , 43.735)	(0.442 , 28.207)	(-0.069 , 0.407)
	p-value	0.217	0.234	0.165
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	3	2.647	0.11
	95% CI	(0.277 , 32.459)	(0.307 , 22.817)	(-0.111 , 0.331)
	p-value	0.366	0.376	0.33
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	0.867	0.882	-0.016
	95% CI	(0.107 , 7.049)	(0.141 , 5.516)	(-0.246 , 0.215)
	p-value	0.894	0.894	0.894
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.102	0.127	-0.2
	95% CI	(0.005 , 2.156)	(0.007 , 2.262)	(-0.465 , 0.065)
	p-value	0.143	0.16	0.184
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	1.867	1.765	0.051
	95% CI	(0.152 , 22.936)	(0.177 , 17.564)	(-0.147 , 0.249)
	p-value	0.626	0.628	0.615
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	2.818	2.657	0.059
	95% CI	(0.107 , 74.514)	(0.117 , 60.585)	(-0.116 , 0.233)
	p-value	0.535	0.54	0.945
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	N/A	N/A	N/A
	95% CI	N/A	N/A	N/A
	p-value	N/A	N/A	N/A

	Result	OR	RR	ARR
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	0.867	0.882	-0.016
	95% CI	(0.107 , 7.049)	(0.141 , 5.516)	(-0.246 , 0.215)
	p-value	0.894	0.894	0.894
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.154	0.177	-0.133
	95% CI	(0.007 , 3.488)	(0.009 , 3.413)	(-0.368 , 0.101)
	p-value	0.24	0.252	0.421
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	2.818	2.657	0.059
	95% CI	(0.107 , 74.514)	(0.117 , 60.585)	(-0.116 , 0.233)
	p-value	0.535	0.54	0.945
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	5	4.429	0.118
	95% CI	(0.221 , 112.89)	(0.23 , 85.331)	(-0.098 , 0.334)
	p-value	0.312	0.324	0.482
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.857	0.882	-0.024
	95% CI	(0.145 , 5.064)	(0.209 , 3.731)	(-0.295 , 0.248)
	p-value	0.865	0.865	0.865
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.857	0.882	-0.024
	95% CI	(0.145 , 5.064)	(0.209 , 3.731)	(-0.295 , 0.248)
	p-value	0.865	0.865	0.865
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	5	4.429	0.118
	95% CI	(0.221 , 112.89)	(0.23 , 85.331)	(-0.098 , 0.334)
	p-value	0.312	0.324	0.482
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	5	4.429	0.118
	95% CI	(0.221 , 112.89)	(0.23 , 85.331)	(-0.098 , 0.334)
	p-value	0.312	0.324	0.482

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded

from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Male_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale (Parent)

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	6 (28.57)	4 (22.22)	10 (31.25)
	No	11 (52.38)	11 (61.11)	22 (68.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	4 (19.05)	2 (11.11)	6 (18.75)
	No	13 (61.90)	13 (72.22)	26 (81.25)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	3 (14.29)	2 (11.11)	5 (15.62)
	No	14 (66.67)	13 (72.22)	27 (84.38)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	0 (0.00)	2 (11.11)	2 (6.25)
	No	17 (80.95)	13 (72.22)	30 (93.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	6 (28.57)	1 (5.56)	7 (21.88)
	No	11 (52.38)	14 (77.78)	25 (78.12)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	6 (28.57)	0 (0.00)	6 (18.75)
	No	11 (52.38)	15 (83.33)	26 (81.25)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	5 (23.81)	0 (0.00)	5 (15.62)
	No	12 (57.14)	15 (83.33)	27 (84.38)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	17 (80.95)	15 (83.33)	32 (100.00)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	4 (19.05)	4 (22.22)	8 (25.00)

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
	No	13 (61.90)	11 (61.11)	24 (75.00)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	4 (19.05)	1 (5.56)	5 (15.62)
	No	13 (61.90)	14 (77.78)	27 (84.38)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	3 (14.29)	1 (5.56)	4 (12.50)
	No	14 (66.67)	14 (77.78)	28 (87.50)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	2 (9.52)	2 (11.11)	4 (12.50)
	No	15 (71.43)	13 (72.22)	28 (87.50)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Yes	0 (0.00)	3 (16.67)	3 (9.38)
	No	17 (80.95)	12 (66.67)	29 (90.62)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Yes	2 (9.52)	1 (5.56)	3 (9.38)
	No	15 (71.43)	14 (77.78)	29 (90.62)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Yes	1 (4.76)	0 (0.00)	1 (3.12)
	No	16 (76.19)	15 (83.33)	31 (96.88)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	0 (0.00)	0 (0.00)	0 (0.00)
	No	17 (80.95)	15 (83.33)	32 (100.00)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Yes	2 (9.52)	2 (11.11)	4 (12.50)
	No	15 (71.43)	13 (72.22)	28 (87.50)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	0 (0.00)	2 (11.11)	2 (6.25)

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
	No	17 (80.95)	13 (72.22)	30 (93.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	1 (4.76)	0 (0.00)	1 (3.12)
	No	16 (76.19)	15 (83.33)	31 (96.88)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	2 (9.52)	0 (0.00)	2 (6.25)
	No	15 (71.43)	15 (83.33)	30 (93.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	3 (14.29)	3 (16.67)	6 (18.75)
	No	14 (66.67)	12 (66.67)	26 (81.25)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Yes	3 (14.29)	3 (16.67)	6 (18.75)
	No	14 (66.67)	12 (66.67)	26 (81.25)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	2 (9.52)	0 (0.00)	2 (6.25)
	No	15 (71.43)	15 (83.33)	30 (93.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Yes	2 (9.52)	0 (0.00)	2 (6.25)
	No	15 (71.43)	15 (83.33)	30 (93.75)
	Missing	4 (19.05)	3 (16.67)	7 (17.95)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab42_44Related_PedsQLFatigueParent_SEX_Male_responsRate

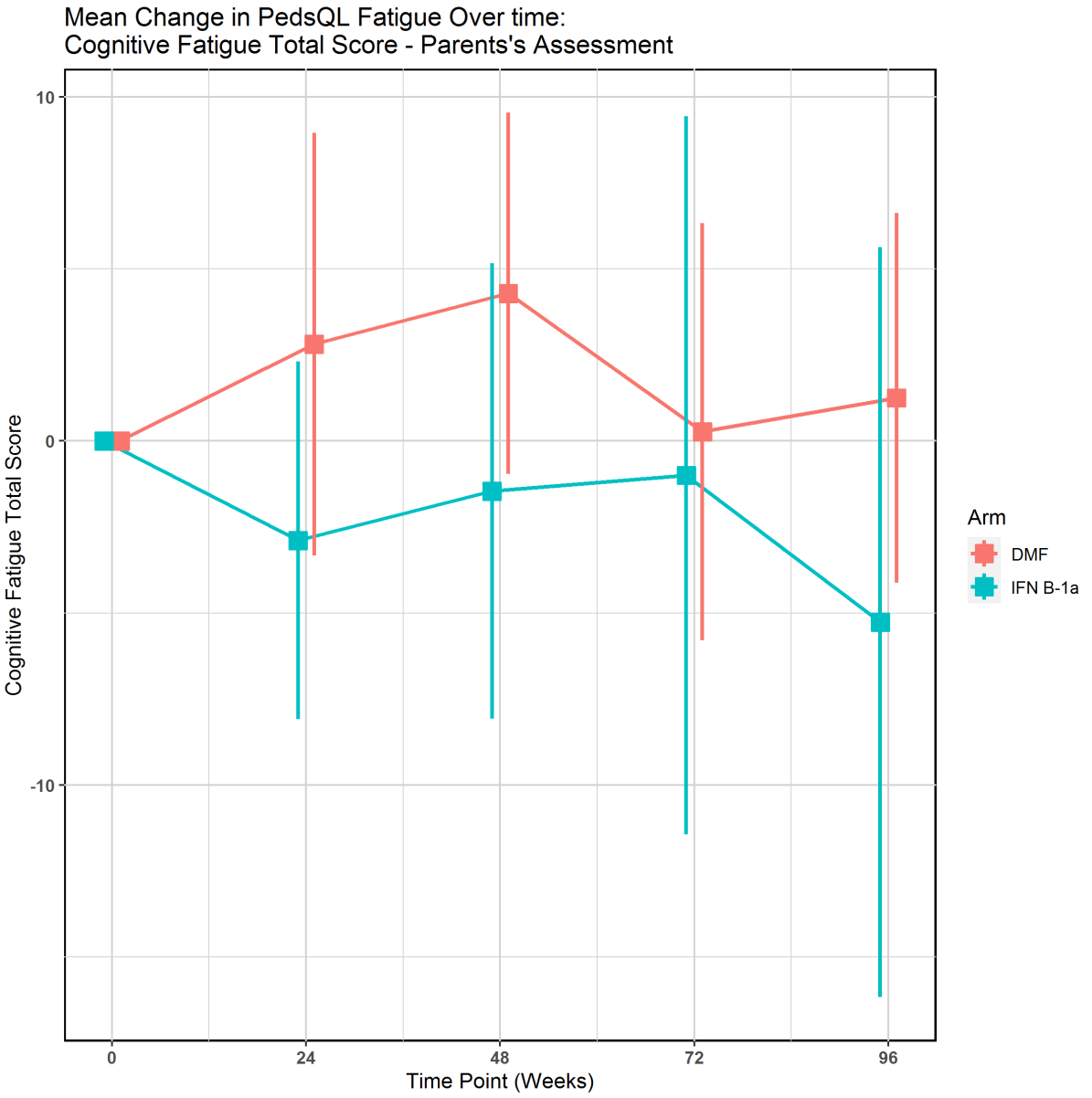
Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
COGNITIVE FATIGUE-Baseline	Yes	17 (80.95)	15 (83.33)	32 (82.05)
	No	4 (19.05)	3 (16.67)	7 (17.95)
COGNITIVE FATIGUE-Week 24	Yes	17 (80.95)	16 (88.89)	33 (84.62)
	No	4 (19.05)	2 (11.11)	6 (15.38)
COGNITIVE FATIGUE-Week 48	Yes	15 (71.43)	11 (61.11)	26 (66.67)
	No	6 (28.57)	7 (38.89)	13 (33.33)
COGNITIVE FATIGUE-Week 72	Yes	14 (66.67)	7 (38.89)	21 (53.85)
	No	7 (33.33)	11 (61.11)	18 (46.15)
COGNITIVE FATIGUE-Week 96	Yes	9 (42.86)	5 (27.78)	14 (35.90)
	No	12 (57.14)	13 (72.22)	25 (64.10)
GENERAL FATIGUE-Baseline	Yes	17 (80.95)	15 (83.33)	32 (82.05)
	No	4 (19.05)	3 (16.67)	7 (17.95)
GENERAL FATIGUE-Week 24	Yes	17 (80.95)	16 (88.89)	33 (84.62)
	No	4 (19.05)	2 (11.11)	6 (15.38)
GENERAL FATIGUE-Week 48	Yes	15 (71.43)	11 (61.11)	26 (66.67)
	No	6 (28.57)	7 (38.89)	13 (33.33)
GENERAL FATIGUE-Week 72	Yes	14 (66.67)	7 (38.89)	21 (53.85)
	No	7 (33.33)	11 (61.11)	18 (46.15)
GENERAL FATIGUE-Week 96	Yes	9 (42.86)	5 (27.78)	14 (35.90)
	No	12 (57.14)	13 (72.22)	25 (64.10)
SLEEP/REST FATIGUE-Baseline	Yes	17 (80.95)	15 (83.33)	32 (82.05)
	No	4 (19.05)	3 (16.67)	7 (17.95)
SLEEP/REST FATIGUE-Week 24	Yes	17 (80.95)	16 (88.89)	33 (84.62)
	No	4 (19.05)	2 (11.11)	6 (15.38)
SLEEP/REST FATIGUE-Week 48	Yes	15 (71.43)	11 (61.11)	26 (66.67)
	No	6 (28.57)	7 (38.89)	13 (33.33)
SLEEP/REST FATIGUE-Week 72	Yes	14 (66.67)	7 (38.89)	21 (53.85)
	No	7 (33.33)	11 (61.11)	18 (46.15)

Response Rate of PedsQL Multidimensional Fatigue Scale (Parent)		Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
SLEEP/REST Week 96	FATIGUE-	Yes	9 (42.86)	5 (27.78)	14 (35.90)
		No	12 (57.14)	13 (72.22)	25 (64.10)

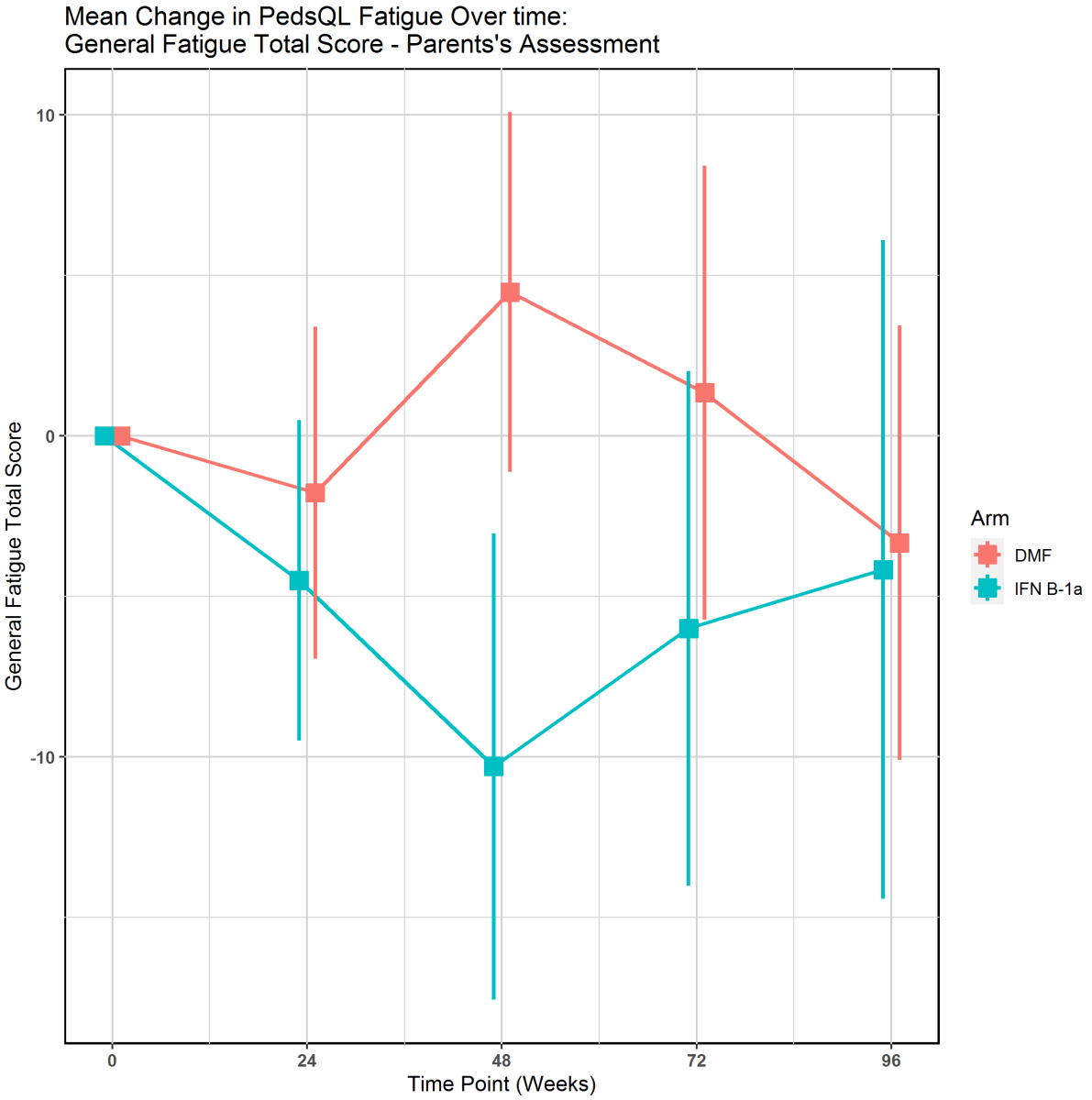
NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

Graphics

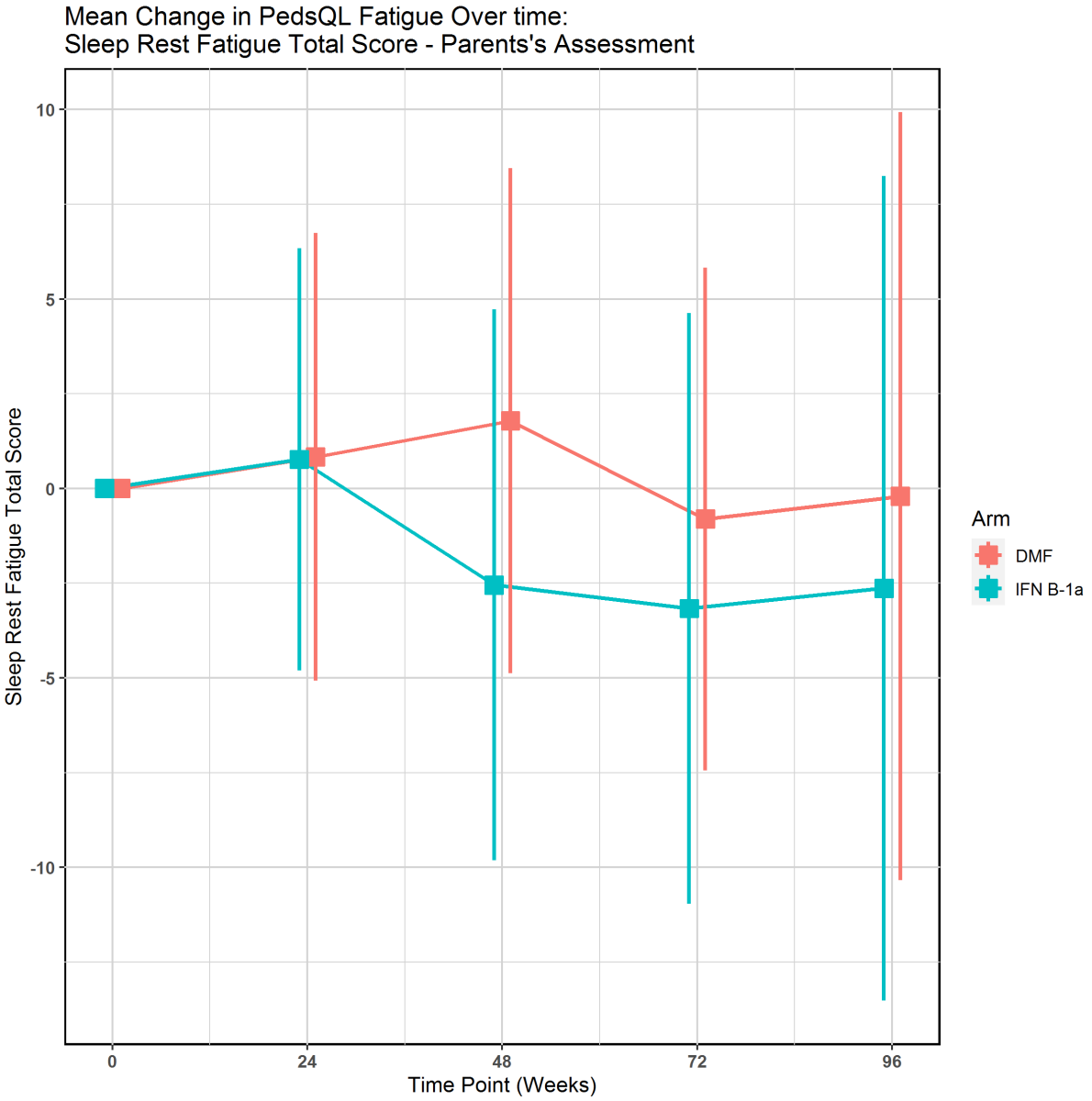
Change from baselineCognitive Fatigue Total Score Parents's Assessment



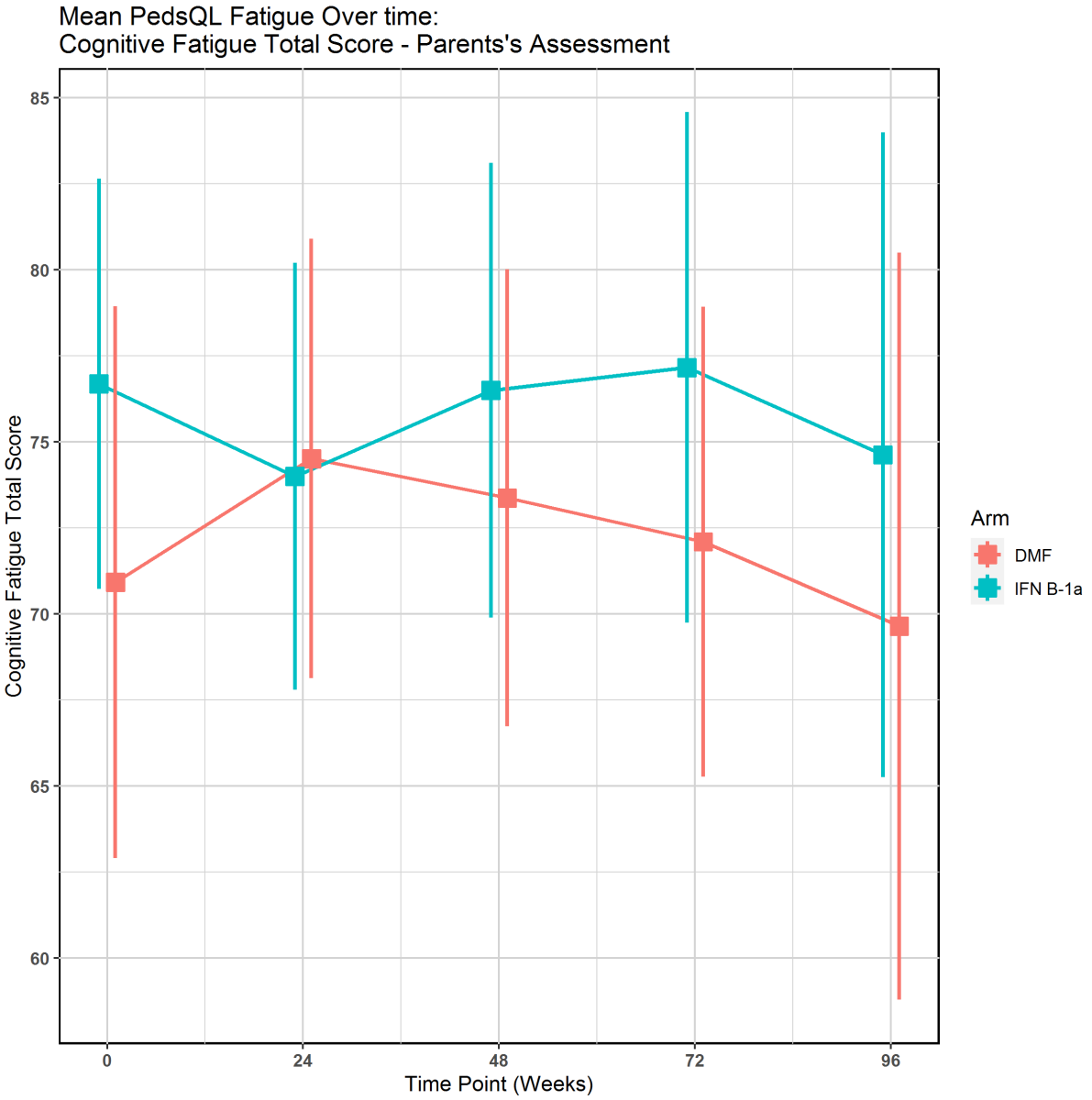
Change from baselineGeneral Fatigue Total Score Parents's Assessment



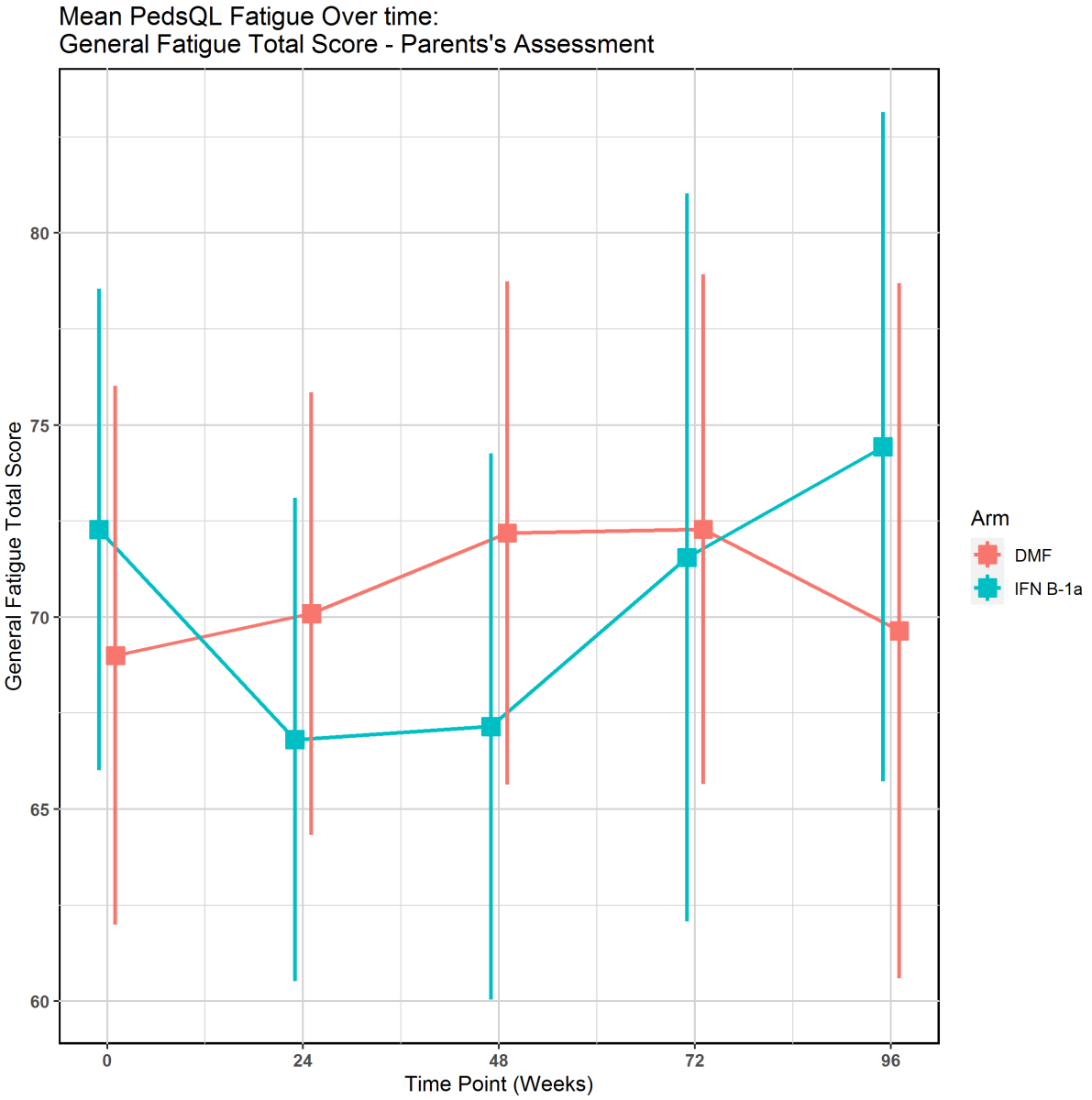
Change from baselineSleep Rest Fatigue Total Score Parents's Assessment



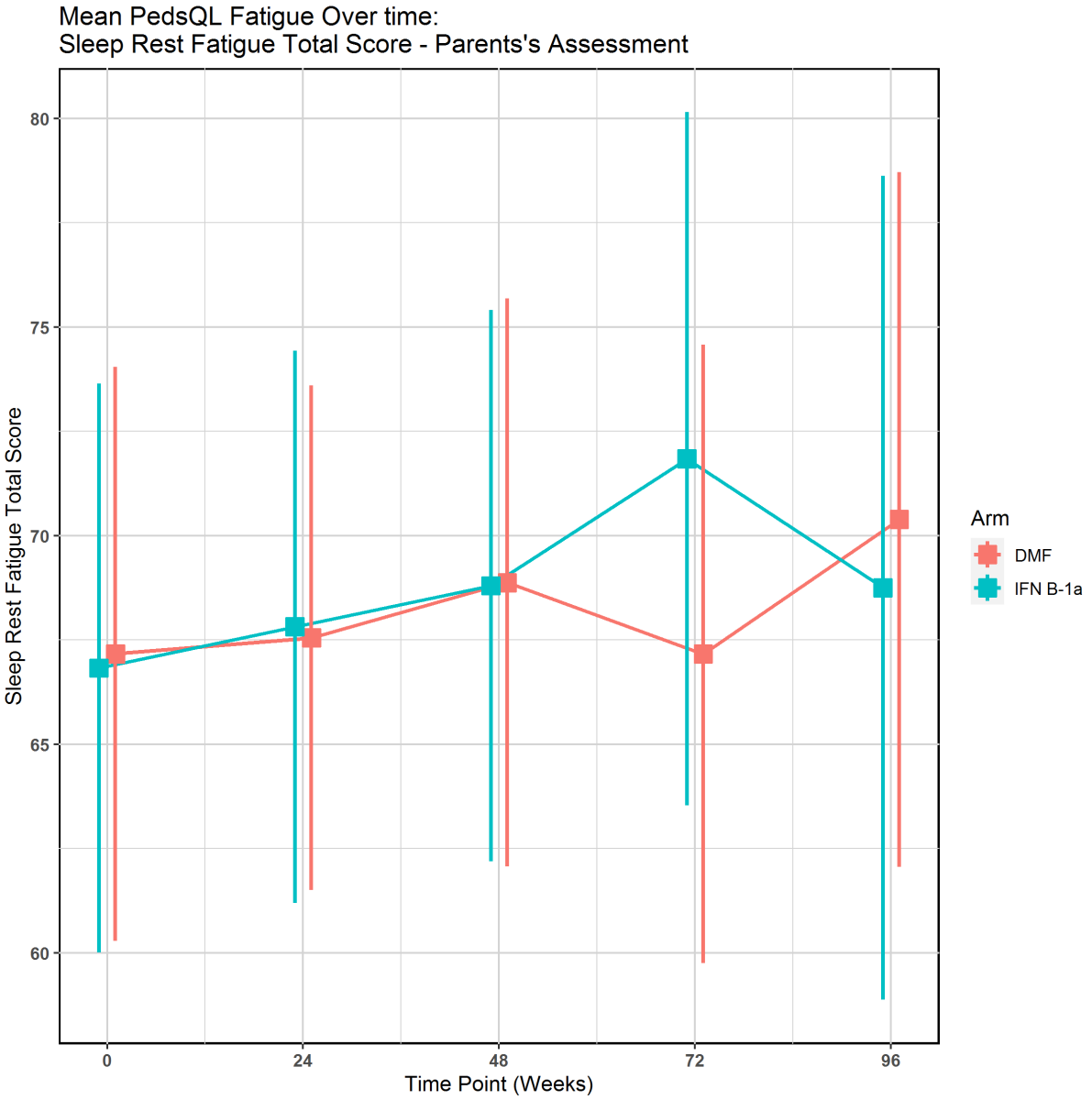
Cognitive Fatigue Total Score Parents's Assessment



General Fatigue Total Score Parents's Assessment



Sleep Rest Fatigue Total Score Parents's Assessment



PedsQL Fatique Participant

109MS306_CSRTab41_43Related_PedsQLFatigue_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigue Scale

		Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	1.46	1.378	0.049
	95% CI	(0.512 , 4.163)	(0.565 , 3.357)	(-0.086 , 0.183)
	p-value	0.479	0.481	0.476
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	1.956	1.768	0.085
	95% CI	(0.668 , 5.728)	(0.703 , 4.444)	(-0.048 , 0.219)
	p-value	0.221	0.226	0.211
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	1.956	1.768	0.085
	95% CI	(0.668 , 5.728)	(0.703 , 4.444)	(-0.048 , 0.219)
	p-value	0.221	0.226	0.211
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	3.056	2.652	0.122
	95% CI	(0.908 , 10.28)	(0.899 , 7.821)	(-0.003 , 0.248)
	p-value	0.071	0.077	0.056
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Effect measure	1.4	1.35	0.032
	95% CI	(0.416 , 4.714)	(0.456 , 3.996)	(-0.084 , 0.149)
	p-value	0.587	0.588	0.584
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	1.46	1.378	0.049
	95% CI	(0.512 , 4.163)	(0.565 , 3.357)	(-0.086 , 0.183)
	p-value	0.479	0.481	0.476

	Result	OR	RR	ARR
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Effect measure	1.633	1.543	0.05
	95% CI	(0.499 , 5.348)	(0.538 , 4.422)	(-0.07 , 0.17)
	p-value	0.418	0.42	0.411
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.714	0.75	-0.042
	95% CI	(0.246 , 2.077)	(0.301 , 1.871)	(-0.174 , 0.09)
	p-value	0.537	0.537	0.536
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	1.143	1.125	0.014
	95% CI	(0.358 , 3.649)	(0.404 , 3.133)	(-0.107 , 0.134)
	p-value	0.822	0.822	0.821
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.806	0.827	-0.022
	95% CI	(0.252 , 2.572)	(0.297 , 2.302)	(-0.143 , 0.098)
	p-value	0.715	0.715	0.715
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	0.821	0.844	-0.023
	95% CI	(0.276 , 2.446)	(0.329 , 2.166)	(-0.152 , 0.105)
	p-value	0.724	0.724	0.724
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	0.615	0.643	-0.04
	95% CI	(0.164 , 2.314)	(0.192 , 2.153)	(-0.147 , 0.068)
	p-value	0.473	0.474	0.47
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Effect measure	0.338	0.386	-0.114
	95% CI	(0.099 , 1.155)	(0.129 , 1.156)	(-0.237 , 0.01)
	p-value	0.084	0.089	0.071
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Effect measure	0.221	0.263	-0.15
	95% CI	(0.058 , 0.844)	(0.078 , 0.891)	(-0.273 , -0.028)

	Result	OR	RR	ARR
	p-value	0.027	0.032	0.016
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Effect measure	0.806	0.827	-0.022
	95% CI	(0.252 , 2.572)	(0.297 , 2.302)	(-0.143 , 0.098)
	p-value	0.715	0.715	0.715
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.956	0.964	-0.007
	95% CI	(0.375 , 2.433)	(0.457 , 2.036)	(-0.157 , 0.142)
	p-value	0.924	0.924	0.924
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Effect measure	1.46	1.378	0.049
	95% CI	(0.512 , 4.163)	(0.565 , 3.357)	(-0.086 , 0.183)
	p-value	0.479	0.481	0.476
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	0.957	0.964	-0.007
	95% CI	(0.363 , 2.521)	(0.436 , 2.131)	(-0.151 , 0.138)
	p-value	0.928	0.928	0.928
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	1.222	1.179	0.03
	95% CI	(0.462 , 3.234)	(0.531 , 2.617)	(-0.114 , 0.174)
	p-value	0.686	0.686	0.685
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.512	1.393	0.065
	95% CI	(0.586 , 3.897)	(0.649 , 2.988)	(-0.083 , 0.214)
	p-value	0.393	0.395	0.388
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Effect measure	0.958	0.964	-0.005
	95% CI	(0.332 , 2.767)	(0.39 , 2.386)	(-0.137 , 0.127)
	p-value	0.937	0.937	0.937
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Effect measure	0.6	0.643	-0.06

	Result	OR	RR	ARR
	95% CI	(0.198 , 1.818)	(0.245 , 1.684)	(-0.188 , 0.069)
	p-value	0.367	0.369	0.363
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	1.087	1.071	0.012
	95% CI	(0.404 , 2.925)	(0.472 , 2.431)	(-0.129 , 0.153)
	p-value	0.869	0.869	0.869
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Effect measure	1.877	1.736	0.068
	95% CI	(0.586 , 6.011)	(0.621 , 4.849)	(-0.055 , 0.192)
	p-value	0.289	0.293	0.279

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab41_43Related_PedsQLFatigue_NPERCENT

Summary statistics PedsQL Multidimensional Fatigue Scale

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 24	Yes	10 (14.08)	7 (10.94)	17 (15.45)
	No	46 (64.79)	47 (73.44)	93 (84.55)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 48	Yes	11 (15.49)	6 (9.38)	17 (15.45)
	No	45 (63.38)	48 (75.00)	93 (84.55)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 72	Yes	11 (15.49)	6 (9.38)	17 (15.45)
	No	45 (63.38)	48 (75.00)	93 (84.55)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	11 (15.49)	4 (6.25)	15 (13.64)
	No	45 (63.38)	50 (78.12)	95 (86.36)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - GENERAL FATIGUE - Week 24	Yes	7 (9.86)	5 (7.81)	12 (10.91)
	No	49 (69.01)	49 (76.56)	98 (89.09)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	10 (14.08)	7 (10.94)	17 (15.45)
	No	46 (64.79)	47 (73.44)	93 (84.55)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - GENERAL FATIGUE - Week 72	Yes	8 (11.27)	5 (7.81)	13 (11.82)
	No	48 (67.61)	49 (76.56)	97 (88.18)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - GENERAL FATIGUE - Week 96	Yes	7 (9.86)	9 (14.06)	16 (14.55)
	No	49 (69.01)	45 (70.31)	94 (85.45)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 24	Yes	7 (9.86)	6 (9.38)	13 (11.82)
	No	49 (69.01)	48 (75.00)	97 (88.18)

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 48	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	6 (8.45)	7 (10.94)	13 (11.82)
	No	50 (70.42)	47 (73.44)	97 (88.18)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 72	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	7 (9.86)	8 (12.50)	15 (13.64)
	No	49 (69.01)	46 (71.88)	95 (86.36)
MCID increase ≥15% - SLEEP/REST FATIGUE - Week 96	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	4 (5.63)	6 (9.38)	10 (9.09)
	No	52 (73.24)	48 (75.00)	100 (90.91)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 24	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	4 (5.63)	10 (15.62)	14 (12.73)
	No	52 (73.24)	44 (68.75)	96 (87.27)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 48	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	3 (4.23)	11 (17.19)	14 (12.73)
	No	53 (74.65)	43 (67.19)	96 (87.27)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 72	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	6 (8.45)	7 (10.94)	13 (11.82)
	No	50 (70.42)	47 (73.44)	97 (88.18)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	11 (15.49)	11 (17.19)	22 (20.00)
	No	45 (63.38)	43 (67.19)	88 (80.00)
MCID decrease ≥15% - GENERAL FATIGUE - Week 24	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	10 (14.08)	7 (10.94)	17 (15.45)
	No	46 (64.79)	47 (73.44)	93 (84.55)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	10 (14.08)	10 (15.62)	20 (18.18)
	No	46 (64.79)	44 (68.75)	90 (81.82)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	11 (15.49)	9 (14.06)	20 (18.18)
	No	45 (63.38)	45 (70.31)	90 (81.82)

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	13 (18.31)	9 (14.06)	22 (20.00)
	No	43 (60.56)	45 (70.31)	88 (80.00)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 24	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	8 (11.27)	8 (12.50)	16 (14.55)
	No	48 (67.61)	46 (71.88)	94 (85.45)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 48	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	6 (8.45)	9 (14.06)	15 (13.64)
	No	50 (70.42)	45 (70.31)	95 (86.36)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	10 (14.08)	9 (14.06)	19 (17.27)
	No	46 (64.79)	45 (70.31)	91 (82.73)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 96	Missing	15 (21.13)	10 (15.62)	25 (18.52)
	Yes	9 (12.68)	5 (7.81)	14 (12.73)
	No	47 (66.20)	49 (76.56)	96 (87.27)
	Missing	15 (21.13)	10 (15.62)	25 (18.52)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigue_responsRate

Response Rate of PedsQL Multidimensional Fatigue Scale

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
COGNITIVE FATIGUE-Baseline	Yes	56 (78.87)	54 (84.38)	110 (81.48)
	No	15 (21.13)	10 (15.62)	25 (18.52)
COGNITIVE FATIGUE-Week 24	Yes	65 (91.55)	62 (96.88)	127 (94.07)
	No	6 (8.45)	2 (3.12)	8 (5.93)
COGNITIVE FATIGUE-Week 48	Yes	61 (85.92)	52 (81.25)	113 (83.70)
	No	10 (14.08)	12 (18.75)	22 (16.30)
COGNITIVE FATIGUE-Week 72	Yes	59 (83.10)	41 (64.06)	100 (74.07)
	No	12 (16.90)	23 (35.94)	35 (25.93)
COGNITIVE FATIGUE-Week 96	Yes	54 (76.06)	38 (59.38)	92 (68.15)
	No	17 (23.94)	26 (40.62)	43 (31.85)
GENERAL FATIGUE-Baseline	Yes	56 (78.87)	54 (84.38)	110 (81.48)
	No	15 (21.13)	10 (15.62)	25 (18.52)
GENERAL FATIGUE-Week 24	Yes	65 (91.55)	62 (96.88)	127 (94.07)
	No	6 (8.45)	2 (3.12)	8 (5.93)
GENERAL FATIGUE-Week 48	Yes	61 (85.92)	52 (81.25)	113 (83.70)
	No	10 (14.08)	12 (18.75)	22 (16.30)
GENERAL FATIGUE-Week 72	Yes	59 (83.10)	41 (64.06)	100 (74.07)
	No	12 (16.90)	23 (35.94)	35 (25.93)
GENERAL FATIGUE-Week 96	Yes	54 (76.06)	38 (59.38)	92 (68.15)
	No	17 (23.94)	26 (40.62)	43 (31.85)
SLEEP/REST FATIGUE-Baseline	Yes	56 (78.87)	54 (84.38)	110 (81.48)
	No	15 (21.13)	10 (15.62)	25 (18.52)
SLEEP/REST FATIGUE-Week 24	Yes	65 (91.55)	62 (96.88)	127 (94.07)
	No	6 (8.45)	2 (3.12)	8 (5.93)
SLEEP/REST FATIGUE-Week 48	Yes	61 (85.92)	52 (81.25)	113 (83.70)
	No	10 (14.08)	12 (18.75)	22 (16.30)

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SLEEP/REST FATIGUE-Week 72	Yes	59 (83.10)	41 (64.06)	100 (74.07)
	No	12 (16.90)	23 (35.94)	35 (25.93)
SLEEP/REST FATIGUE-Week 96	Yes	54 (76.06)	38 (59.38)	92 (68.15)
	No	17 (23.94)	26 (40.62)	43 (31.85)

NOTE1: Scale of the measure is 0 to 100.Response rates are yes when patients report non-missing data for the given timepoint

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline;

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline
General Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 24			
n (%)	53 (75)	52 (81)	105 (78)
Mean (SD)	0.7 (17.82)	-1.7 (13.44)	-0.5 (15.77)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-8.3, 4.2	-8.3, 4.2
Min, Max	-29, 75	-29, 29	-29, 75
Week 48			
n (%)	49 (69)	43 (67)	92 (68)
Mean (SD)	2.0 (18.06)	-3.5 (18.14)	-0.5 (18.21)
Median	4.2	0.0	0.0
Q1,Q3	-12.5, 8.3	-12.5, 8.3	-12.5, 8.3
Min, Max	-29, 63	-58, 29	-58, 63

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 72			
n (%)	48 (68)	35 (55)	83 (61)
Mean (SD)	-1.0 (15.74)	-2.6 (17.74)	-1.7 (16.53)
Median	-4.2	0.0	0.0
Q1,Q3	-12.5, 6.3	-16.7, 8.3	-12.5, 8.3
Min, Max	-33, 46	-29, 50	-33, 50
Week 96			
n (%)	42 (59)	34 (53)	76 (56)
Mean (SD)	-5.1 (21.38)	-3.9 (20.18)	-4.6 (20.72)
Median	-2.1	-4.2	-4.2
Q1,Q3	-16.7, 8.3	-20.8, 16.7	-18.8, 8.3
Min, Max	-71, 42	-46, 38	-71, 42

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline;

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline
Sleep/Rest Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 24			
n (%)	53 (75)	52 (81)	105 (78)
Mean (SD)	1.2 (19.10)	-1.2 (15.06)	0.0 (17.18)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-8.3, 8.3	-8.3, 8.3
Min, Max	-46, 79	-42, 25	-46, 79
Week 48			
n (%)	49 (69)	43 (67)	92 (68)
Mean (SD)	1.1 (15.10)	-0.4 (18.54)	0.4 (16.72)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-12.5, 12.5	-8.3, 8.3
Min, Max	-29, 42	-46, 50	-46, 50

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	48 (68)	35 (55)	83 (61)
Mean (SD)	0.4 (18.44)	-0.9 (19.11)	-0.1 (18.62)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 12.5	-16.7, 12.5	-12.5, 12.5
Min, Max	-46, 58	-46, 42	-46, 58
Week 96			
n (%)	42 (59)	34 (53)	76 (56)
Mean (SD)	-3.5 (18.15)	-1.0 (17.89)	-2.4 (17.95)
Median	-2.1	-2.1	-2.1
Q1,Q3	-12.5, 8.3	-12.5, 12.5	-12.5, 8.3
Min, Max	-58, 33	-54, 38	-58, 38

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline;

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline
Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 24			
n (%)	53 (75)	52 (81)	105 (78)
Mean (SD)	5.0 (18.35)	-1.9 (16.57)	1.6 (17.76)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 12.5	-8.3, 4.2	-8.3, 8.3
Min, Max	-21, 100	-50, 38	-50, 100
Week 48			
n (%)	49 (69)	43 (67)	92 (68)
Mean (SD)	2.6 (15.84)	-3.2 (21.03)	-0.1 (18.57)
Median	0.0	-4.2	-4.2
Q1,Q3	-8.3, 12.5	-16.7, 8.3	-8.3, 12.5
Min, Max	-29, 58	-58, 63	-58, 63

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	48 (68)	35 (55)	83 (61)
Mean (SD)	3.0 (20.84)	-4.2 (17.18)	0.0 (19.60)
Median	-2.1	0.0	0.0
Q1,Q3	-8.3, 12.5	-12.5, 4.2	-12.5, 12.5
Min, Max	-25, 100	-46, 33	-46, 100
Week 96			
n (%)	42 (59)	34 (53)	76 (56)
Mean (SD)	0.1 (18.55)	-7.1 (21.13)	-3.1 (19.94)
Median	-2.1	-4.2	-4.2
Q1,Q3	-16.7, 16.7	-20.8, 4.2	-16.7, 8.3
Min, Max	-29, 50	-54, 46	-54, 50

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

109MS306_table41_43_CHG_DESCRIBE

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)
General Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	56 (79)	54 (84)	110 (81)
Mean (SD)	70.4 (24.78)	74.9 (20.96)	72.6 (22.99)
Median	75.0	79.2	79.2
Q1,Q3	58.3, 91.7	62.5, 91.7	58.3, 91.7
Min, Max	0, 100	8, 100	0, 100
Week 24			
n (%)	65 (92)	62 (97)	127 (94)
Mean (SD)	68.5 (21.84)	71.4 (21.89)	69.9 (21.82)
Median	70.8	75.0	75.0
Q1,Q3	54.2, 83.3	58.3, 87.5	58.3, 87.5
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	61 (86)	52 (81)	113 (84)
Mean (SD)	69.9 (20.29)	73.1 (21.60)	71.4 (20.87)
Median	70.8	77.1	70.8
Q1,Q3	54.2, 83.3	60.4, 91.7	58.3, 91.7
Min, Max	25, 100	13, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	41 (64)	100 (74)
Mean (SD)	67.9 (22.33)	74.3 (22.22)	70.5 (22.40)
Median	70.8	79.2	70.8
Q1,Q3	54.2, 87.5	62.5, 91.7	54.2, 89.6
Min, Max	17, 100	17, 100	17, 100
Week 96			
n (%)	54 (76)	38 (59)	92 (68)
Mean (SD)	67.7 (24.04)	73.5 (20.61)	70.1 (22.74)
Median	64.6	70.8	68.8
Q1,Q3	54.2, 91.7	58.3, 95.8	54.2, 91.7
Min, Max	0, 100	21, 100	0, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)
Sleep/Rest Fatigue

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	56 (79)	54 (84)	110 (81)
Mean (SD)	66.4 (20.65)	65.4 (23.54)	65.9 (22.02)
Median	68.8	66.7	66.7
Q1,Q3	54.2, 83.3	45.8, 83.3	50.0, 83.3
Min, Max	13, 100	21, 100	13, 100
Week 24			
n (%)	65 (92)	62 (97)	127 (94)
Mean (SD)	65.2 (20.20)	63.9 (22.34)	64.6 (21.20)
Median	62.5	66.7	62.5
Q1,Q3	50.0, 79.2	50.0, 79.2	50.0, 79.2
Min, Max	21, 100	8, 100	8, 100
Week 48			
n (%)	61 (86)	52 (81)	113 (84)
Mean (SD)	66.4 (21.17)	69.5 (21.45)	67.8 (21.26)
Median	66.7	68.8	66.7
Q1,Q3	54.2, 79.2	58.3, 91.7	54.2, 87.5
Min, Max	13, 100	21, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	41 (64)	100 (74)
Mean (SD)	65.4 (22.61)	69.9 (21.87)	67.2 (22.31)
Median	66.7	66.7	66.7
Q1,Q3	50.0, 83.3	58.3, 87.5	54.2, 85.4
Min, Max	13, 100	8, 100	8, 100
Week 96			
n (%)	54 (76)	38 (59)	92 (68)
Mean (SD)	65.0 (22.20)	68.6 (21.20)	66.5 (21.75)
Median	64.6	68.8	66.7
Q1,Q3	50.0, 83.3	54.2, 87.5	50.0, 87.5
Min, Max	21, 100	8, 100	8, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)
Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Baseline			
n (%)	56 (79)	54 (84)	110 (81)
Mean (SD)	67.8 (25.03)	75.8 (20.96)	71.7 (23.37)
Median	72.9	79.2	75.0
Q1,Q3	50.0, 87.5	58.3, 95.8	54.2, 91.7
Min, Max	0, 100	17, 100	0, 100
Week 24			
n (%)	65 (92)	62 (97)	127 (94)
Mean (SD)	71.7 (22.50)	72.4 (24.37)	72.1 (23.34)
Median	75.0	75.0	75.0
Q1,Q3	58.3, 91.7	58.3, 91.7	58.3, 91.7
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	61 (86)	52 (81)	113 (84)
Mean (SD)	68.2 (23.29)	73.3 (22.11)	70.6 (22.80)
Median	70.8	75.0	75.0
Q1,Q3	50.0, 83.3	58.3, 95.8	54.2, 91.7
Min, Max	0, 100	21, 100	0, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	41 (64)	100 (74)
Mean (SD)	66.9 (25.25)	72.6 (21.08)	69.3 (23.68)
Median	70.8	70.8	70.8
Q1,Q3	45.8, 87.5	54.2, 91.7	50.0, 91.7
Min, Max	0, 100	29, 100	0, 100
Week 96			
n (%)	54 (76)	38 (59)	92 (68)
Mean (SD)	67.1 (24.22)	72.1 (24.16)	69.2 (24.19)
Median	66.7	70.8	68.8
Q1,Q3	45.8, 87.5	62.5, 100.0	50.0, 89.6
Min, Max	17, 100	13, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-subj.sas Run Date: 25MAR2021

109MS306_table41_43_CHG_HEDGESCI

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Subject's Assessment - mITT Population, Aged 13 years and older (n=135)

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24 Weeks	0.398	0.011	0.784
	48 Weeks	0.316	-0.096	0.728
	72 Weeks	0.372	-0.068	0.811
	96 Weeks	0.365	-0.091	0.821
GENERAL FATIGUE	24 Weeks	0.151	-0.232	0.534
	48 Weeks	0.306	-0.106	0.717
	72 Weeks	0.1	-0.336	0.536
	96 Weeks	-0.055	-0.507	0.398
SLEEP/REST FATIGU	24 Weeks	0.138	-0.245	0.521
	48 Weeks	0.086	-0.324	0.496
	72 Weeks	0.071	-0.364	0.507
	96 Weeks	-0.138	-0.591	0.315

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.

Source: W:\Biogen\109MS306\TFLs\MainQCd\T41_43/109MS306_table41_43_CHG_HEDGESCI.sa

109MS306_table41_43_CHG_LSMEANS

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135);

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Subject's Assessment - ITT Population, Aged 13 years and older (n=135)

General Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	53 (75)	52 (81)
Lsmean (SE)	00.75 (2.228)	-0.06 (2.208)
Lsmean_95 % CI	(-3.668, 05.170)	(-4.439, 04.319)
Diffrence (95% CI)	0.81 (-4.743, 6.365)	
SE_Difference	2.7999	
p-value	0.7727	
Week 48		
n (%)	49 (69)	43 (67)
Lsmean (SE)	01.14 (2.715)	-1.65 (2.764)
Lsmean_95 % CI	(-4.259, 06.532)	(-7.141, 03.844)
Diffrence (95% CI)	2.78 (-4.018, 9.588)	
SE_Difference	3.4232	

	DMF (N= 71)	**IFN B-1a (N= 64)**
p-value	0.4181	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	48 (68)	35 (55)
Lsmean (SE)	00.67 (2.287)	01.95 (2.618)
Lsmean_95 % CI	(-3.884, 05.222)	(-3.261, 07.160)
Diffrence (95% CI)	-1.28 (-7.545, 4.984)	
SE_Difference	3.1472	
p-value	0.6851	
Week 96		
n (%)	42 (59)	34 (53)
Lsmean (SE)	-5.06 (3.220)	-1.54 (3.634)
Lsmean_95 % CI	(-11.48, 01.355)	(-8.778, 05.708)
Diffrence (95% CI)	-3.53 (-12.301, 5.244)	
SE_Difference	4.4006	
p-value	0.4253	

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135);

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Subject's Assessment - ITT Population, Aged 13 years and older (n=135)

Sleep/Rest Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	53 (75)	52 (81)
Lsmean (SE)	03.49 (2.395)	00.91 (2.341)
Lsmean_95 % CI	(-1.257, 08.245)	(-3.737, 05.551)
Diffrence (95% CI)	2.59 (-3.297, 8.471)	
SE_Difference	2.9659	
p-value	0.3851	
Week 48		
n (%)	49 (69)	43 (67)
Lsmean (SE)	00.32 (2.663)	00.07 (2.691)
Lsmean_95 % CI	(-4.977, 05.607)	(-5.277, 05.417)
Diffrence (95% CI)	0.25 (-6.352, 6.843)	
SE_Difference	3.3198	
p-value	0.9413	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	48 (68)	35 (55)
Lsmean (SE)	01.74 (2.848)	01.93 (3.239)
Lsmean_95 % CI	(-3.930, 07.406)	(-4.517, 08.377)
Diffrence (95% CI)	-0.19 (-7.909, 7.526)	
SE_Difference	3.8773	
p-value	0.9606	
Week 96		
n (%)	42 (59)	34 (53)
Lsmean (SE)	-3.03 (2.852)	00.08 (3.191)
Lsmean_95 % CI	(-8.718, 02.655)	(-6.282, 06.439)
Diffrence (95% CI)	-3.11 (-10.805, 4.584)	
SE_Difference	3.8600	
p-value	0.4230	

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135);

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Subject's Assessment - ITT Population, Aged 13 years and older (n=135)

Cognitive Fatigue

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	53 (75)	52 (81)
Lsmean (SE)	05.93 (2.554)	00.95 (2.540)
Lsmean_95 % CI	(00.867, 10.998)	(-4.087, 05.991)
Diffrence (95% CI)	4.98 (-1.434, 11.394)	
SE_Difference	3.2335	
p-value	0.1267	
Week 48		
n (%)	49 (69)	43 (67)
Lsmean (SE)	02.74 (2.826)	00.10 (2.887)
Lsmean_95 % CI	(-2.880, 08.354)	(-5.634, 05.841)
Diffrence (95% CI)	2.63 (-4.516, 9.782)	
SE_Difference	3.5973	
p-value	0.4661	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	48 (68)	35 (55)
Lsmean (SE)	03.50 (2.814)	00.96 (3.248)
Lsmean_95 % CI	(-2.097, 09.105)	(-5.505, 07.425)
Diffrence (95% CI)	2.54 (-5.282, 10.370)	
SE_Difference	3.9319	
p-value	0.5195	
Week 96		
n (%)	42 (59)	34 (53)
Lsmean (SE)	00.27 (3.129)	-2.64 (3.588)
Lsmean_95 % CI	(-5.967, 06.507)	(-9.790, 04.515)
Diffrence (95% CI)	2.91 (-5.822, 11.637)	
SE_Difference	4.3789	
p-value	0.5088	

Sub groups

Change

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_age13to14

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 13 TO 14. General Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	10 (56)	12 (86)	22 (69)
Mean (SD)	-5.4 (15.35)	2.4 (8.23)	-1.1 (12.35)
Median	-2.1	0.0	0.0
Q1,Q3	-16.7, 0.0	0.0, 6.3	-4.2, 0.0
Min, Max	-29, 25	-8, 21	-29, 25
Week 48			
n (%)	8 (44)	10 (71)	18 (56)
Mean (SD)	0.0 (6.68)	-6.3 (21.18)	-3.5 (16.31)
Median	4.2	-4.2	0.0
Q1,Q3	-4.2, 4.2	-12.5, 8.3	-8.3, 4.2
Min, Max	-13, 4	-58, 21	-58, 21

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	2.5 (11.15)	3.1 (8.55)	2.8 (9.80)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 0.0	0.0, 6.3	-4.2, 4.2
Min, Max	-8, 25	-8, 21	-8, 25
Week 96			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	-4.2 (28.12)	-6.0 (12.92)	-4.9 (22.55)
Median	2.1	-4.2	-4.2
Q1,Q3	-16.7, 8.3	-12.5, 0.0	-12.5, 4.2
Min, Max	-71, 33	-25, 17	-71, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	10 (56)	12 (86)	22 (69)
Mean (SD)	-1.7 (20.62)	3.5 (9.03)	1.1 (15.22)
Median	-4.2	6.3	0.0
Q1,Q3	-16.7, 8.3	0.0, 10.4	-4.2, 8.3
Min, Max	-29, 46	-17, 13	-29, 46
Week 48			
n (%)	8 (44)	10 (71)	18 (56)
Mean (SD)	-2.1 (9.96)	-4.2 (12.11)	-3.2 (10.94)
Median	0.0	2.1	0.0
Q1,Q3	-8.3, 6.3	-16.7, 4.2	-8.3, 4.2
Min, Max	-21, 8	-25, 8	-25, 8

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	-0.4 (9.10)	4.2 (12.20)	1.6 (10.52)
Median	0.0	6.3	2.1
Q1,Q3	-8.3, 4.2	-4.2, 12.5	-8.3, 12.5
Min, Max	-13, 13	-17, 21	-17, 21
Week 96			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	-5.0 (14.14)	-1.2 (9.83)	-3.4 (12.35)
Median	-2.1	0.0	0.0
Q1,Q3	-4.2, 4.2	-8.3, 8.3	-4.2, 4.2
Min, Max	-38, 8	-17, 13	-38, 13

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	10 (56)	12 (86)	22 (69)
Mean (SD)	4.2 (14.03)	4.2 (14.65)	4.2 (14.03)
Median	4.2	0.0	0.0
Q1,Q3	-4.2, 8.3	0.0, 6.3	0.0, 8.3
Min, Max	-21, 33	-25, 38	-25, 38
Week 48			
n (%)	8 (44)	10 (71)	18 (56)
Mean (SD)	2.6 (18.89)	-0.4 (16.83)	0.9 (17.30)
Median	2.1	0.0	0.0
Q1,Q3	-8.3, 14.6	-8.3, 4.2	-8.3, 12.5
Min, Max	-29, 33	-25, 33	-29, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	8 (57)	18 (56)
Mean (SD)	6.3 (15.37)	0.0 (13.91)	3.5 (14.66)
Median	8.3	0.0	2.1
Q1,Q3	-4.2, 12.5	-6.3, 10.4	-4.2, 12.5
Min, Max	-13, 38	-25, 17	-25, 38
Week 96			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	3.8 (18.47)	-4.8 (14.12)	0.2 (16.89)
Median	6.3	0.0	0.0
Q1,Q3	-12.5, 20.8	-20.8, 0.0	-12.5, 16.7
Min, Max	-21, 25	-25, 17	-25, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_age15to17

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 15 TO 17. General Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	43 (81)	40 (80)	83 (81)
Mean (SD)	2.1 (18.22)	-2.9 (14.50)	-0.3 (16.63)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 8.3	-12.5, 4.2	-12.5, 8.3
Min, Max	-25, 75	-29, 29	-29, 75
Week 48			
n (%)	41 (77)	33 (66)	74 (72)
Mean (SD)	2.4 (19.57)	-2.7 (17.39)	0.2 (18.68)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 12.5	-16.7, 8.3	-16.7, 12.5
Min, Max	-29, 63	-33, 29	-33, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	38 (72)	27 (54)	65 (63)
Mean (SD)	-1.9 (16.74)	-4.3 (19.46)	-2.9 (17.81)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 8.3	-25.0, 8.3	-16.7, 8.3
Min, Max	-33, 46	-29, 50	-33, 50
Week 96			
n (%)	32 (60)	27 (54)	59 (57)
Mean (SD)	-5.3 (19.35)	-3.4 (21.84)	-4.4 (20.37)
Median	-6.3	0.0	-4.2
Q1,Q3	-20.8, 6.3	-20.8, 16.7	-20.8, 8.3
Min, Max	-38, 42	-46, 38	-46, 42

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	43 (81)	40 (80)	83 (81)
Mean (SD)	1.8 (18.93)	-2.6 (16.28)	-0.3 (17.73)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-10.4, 8.3	-8.3, 8.3
Min, Max	-46, 79	-42, 25	-46, 79
Week 48			
n (%)	41 (77)	33 (66)	74 (72)
Mean (SD)	1.7 (15.93)	0.8 (20.10)	1.3 (17.79)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-8.3, 12.5	-8.3, 12.5
Min, Max	-29, 42	-46, 50	-46, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	38 (72)	27 (54)	65 (63)
Mean (SD)	0.7 (20.29)	-2.4 (20.67)	-0.6 (20.34)
Median	0.0	-4.2	0.0
Q1,Q3	-16.7, 12.5	-16.7, 16.7	-16.7, 12.5
Min, Max	-46, 58	-46, 42	-46, 58
Week 96			
n (%)	32 (60)	27 (54)	59 (57)
Mean (SD)	-3.0 (19.41)	-0.9 (19.59)	-2.0 (19.35)
Median	-2.1	-4.2	-4.2
Q1,Q3	-12.5, 10.4	-12.5, 12.5	-12.5, 12.5
Min, Max	-58, 33	-54, 38	-58, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	43 (81)	40 (80)	83 (81)
Mean (SD)	5.2 (19.35)	-3.8 (16.85)	0.9 (18.63)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 12.5	-12.5, 4.2	-8.3, 8.3
Min, Max	-17, 100	-50, 33	-50, 100
Week 48			
n (%)	41 (77)	33 (66)	74 (72)
Mean (SD)	2.6 (15.44)	-4.0 (22.30)	-0.3 (18.97)
Median	0.0	-4.2	-4.2
Q1,Q3	-8.3, 12.5	-16.7, 8.3	-12.5, 12.5
Min, Max	-21, 58	-58, 63	-58, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	38 (72)	27 (54)	65 (63)
Mean (SD)	2.2 (22.15)	-5.4 (18.08)	-1.0 (20.75)
Median	-4.2	-4.2	-4.2
Q1,Q3	-8.3, 12.5	-12.5, 4.2	-12.5, 12.5
Min, Max	-25, 100	-46, 33	-46, 100
Week 96			
n (%)	32 (60)	27 (54)	59 (57)
Mean (SD)	-1.0 (18.72)	-7.7 (22.78)	-4.1 (20.77)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 6.3	-25.0, 4.2	-16.7, 4.2
Min, Max	-29, 50	-54, 46	-54, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_female

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for FEMALE SEX. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	38 (76)	37 (80)	75 (78)
Mean (SD)	0.5 (19.45)	-1.8 (12.79)	-0.6 (16.44)
Median	0.0	-4.2	0.0
Q1,Q3	-12.5, 4.2	-8.3, 4.2	-12.5, 4.2
Min, Max	-25, 75	-29, 25	-29, 75
Week 48			
n (%)	35 (70)	31 (67)	66 (69)
Mean (SD)	-0.5 (15.58)	-4.0 (20.05)	-2.1 (17.77)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 8.3	-12.5, 12.5	-12.5, 8.3
Min, Max	-29, 42	-58, 29	-58, 42

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	33 (66)	26 (57)	59 (61)
Mean (SD)	-2.8 (14.57)	-2.1 (19.23)	-2.5 (16.63)
Median	-4.2	0.0	-4.2
Q1,Q3	-12.5, 4.2	-16.7, 8.3	-16.7, 8.3
Min, Max	-25, 46	-29, 50	-29, 50
Week 96			
n (%)	29 (58)	25 (54)	54 (56)
Mean (SD)	-8.9 (22.35)	-3.0 (20.47)	-6.2 (21.50)
Median	-12.5	-4.2	-6.3
Q1,Q3	-20.8, 4.2	-20.8, 16.7	-20.8, 4.2
Min, Max	-71, 42	-38, 38	-71, 42

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	38 (76)	37 (80)	75 (78)
Mean (SD)	0.3 (21.10)	0.6 (14.17)	0.4 (17.90)
Median	-2.1	4.2	0.0
Q1,Q3	-8.3, 8.3	0.0, 8.3	-8.3, 8.3
Min, Max	-46, 79	-42, 21	-46, 79
Week 48			
n (%)	35 (70)	31 (67)	66 (69)
Mean (SD)	1.1 (13.17)	0.4 (20.79)	0.8 (17.04)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-8.3, 12.5	-8.3, 8.3
Min, Max	-29, 38	-46, 50	-46, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	33 (66)	26 (57)	59 (61)
Mean (SD)	-0.6 (18.28)	-0.2 (20.77)	-0.4 (19.25)
Median	-4.2	0.0	0.0
Q1,Q3	-12.5, 12.5	-16.7, 16.7	-16.7, 12.5
Min, Max	-25, 58	-46, 42	-46, 58
Week 96			
n (%)	29 (58)	25 (54)	54 (56)
Mean (SD)	-4.6 (17.34)	-1.5 (19.09)	-3.2 (18.06)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 8.3	-12.5, 12.5	-12.5, 12.5
Min, Max	-42, 25	-54, 38	-54, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	38 (76)	37 (80)	75 (78)
Mean (SD)	4.8 (20.38)	-3.2 (15.32)	0.9 (18.38)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 12.5	-12.5, 4.2	-8.3, 8.3
Min, Max	-21, 100	-38, 38	-38, 100
Week 48			
n (%)	35 (70)	31 (67)	66 (69)
Mean (SD)	2.3 (15.99)	-3.6 (21.29)	-0.5 (18.76)
Median	0.0	-4.2	-4.2
Q1,Q3	-8.3, 12.5	-16.7, 4.2	-12.5, 8.3
Min, Max	-29, 58	-58, 63	-58, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	33 (66)	26 (57)	59 (61)
Mean (SD)	3.4 (21.91)	-7.7 (15.93)	-1.5 (20.13)
Median	0.0	-4.2	-4.2
Q1,Q3	-8.3, 12.5	-16.7, 4.2	-12.5, 4.2
Min, Max	-21, 100	-46, 17	-46, 100
Week 96			
n (%)	29 (58)	25 (54)	54 (56)
Mean (SD)	-0.6 (18.82)	-9.8 (19.98)	-4.9 (19.74)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 8.3	-25.0, 0.0	-16.7, 4.2
Min, Max	-29, 50	-42, 46	-42, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_male

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for MALE SEX. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	15 (83)	30 (77)
Mean (SD)	1.1 (13.41)	-1.4 (15.40)	-0.1 (14.25)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 8.3	-8.3, 8.3	-4.2, 8.3
Min, Max	-29, 33	-29, 29	-29, 33
Week 48			
n (%)	14 (67)	12 (67)	26 (67)
Mean (SD)	8.3 (22.59)	-2.1 (12.50)	3.5 (19.03)
Median	4.2	0.0	0.0
Q1,Q3	-8.3, 20.8	-14.6, 4.2	-8.3, 8.3
Min, Max	-25, 63	-17, 25	-25, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	9 (50)	24 (62)
Mean (SD)	3.1 (17.92)	-4.2 (13.34)	0.3 (16.43)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 16.7	-8.3, 4.2	-8.3, 12.5
Min, Max	-33, 33	-29, 17	-33, 33
Week 96			
n (%)	13 (62)	9 (50)	22 (56)
Mean (SD)	3.5 (16.74)	-6.5 (20.32)	-0.6 (18.51)
Median	8.3	-4.2	0.0
Q1,Q3	-4.2, 20.8	-12.5, 0.0	-8.3, 16.7
Min, Max	-29, 21	-46, 21	-46, 21

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	15 (83)	30 (77)
Mean (SD)	3.3 (13.10)	-5.6 (16.79)	-1.1 (15.47)
Median	8.3	-4.2	0.0
Q1,Q3	-4.2, 8.3	-16.7, 8.3	-12.5, 8.3
Min, Max	-21, 29	-38, 25	-38, 29
Week 48			
n (%)	14 (67)	12 (67)	26 (67)
Mean (SD)	0.9 (19.69)	-2.4 (11.30)	-0.6 (16.15)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 12.5	-12.5, 6.3	-12.5, 8.3
Min, Max	-25, 42	-21, 17	-25, 42

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	9 (50)	24 (62)
Mean (SD)	2.8 (19.20)	-3.1 (14.06)	0.6 (17.36)
Median	4.2	-4.2	2.1
Q1,Q3	-8.3, 12.5	-12.5, 5.8	-10.4, 12.5
Min, Max	-46, 33	-21, 21	-46, 33
Week 96			
n (%)	13 (62)	9 (50)	22 (56)
Mean (SD)	-1.0 (20.35)	0.5 (14.94)	-0.4 (17.95)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 8.3	-4.2, 8.3	-4.2, 8.3
Min, Max	-58, 33	-25, 29	-58, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for MALE SEX. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	15 (83)	30 (77)
Mean (SD)	5.6 (12.37)	1.1 (19.57)	3.3 (16.24)
Median	4.2	0.0	2.1
Q1,Q3	0.0, 12.5	-8.3, 12.5	-4.2, 12.5
Min, Max	-17, 29	-50, 33	-50, 33
Week 48			
n (%)	14 (67)	12 (67)	26 (67)
Mean (SD)	3.6 (16.00)	-2.1 (21.21)	1.0 (18.42)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 16.7	-14.6, 14.6	-8.3, 16.7
Min, Max	-17, 33	-42, 33	-42, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	9 (50)	24 (62)
Mean (SD)	2.2 (18.96)	6.0 (17.44)	3.6 (18.11)
Median	-4.2	0.0	0.0
Q1,Q3	-12.5, 12.5	-12.5, 16.7	-12.5, 16.7
Min, Max	-25, 38	-13, 33	-25, 38
Week 96			
n (%)	13 (62)	9 (50)	22 (56)
Mean (SD)	1.6 (18.60)	0.5 (23.61)	1.1 (20.26)
Median	0.0	4.2	0.0
Q1,Q3	-8.3, 16.7	0.0, 12.5	-8.3, 16.7
Min, Max	-29, 29	-54, 29	-54, 29

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE_age13to14

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. General Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	11 (61)	13 (93)	24 (75)
Mean (SD)	82.6 (12.33)	80.8 (15.82)	81.6 (14.06)
Median	79.2	83.3	81.3
Q1,Q3	70.8, 95.8	70.8, 91.7	70.8, 95.8
Min, Max	67, 100	50, 100	50, 100
Week 24			
n (%)	15 (83)	13 (93)	28 (88)
Mean (SD)	70.6 (21.27)	76.0 (27.49)	73.1 (24.04)
Median	70.8	79.2	75.0
Q1,Q3	58.3, 91.7	70.8, 95.8	66.7, 95.8
Min, Max	29, 100	0, 100	0, 100
Week 48			
n (%)	12 (67)	10 (71)	22 (69)
Mean (SD)	79.5 (15.43)	75.8 (28.79)	77.8 (21.99)

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Median	75.0	89.6	77.1
Q1,Q3	70.8, 95.8	58.3, 100.0	70.8, 100.0
Min, Max	50, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	14 (78)	8 (57)	22 (69)
Mean (SD)	80.4 (19.16)	85.4 (16.96)	82.2 (18.15)
Median	83.3	91.7	89.6
Q1,Q3	70.8, 91.7	77.1, 97.9	70.8, 95.8
Min, Max	29, 100	50, 100	29, 100
Week 96			
n (%)	16 (89)	7 (50)	23 (72)
Mean (SD)	76.0 (27.49)	76.2 (19.80)	76.1 (24.94)
Median	83.3	75.0	79.2
Q1,Q3	60.4, 100.0	58.3, 95.8	58.3, 100.0
Min, Max	0, 100	46, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	11 (61)	13 (93)	24 (75)
Mean (SD)	80.7 (17.80)	76.0 (16.94)	78.1 (17.12)
Median	87.5	70.8	81.3
Q1,Q3	70.8, 95.8	62.5, 91.7	66.7, 93.8
Min, Max	46, 100	46, 96	46, 100
Week 24			
n (%)	15 (83)	13 (93)	28 (88)
Mean (SD)	67.8 (22.07)	73.4 (24.68)	70.4 (23.06)
Median	75.0	79.2	77.1
Q1,Q3	45.8, 83.3	66.7, 87.5	54.2, 85.4
Min, Max	29, 100	8, 100	8, 100
Week 48			
n (%)	12 (67)	10 (71)	22 (69)
Mean (SD)	71.9 (20.58)	72.9 (20.99)	72.3 (20.27)
Median	70.8	68.8	70.8

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Q1,Q3	54.2, 91.7	58.3, 100.0	54.2, 95.8
Min, Max	42, 100	46, 100	42, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	14 (78)	8 (57)	22 (69)
Mean (SD)	72.3 (23.77)	79.7 (17.03)	75.0 (21.44)
Median	70.8	83.3	77.1
Q1,Q3	62.5, 91.7	64.6, 93.8	62.5, 91.7
Min, Max	21, 100	54, 100	21, 100
Week 96			
n (%)	16 (89)	7 (50)	23 (72)
Mean (SD)	72.9 (23.07)	71.4 (18.85)	72.5 (21.46)
Median	77.1	62.5	75.0
Q1,Q3	52.1, 95.8	54.2, 87.5	54.2, 95.8
Min, Max	25, 100	50, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	11 (61)	13 (93)	24 (75)
Mean (SD)	73.9 (24.01)	85.6 (16.81)	80.2 (20.82)
Median	83.3	91.7	85.4
Q1,Q3	62.5, 87.5	75.0, 100.0	68.8, 100.0
Min, Max	17, 100	54, 100	17, 100
Week 24			
n (%)	15 (83)	13 (93)	28 (88)
Mean (SD)	71.1 (22.02)	82.4 (29.52)	76.3 (25.91)
Median	70.8	95.8	81.3
Q1,Q3	54.2, 95.8	79.2, 100.0	62.5, 100.0
Min, Max	29, 100	0, 100	0, 100
Week 48			
n (%)	12 (67)	10 (71)	22 (69)
Mean (SD)	74.3 (17.84)	84.2 (17.55)	78.8 (18.00)
Median	75.0	89.6	81.3

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Q1,Q3	58.3, 87.5	75.0, 100.0	62.5, 95.8
Min, Max	50, 100	46, 100	46, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	14 (78)	8 (57)	22 (69)
Mean (SD)	72.0 (24.37)	84.4 (18.20)	76.5 (22.70)
Median	77.1	89.6	79.2
Q1,Q3	54.2, 95.8	72.9, 100.0	70.8, 95.8
Min, Max	17, 100	50, 100	17, 100
Week 96			
n (%)	16 (89)	7 (50)	23 (72)
Mean (SD)	72.4 (24.29)	83.9 (18.70)	75.9 (22.96)
Median	79.2	87.5	79.2
Q1,Q3	50.0, 93.8	75.0, 100.0	54.2, 100.0
Min, Max	29, 100	50, 100	29, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE_age15to17

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. General Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	45 (85)	41 (82)	86 (83)
Mean (SD)	67.4 (26.21)	73.1 (22.19)	70.1 (24.40)
Median	75.0	79.2	75.0
Q1,Q3	54.2, 91.7	58.3, 91.7	54.2, 91.7
Min, Max	0, 100	8, 100	0, 100
Week 24			
n (%)	50 (94)	49 (98)	99 (96)
Mean (SD)	67.9 (22.18)	70.2 (20.31)	69.0 (21.20)
Median	70.8	75.0	70.8
Q1,Q3	54.2, 83.3	58.3, 87.5	54.2, 87.5
Min, Max	13, 100	25, 100	13, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	67.6 (20.77)	72.4 (19.91)	69.8 (20.41)

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Median	66.7	75.0	70.8
Q1,Q3	50.0, 83.3	62.5, 87.5	54.2, 87.5
Min, Max	25, 100	17, 100	17, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	45 (85)	33 (66)	78 (76)
Mean (SD)	64.1 (22.02)	71.6 (22.71)	67.3 (22.48)
Median	62.5	70.8	68.8
Q1,Q3	45.8, 79.2	58.3, 87.5	54.2, 87.5
Min, Max	17, 100	17, 100	17, 100
Week 96			
n (%)	38 (72)	31 (62)	69 (67)
Mean (SD)	64.3 (21.89)	72.8 (21.05)	68.1 (21.79)
Median	60.4	70.8	66.7
Q1,Q3	50.0, 83.3	58.3, 95.8	54.2, 91.7
Min, Max	25, 100	21, 100	21, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	45 (85)	41 (82)	86 (83)
Mean (SD)	63.0 (19.95)	62.1 (24.51)	62.5 (22.11)
Median	62.5	62.5	62.5
Q1,Q3	50.0, 75.0	41.7, 79.2	45.8, 79.2
Min, Max	13, 96	21, 100	13, 100
Week 24			
n (%)	50 (94)	49 (98)	99 (96)
Mean (SD)	64.4 (19.78)	61.4 (21.24)	62.9 (20.47)
Median	62.5	62.5	62.5
Q1,Q3	54.2, 79.2	45.8, 75.0	50.0, 79.2
Min, Max	21, 100	21, 100	21, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	65.0 (21.30)	68.7 (21.72)	66.7 (21.46)
Median	66.7	68.8	66.7

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Q1,Q3	54.2, 79.2	58.3, 91.7	54.2, 87.5
Min, Max	13, 100	21, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	45 (85)	33 (66)	78 (76)
Mean (SD)	63.2 (22.07)	67.5 (22.45)	65.0 (22.19)
Median	62.5	66.7	66.7
Q1,Q3	50.0, 75.0	54.2, 87.5	50.0, 83.3
Min, Max	13, 100	8, 100	8, 100
Week 96			
n (%)	38 (72)	31 (62)	69 (67)
Mean (SD)	61.7 (21.26)	68.0 (21.93)	64.6 (21.63)
Median	62.5	70.8	66.7
Q1,Q3	45.8, 75.0	54.2, 87.5	45.8, 79.2
Min, Max	21, 100	8, 96	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	45 (85)	41 (82)	86 (83)
Mean (SD)	66.3 (25.31)	72.8 (21.37)	69.4 (23.60)
Median	70.8	75.0	75.0
Q1,Q3	50.0, 87.5	54.2, 91.7	54.2, 91.7
Min, Max	0, 100	17, 100	0, 100
Week 24			
n (%)	50 (94)	49 (98)	99 (96)
Mean (SD)	71.9 (22.87)	69.8 (22.43)	70.9 (22.56)
Median	75.0	70.8	75.0
Q1,Q3	58.3, 91.7	58.3, 91.7	58.3, 91.7
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	66.8 (24.36)	70.7 (22.48)	68.6 (23.47)
Median	66.7	72.9	70.8

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Q1,Q3	50.0, 83.3	58.3, 91.7	50.0, 87.5
Min, Max	0, 100	21, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	45 (85)	33 (66)	78 (76)
Mean (SD)	65.4 (25.57)	69.7 (20.97)	67.2 (23.69)
Median	70.8	70.8	70.8
Q1,Q3	45.8, 83.3	50.0, 91.7	50.0, 87.5
Min, Max	0, 100	29, 100	0, 100
Week 96			
n (%)	38 (72)	31 (62)	69 (67)
Mean (SD)	64.8 (24.15)	69.5 (24.71)	66.9 (24.34)
Median	66.7	66.7	66.7
Q1,Q3	45.8, 87.5	54.2, 91.7	50.0, 87.5
Min, Max	17, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE_female

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	69.6 (24.52)	72.6 (21.95)	71.0 (23.19)
Median	70.8	77.1	75.0
Q1,Q3	58.3, 91.7	58.3, 91.7	58.3, 91.7
Min, Max	0, 96	8, 100	0, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	67.3 (21.28)	68.3 (22.67)	67.8 (21.85)
Median	70.8	75.0	70.8
Q1,Q3	52.1, 81.3	54.2, 87.5	54.2, 83.3
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	67.2 (19.68)	70.7 (22.02)	68.9 (20.74)

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Median	70.8	75.0	70.8
Q1,Q3	50.0, 79.2	58.3, 87.5	54.2, 87.5
Min, Max	25, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	41 (82)	30 (65)	71 (74)
Mean (SD)	66.2 (22.62)	71.7 (23.66)	68.5 (23.06)
Median	66.7	77.1	70.8
Q1,Q3	50.0, 83.3	58.3, 91.7	54.2, 87.5
Min, Max	17, 100	17, 100	17, 100
Week 96			
n (%)	37 (74)	28 (61)	65 (68)
Mean (SD)	64.9 (25.03)	72.2 (20.13)	68.0 (23.17)
Median	62.5	70.8	66.7
Q1,Q3	50.0, 83.3	58.3, 93.8	54.2, 87.5
Min, Max	0, 100	21, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	64.9 (20.78)	63.8 (24.64)	64.3 (22.63)
Median	66.7	66.7	66.7
Q1,Q3	50.0, 79.2	45.8, 83.3	45.8, 79.2
Min, Max	13, 96	21, 100	13, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	63.1 (21.05)	63.1 (23.70)	63.1 (22.25)
Median	62.5	62.5	62.5
Q1,Q3	47.9, 79.2	50.0, 83.3	50.0, 79.2
Min, Max	21, 100	8, 100	8, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	64.4 (19.81)	68.3 (22.81)	66.2 (21.21)

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Median	61.3	68.8	66.7
Q1,Q3	52.1, 75.0	54.2, 91.7	54.2, 87.5
Min, Max	21, 100	21, 100	21, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	41 (82)	30 (65)	71 (74)
Mean (SD)	62.7 (21.83)	68.1 (23.68)	65.0 (22.62)
Median	62.5	66.7	66.7
Q1,Q3	50.0, 75.0	54.2, 87.5	50.0, 83.3
Min, Max	21, 100	8, 100	8, 100
Week 96			
n (%)	37 (74)	28 (61)	65 (68)
Mean (SD)	61.9 (22.36)	66.7 (22.48)	64.0 (22.36)
Median	58.3	68.8	62.5
Q1,Q3	45.8, 79.2	50.0, 87.5	50.0, 83.3
Min, Max	21, 100	8, 96	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	67.3 (24.68)	76.8 (22.48)	72.0 (23.94)
Median	70.8	83.3	75.0
Q1,Q3	50.0, 87.5	58.3, 95.8	54.2, 91.7
Min, Max	0, 100	17, 100	0, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	70.9 (21.92)	71.8 (24.05)	71.3 (22.85)
Median	75.0	75.0	75.0
Q1,Q3	54.2, 87.5	58.3, 91.7	58.3, 91.7
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	67.8 (21.91)	73.2 (22.13)	70.3 (22.04)
Median	68.8	75.0	72.9

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Q1,Q3	52.1, 83.3	58.3, 95.8	54.2, 87.5
Min, Max	0, 100	29, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	41 (82)	30 (65)	71 (74)
Mean (SD)	67.3 (25.01)	70.8 (22.32)	68.8 (23.81)
Median	70.8	70.8	70.8
Q1,Q3	45.8, 83.3	50.0, 91.7	50.0, 91.7
Min, Max	0, 100	29, 100	0, 100
Week 96			
n (%)	37 (74)	28 (61)	65 (68)
Mean (SD)	66.9 (22.22)	71.1 (23.32)	68.7 (22.62)
Median	66.7	70.8	66.7
Q1,Q3	45.8, 87.5	52.1, 89.6	50.0, 87.5
Min, Max	21, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 08MAR2022

109MS306_table41_43_CHG_DESCRIBE_male

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	16 (89)	33 (85)
Mean (SD)	72.3 (26.02)	80.5 (17.79)	76.3 (22.45)
Median	79.2	81.3	79.2
Q1,Q3	70.8, 91.7	70.8, 95.8	70.8, 91.7
Min, Max	13, 100	46, 100	13, 100
Week 24			
n (%)	17 (81)	17 (94)	34 (87)
Mean (SD)	72.1 (23.65)	79.4 (17.83)	75.7 (20.96)
Median	70.8	75.0	75.0
Q1,Q3	62.5, 91.7	62.5, 100.0	62.5, 95.8
Min, Max	21, 100	50, 100	21, 100
Week 48			
n (%)	17 (81)	14 (78)	31 (79)
Mean (SD)	77.0 (20.74)	79.5 (19.78)	78.1 (20.01)

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Median	83.3	83.3	83.3
Q1,Q3	66.7, 95.8	62.5, 100.0	62.5, 100.0
Min, Max	33, 100	42, 100	33, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107. Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_HEDGESCI_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	18 (86)	11 (61)	29 (74)
Mean (SD)	72.0 (21.76)	81.4 (16.60)	75.6 (20.19)
Median	70.8	87.5	70.8
Q1,Q3	62.5, 91.7	70.8, 95.8	62.5, 91.7
Min, Max	29, 100	50, 100	29, 100
Week 96			
n (%)	17 (81)	10 (56)	27 (69)
Mean (SD)	74.0 (21.07)	77.1 (22.59)	75.2 (21.26)
Median	70.8	79.2	70.8
Q1,Q3	58.3, 91.7	58.3, 100.0	58.3, 100.0
Min, Max	38, 100	42, 100	38, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	16 (89)	33 (85)
Mean (SD)	70.1 (20.48)	69.3 (20.91)	69.7 (20.37)
Median	75.0	66.7	70.8
Q1,Q3	58.3, 87.5	52.1, 87.5	54.2, 87.5
Min, Max	25, 100	38, 100	25, 100
Week 24			
n (%)	17 (81)	17 (94)	34 (87)
Mean (SD)	71.1 (16.76)	65.9 (18.76)	68.5 (17.71)
Median	75.0	70.8	70.8
Q1,Q3	58.3, 83.3	45.8, 79.2	58.3, 79.2
Min, Max	33, 100	38, 100	33, 100
Week 48			
n (%)	17 (81)	14 (78)	31 (79)
Mean (SD)	71.3 (24.29)	72.6 (17.58)	71.9 (21.19)
Median	75.0	68.8	70.8

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Q1,Q3	66.7, 87.5	62.5, 87.5	62.5, 87.5
Min, Max	13, 100	42, 100	13, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	18 (86)	11 (61)	29 (74)
Mean (SD)	71.5 (23.80)	74.8 (15.81)	72.8 (20.87)
Median	72.9	66.7	70.8
Q1,Q3	62.5, 91.7	62.5, 87.5	62.5, 87.5
Min, Max	13, 100	50, 100	13, 100
Week 96			
n (%)	17 (81)	10 (56)	27 (69)
Mean (SD)	71.8 (20.91)	74.2 (16.87)	72.7 (19.21)
Median	70.8	68.8	70.8
Q1,Q3	58.3, 83.3	58.3, 91.7	58.3, 91.7
Min, Max	29, 100	54, 100	29, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	16 (89)	33 (85)
Mean (SD)	68.9 (26.56)	73.7 (17.26)	71.2 (22.33)
Median	75.0	72.9	75.0
Q1,Q3	50.0, 87.5	60.4, 85.4	54.2, 87.5
Min, Max	17, 100	46, 100	17, 100
Week 24			
n (%)	17 (81)	17 (94)	34 (87)
Mean (SD)	74.0 (24.63)	74.3 (25.86)	74.1 (24.87)
Median	75.0	83.3	79.2
Q1,Q3	58.3, 100.0	62.5, 91.7	58.3, 95.8
Min, Max	25, 100	0, 100	0, 100
Week 48			
n (%)	17 (81)	14 (78)	31 (79)
Mean (SD)	69.4 (27.24)	73.5 (22.92)	71.2 (25.05)
Median	75.0	75.0	75.0

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Q1,Q3	50.0, 95.8	62.5, 95.8	54.2, 95.8
Min, Max	13, 100	21, 100	13, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	18 (86)	11 (61)	29 (74)
Mean (SD)	66.2 (26.50)	77.3 (17.32)	70.4 (23.74)
Median	68.8	75.0	70.8
Q1,Q3	50.0, 95.8	70.8, 100.0	54.2, 95.8
Min, Max	13, 100	50, 100	13, 100
Week 96			
n (%)	17 (81)	10 (56)	27 (69)
Mean (SD)	67.4 (28.84)	75.0 (27.50)	70.2 (28.06)
Median	75.0	72.9	75.0
Q1,Q3	41.7, 100.0	62.5, 100.0	50.0, 100.0
Min, Max	17, 100	13, 100	13, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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109MS306_table41_43_CHG_HEDGESCI_age13to14

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0	-0.839	0.839
	48	0.17	-0.761	1.102
	72	0.424	-0.517	1.365
	96	0.505	-0.478	1.487
GENERAL FATIGUE	24	-0.656	-1.519	0.208
	48	0.379	-0.560	1.318
	72	-0.062	-0.992	0.868
	96	0.077	-0.890	1.043
SLEEP/REST FATIGUE	24	-0.334	-1.180	0.511
	48	0.186	-0.746	1.118
	72	-0.434	-1.376	0.508
	96	-0.302	-1.274	0.669

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.

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109MS306_table41_43_CHG_HEDGESCI_age15to17

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.494	0.057	0.931
	48	0.355	-0.107	0.817
	72	0.369	-0.128	0.867
	96	0.323	-0.193	0.838
GENERAL FATIGUE	24	0.305	-0.128	0.738
	48	0.273	-0.187	0.734
	72	0.137	-0.357	0.631
	96	-0.095	-0.607	0.418
SLEEP/REST FATIGUE	24	0.251	-0.181	0.683
	48	0.051	-0.408	0.509
	72	0.15	-0.344	0.644
	96	-0.106	-0.619	0.406

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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109MS306_table41_43_CHG_HEDGESCI_female

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.442	-0.017	0.900
	48	0.316	-0.171	0.802
	72	0.569	0.044	1.093
	96	0.478	-0.065	1.021
GENERAL FATIGUE	24	0.142	-0.311	0.596
	48	0.2	-0.285	0.684
	72	-0.041	-0.555	0.473
	96	-0.275	-0.812	0.263
SLEEP/REST FATIGUE	24	-0.013	-0.466	0.440
	48	0.042	-0.442	0.525
	72	-0.024	-0.538	0.490
	96	-0.171	-0.706	0.365

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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109MS306_table41_43_CHG_HEDGESCI_male

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.271	-0.448	0.991
	48	0.305	-0.471	1.080
	72	-0.206	-1.035	0.623
	96	0.055	-0.795	0.905
GENERAL FATIGUE	24	0.173	-0.544	0.890
	48	0.558	-0.229	1.345
	72	0.44	-0.396	1.277
	96	0.548	-0.319	1.415
SLEEP/REST FATIGUE	24	0.59	-0.142	1.322
	48	0.203	-0.570	0.976
	72	0.333	-0.499	1.165
	96	-0.078	-0.928	0.773

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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109MS306_table41_43_CHG_LSMEANS_age13to14

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 13 TO 14. General Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	10 (56)	12 (86)
Lsmean (SE)	-5.20 (3.843)	02.25 (3.506)
Lsmean_95 % CI	(-13.24, 02.847)	(-5.092, 09.585)
Diffrence (95% CI)	-7.44 (-18.361, 3.476)	
SE_Difference	5.2166	
p-value	0.1699	
Week 48		
n (%)	8 (44)	10 (71)
Lsmean (SE)	-0.10 (5.897)	-6.17 (5.275)
Lsmean_95 % CI	(-12.67, 12.473)	(-17.41, 05.070)
Diffrence (95% CI)	6.07 (-10.793, 22.943)	
SE_Difference	7.9136	
p-value	0.4546	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
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	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	8 (57)
Lsmean (SE)	02.40 (3.159)	03.25 (3.532)
Lsmean_95 % CI	(-4.331, 09.135)	(-4.281, 10.776)
Diffrence (95% CI)	-0.85 (-10.950, 9.258)	
SE_Difference	4.7405	
p-value	0.8607	
Week 96		
n (%)	10 (56)	7 (50)
Lsmean (SE)	-4.14 (7.613)	-5.98 (9.100)
Lsmean_95 % CI	(-20.47, 12.183)	(-25.50, 13.534)
Diffrence (95% CI)	1.84 (-23.615, 27.292)	
SE_Difference	1.8673	
p-value	0.8791	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 13 TO 14. Sleep/Rest Fatigue

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	10 (56)	12 (86)
Lsmean (SE)	-0.51 (4.062)	02.51 (3.706)
Lsmean_95 % CI	(-9.010, 07.994)	(-5.249, 10.263)
Diffrence (95% CI)	-3.01 (-14.566, 8.537)	
SE_Difference	5.5189	
p-value	0.5912	
Week 48		
n (%)	8 (44)	10 (71)
Lsmean (SE)	-2.08 (4.097)	-4.17 (3.665)
Lsmean_95 % CI	(-10.81, 06.654)	(-11.98, 03.641)
Diffrence (95% CI)	2.09 (-9.630, 13.810)	
SE_Difference	5.4985	
p-value	0.7091	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
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	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	8 (57)
Lsmean (SE)	-0.32 (3.445)	04.05 (3.854)
Lsmean_95 % CI	(-7.666, 07.019)	(-4.164, 12.265)
Diffrence (95% CI)	-4.37 (-15.425, 6.677)	
SE_Difference	5.1848	
p-value	0.4121	
Week 96		
n (%)	10 (56)	7 (50)
Lsmean (SE)	-5.43 (4.060)	-0.58 (4.869)
Lsmean_95 % CI	(-14.13, 03.280)	(-11.02, 09.862)
Diffrence (95% CI)	-4.85 (-18.573, 8.880)	
SE_Difference	6.3998	
p-value	0.4615	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 13 TO 14. Cognitive Fatigue

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	10 (56)	12 (86)
Lsmean (SE)	02.25 (4.319)	05.76 (3.928)
Lsmean_95 % CI	(-6.788, 11.293)	(-2.459, 13.982)
Diffrence (95% CI)	-3.51 (-15.985, 8.966)	
SE_Difference	5.9604	
p-value	0.5629	
Week 48		
n (%)	8 (44)	10 (71)
Lsmean (SE)	-0.30 (5.306)	01.91 (4.728)
Lsmean_95 % CI	(-11.61, 11.005)	(-8.168, 11.989)
Diffrence (95% CI)	-2.21 (-17.607, 13.178)	
SE_Difference	7.2215	
p-value	0.7633	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
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	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	8 (57)
Lsmean (SE)	04.33 (4.068)	02.40 (4.567)
Lsmean_95 % CI	(-4.342, 13.001)	(-7.334, 12.135)
Diffrence (95% CI)	1.93 (-11.344, 15.201)	
SE_Difference	6.2269	
p-value	0.7610	
Week 96		
n (%)	10 (56)	7 (50)
Lsmean (SE)	01.63 (5.188)	-1.73 (6.279)
Lsmean_95 % CI	(-9.498, 12.758)	(-15.20, 11.734)
Diffrence (95% CI)	3.36 (-14.692, 21.420)	
SE_Difference	8.4183	
p-value	0.6955	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
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109MS306_table41_43_CHG_LSMEANS_age15to17

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 15 TO 17. General Fatigue

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	43 (81)	40 (80)
Lsmean (SE)	01.04 (2.243)	-1.74 (2.327)
Lsmean_95 % CI	(-3.424, 05.505)	(-6.375, 02.887)
Diffrence (95% CI)	2.78 (-3.682, 9.251)	
SE_Difference	3.2493	
p-value	0.3941	
Week 48		
n (%)	41 (77)	33 (66)
Lsmean (SE)	00.83 (2.466)	-0.65 (2.753)
Lsmean_95 % CI	(-4.087, 05.746)	(-6.141, 04.837)
Diffrence (95% CI)	1.48 (-5.944, 8.907)	
SE_Difference	3.7239	
p-value	0.6920	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	38 (72)	27 (54)
Lsmean (SE)	-3.50 (2.439)	-2.02 (2.902)
Lsmean_95 % CI	(-8.373, 01.376)	(-7.822, 03.781)
Diffrence (95% CI)	-1.48 (-9.124, 6.168)	
SE_Difference	3.8248	
p-value	0.7005	
Week 96		
n (%)	32 (60)	27 (54)
Lsmean (SE)	-6.85 (3.074)	-1.61 (3.349)
Lsmean_95 % CI	(-13.00, -0.689)	(-8.318, 05.100)
Diffrence (95% CI)	-5.24 (-14.392, 3.918)	
SE_Difference	4.5701	
p-value	0.2567	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 15 TO 17. Sleep/Rest Fatigue

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	43 (81)	40 (80)
Lsmean (SE)	01.72 (2.400)	-2.47 (2.488)
Lsmean_95 % CI	(-3.055, 06.495)	(-7.425, 02.477)
Diffrence (95% CI)	4.19 (-2.685, 11.073)	
SE_Difference	3.4567	
p-value	0.2286	
Week 48		
n (%)	41 (77)	33 (66)
Lsmean (SE)	01.06 (2.589)	01.51 (2.887)
Lsmean_95 % CI	(-4.101, 06.223)	(-4.247, 07.267)
Diffrence (95% CI)	-0.45 (-8.199, 7.300)	
SE_Difference	3.8866	
p-value	0.9083	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	38 (72)	27 (54)
Lsmean (SE)	-0.44 (3.033)	-0.86 (3.605)
Lsmean_95 % CI	(-6.506, 05.621)	(-8.066, 06.348)
Diffrence (95% CI)	0.42 (-9.053, 9.886)	
SE_Difference	4.7372	
p-value	0.9302	
Week 96		
n (%)	32 (60)	27 (54)
Lsmean (SE)	-3.82 (3.044)	00.06 (3.315)
Lsmean_95 % CI	(-9.921, 02.275)	(-6.586, 06.697)
Diffrence (95% CI)	-3.88 (-12.915, 5.159)	
SE_Difference	4.5112	
p-value	0.3936	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for AGES 15 TO 17. Cognitive Fatigue

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	43 (81)	40 (80)
Lsmean (SE)	04.36 (2.599)	-2.81 (2.696)
Lsmean_95 % CI	(-0.816, 09.530)	(-8.174, 02.557)
Diffrence (95% CI)	7.17 (-0.321, 14.652)	
SE_Difference	3.7620	
p-value	0.0604	
Week 48		
n (%)	41 (77)	33 (66)
Lsmean (SE)	01.31 (2.729)	-2.38 (3.049)
Lsmean_95 % CI	(-4.134, 06.750)	(-8.461, 03.696)
Diffrence (95% CI)	3.69 (-4.546, 11.927)	
SE_Difference	4.1307	
p-value	0.3746	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	38 (72)	27 (54)
Lsmean (SE)	00.18 (3.007)	-2.56 (3.586)
Lsmean_95 % CI	(-5.835, 06.188)	(-9.731, 04.605)
Diffrence (95% CI)	2.74 (-6.754, 12.233)	
SE_Difference	4.7490	
p-value	0.5661	
Week 96		
n (%)	32 (60)	27 (54)
Lsmean (SE)	-2.80 (3.435)	-5.63 (3.748)
Lsmean_95 % CI	(-9.683, 04.078)	(-13.14, 01.879)
Diffrence (95% CI)	2.83 (-7.497, 13.151)	
SE_Difference	5.1537	
p-value	0.5855	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

109MS306_table41_43_CHG_LSMEANS_female

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for FEMALE SEX. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	38 (76)	37 (80)
Lsmean (SE)	01.65 (2.773)	00.02 (2.648)
Lsmean_95 % CI	(-3.884, 07.175)	(-5.257, 05.301)
Diffrence (95% CI)	1.62 (-5.128, 8.375)	
SE_Difference	3.3859	
p-value	0.6331	
Week 48		
n (%)	35 (70)	31 (67)
Lsmean (SE)	-1.64 (3.287)	-2.95 (3.262)
Lsmean_95 % CI	(-8.209, 04.934)	(-9.470, 03.571)
Diffrence (95% CI)	1.31 (-6.727, 9.352)	
SE_Difference	4.0219	
p-value	0.7453	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
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	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	33 (66)	26 (57)
Lsmean (SE)	00.06 (3.014)	01.88 (3.137)
Lsmean_95 % CI	(-5.982, 06.099)	(-4.403, 08.169)
Diffrence (95% CI)	-1.82 (-9.444, 5.795)	
SE_Difference	3.8021	
p-value	0.6332	
Week 96		
n (%)	29 (58)	25 (54)
Lsmean (SE)	-9.63 (4.259)	-2.66 (4.427)
Lsmean_95 % CI	(-18.19, -1.080)	(-11.55, 06.229)
Diffrence (95% CI)	-6.97 (-17.671, 3.728)	
SE_Difference	5.3269	
p-value	0.1966	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for FEMALE SEX. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	38 (76)	37 (80)
Lsmean (SE)	02.50 (3.111)	01.91 (2.937)
Lsmean_95 % CI	(-3.706, 08.702)	(-3.946, 07.767)
Diffrence (95% CI)	0.59 (-6.931, 8.106)	
SE_Difference	3.7707	
p-value	0.8766	
Week 48		
n (%)	35 (70)	31 (67)
Lsmean (SE)	-0.64 (3.278)	-0.15 (3.229)
Lsmean_95 % CI	(-7.196, 05.910)	(-6.609, 06.300)
Diffrence (95% CI)	-0.49 (-8.448, 7.471)	
SE_Difference	3.9818	
p-value	0.9027	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	33 (66)	26 (57)
Lsmean (SE)	-0.20 (3.748)	01.34 (3.882)
Lsmean_95 % CI	(-7.708, 07.315)	(-6.440, 09.121)
Diffrence (95% CI)	-1.54 (-10.983, 7.909)	
SE_Difference	4.7135	
p-value	0.7456	
Week 96		
n (%)	29 (58)	25 (54)
Lsmean (SE)	-6.21 (3.634)	-2.63 (3.765)
Lsmean_95 % CI	(-13.50, 01.093)	(-10.20, 04.929)
Diffrence (95% CI)	-3.57 (-12.693, 5.550)	
SE_Difference	4.5413	
p-value	0.4353	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for FEMALE SEX. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	38 (76)	37 (80)
Lsmean (SE)	06.30 (3.067)	00.97 (2.982)
Lsmean_95 % CI	(00.185, 12.417)	(-4.977, 06.915)
Diffrence (95% CI)	5.33 (-2.262, 12.927)	
SE_Difference	3.8088	
p-value	0.1659	
Week 48		
n (%)	35 (70)	31 (67)
Lsmean (SE)	00.84 (3.324)	-0.73 (3.340)
Lsmean_95 % CI	(-5.801, 07.487)	(-7.406, 05.946)
Diffrence (95% CI)	1.57 (-6.680, 9.825)	
SE_Difference	4.1284	
p-value	0.7046	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	33 (66)	26 (57)
Lsmean (SE)	03.86 (3.511)	-2.00 (3.752)
Lsmean_95 % CI	(-3.174, 10.898)	(-9.520, 05.517)
Diffrence (95% CI)	5.86 (-3.271, 14.999)	
SE_Difference	4.5582	
p-value	0.2037	
Week 96		
n (%)	29 (58)	25 (54)
Lsmean (SE)	-2.43 (3.742)	-6.57 (4.038)
Lsmean_95 % CI	(-9.942, 05.092)	(-14.68, 01.537)
Diffrence (95% CI)	4.15 (-5.581, 13.876)	
SE_Difference	4.8435	
p-value	0.3959	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

109MS306_table41_43_CHG_LSMEANS_male

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for MALE SEX. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)
Week 24		
n (%)	15 (71)	15 (83)
Lsmean (SE)	-0.50 (3.863)	-0.70 (4.168)
Lsmean_95 % CI	(-8.445, 07.437)	(-9.271, 07.866)
Diffrence (95% CI)	0.20 (-10.644, 11.041)	
SE_Difference	5.2748	
p-value	0.9702	
Week 48		
n (%)	14 (67)	12 (67)
Lsmean (SE)	07.07 (4.770)	01.58 (5.158)
Lsmean_95 % CI	(-2.828, 16.959)	(-9.113, 12.282)
Diffrence (95% CI)	5.48 (-7.921, 18.883)	
SE_Difference	6.4622	
p-value	0.4054	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	15 (71)	9 (50)
Lsmean (SE)	01.68 (3.708)	02.58 (5.194)
Lsmean_95 % CI	(-6.051, 09.418)	(-8.257, 13.410)
Diffrence (95% CI)	-0.89 (-13.921, 12.135)	
SE_Difference	6.2452	
p-value	0.8877	
Week 96		
n (%)	13 (62)	9 (50)
Lsmean (SE)	01.96 (4.913)	-1.03 (6.555)
Lsmean_95 % CI	(-8.360, 12.284)	(-14.80, 12.746)
Diffrence (95% CI)	2.99 (-14.188, 20.163)	
SE_Difference	8.1750	
p-value	0.7190	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for MALE SEX. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)
Week 24		
n (%)	15 (71)	15 (83)
Lsmean (SE)	05.29 (3.570)	-1.41 (3.834)
Lsmean_95 % CI	(-2.052, 12.624)	(-9.291, 06.473)
Diffrence (95% CI)	6.69 (-2.996, 16.385)	
SE_Difference	4.7142	
p-value	0.1675	
Week 48		
n (%)	14 (67)	12 (67)
Lsmean (SE)	01.82 (4.820)	00.32 (5.238)
Lsmean_95 % CI	(-8.174, 11.820)	(-10.54, 11.186)
Diffrence (95% CI)	1.50 (-11.788, 14.787)	
SE_Difference	6.4069	
p-value	0.8171	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	15 (71)	9 (50)
Lsmean (SE)	03.73 (4.564)	02.58 (6.489)
Lsmean_95 % CI	(-5.791, 13.252)	(-10.96, 16.113)
Diffrence (95% CI)	1.15 (-14.687, 16.993)	
SE_Difference	7.5934	
p-value	0.8808	
Week 96		
n (%)	13 (62)	9 (50)
Lsmean (SE)	00.06 (4.458)	07.23 (5.899)
Lsmean_95 % CI	(-9.303, 09.427)	(-5.168, 19.621)
Diffrence (95% CI)	-7.16 (-22.148, 7.820)	
SE_Difference	7.1320	
p-value	0.3284	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for MALE SEX. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 18)
Week 24		
n (%)	15 (71)	15 (83)
Lsmean (SE)	05.80 (4.673)	01.81 (4.887)
Lsmean_95 % CI	(-3.808, 15.404)	(-8.233, 11.857)
Diffrence (95% CI)	3.99 (-8.752, 16.723)	
SE_Difference	6.1967	
p-value	0.5257	
Week 48		
n (%)	14 (67)	12 (67)
Lsmean (SE)	06.36 (5.488)	01.64 (5.807)
Lsmean_95 % CI	(-5.019, 17.742)	(-10.40, 13.686)
Diffrence (95% CI)	4.72 (-10.522, 19.959)	
SE_Difference	7.3485	
p-value	0.5274	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_LSMEANS_SubGr.sas date: 08MAR2022

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	15 (71)	9 (50)
Lsmean (SE)	03.01 (4.844)	09.94 (6.496)
Lsmean_95 % CI	(-7.098, 13.109)	(-3.614, 23.486)
Diffrence (95% CI)	-6.93 (-23.144, 9.284)	
SE_Difference	7.7727	
p-value	0.3832	
Week 96		
n (%)	13 (62)	9 (50)
Lsmean (SE)	03.47 (5.657)	05.78 (7.225)
Lsmean_95 % CI	(-8.417, 15.355)	(-9.394, 20.964)
Diffrence (95% CI)	-2.32 (-21.183, 16.552)	
SE_Difference	8.9804	
p-value	0.7994	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
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MCID

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_AGEGRN_Age1314_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Aged between 13 and 14 years old

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	0 (0.00)	1 (7.14)	1 (4.17)
-	No	11 (61.11)	12 (85.71)	23 (95.83)
-	Missing	7 (38.89)	1 (7.14)	8 (25.00)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	0 (0.00)	1 (7.14)	1 (4.17)
-	No	11 (61.11)	12 (85.71)	23 (95.83)
-	Missing	7 (38.89)	1 (7.14)	8 (25.00)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	0 (0.00)	0 (0.00)	0 (0.00)
-	No	11 (61.11)	13 (92.86)	24 (100.00)
-	Missing	7 (38.89)	1 (7.14)	8 (25.00)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	3 (16.67)	1 (7.14)	4 (16.67)
-	No	8 (44.44)	12 (85.71)	20 (83.33)
-	Missing	7 (38.89)	1 (7.14)	8 (25.00)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	0 (0.00)	1 (7.14)	1 (4.17)
-	No	11 (61.11)	12 (85.71)	23 (95.83)
-	Missing	7 (38.89)	1 (7.14)	8 (25.00)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_AGEGRN_Age1314_responsRate

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Aged between 13 and 14 years old

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
GENERAL FATIGUE-Week 48	Yes	12 (66.67)	10 (71.43)	22 (68.75)
-	No	6 (33.33)	4 (28.57)	10 (31.25)
GENERAL FATIGUE-Week 72	Yes	14 (77.78)	8 (57.14)	22 (68.75)
-	No	4 (22.22)	6 (42.86)	10 (31.25)
GENERAL FATIGUE-Week 96	Yes	16 (88.89)	7 (50.00)	23 (71.88)
-	No	2 (11.11)	7 (50.00)	9 (28.12)
SLEEP/REST FATIGUE-Week 72	Yes	14 (77.78)	8 (57.14)	22 (68.75)
-	No	4 (22.22)	6 (42.86)	10 (31.25)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_AGEGRN_Age1517_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigure Scale (Participant) - Aged between 15 and 17 years old

	Result	OR	RR	ARR
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Effect measure	1.667	1.519	0.076
-	95% CI	(0.546 , 5.084)	(0.606 , 3.808)	(-0.087 , 0.239)
-	p-value	0.369	0.373	0.361
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Effect measure	1.016	1.012	0.003
-	95% CI	(0.366 , 2.818)	(0.457 , 2.242)	(-0.173 , 0.178)
-	p-value	0.976	0.976	0.976
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Effect measure	1.15	1.114	0.025
-	95% CI	(0.421 , 3.141)	(0.514 , 2.411)	(-0.153 , 0.203)
-	p-value	0.785	0.785	0.784
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.179	1.139	0.027
-	95% CI	(0.415 , 3.349)	(0.498 , 2.606)	(-0.145 , 0.199)
-	p-value	0.758	0.758	0.757
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Effect measure	1.179	1.139	0.027
-	95% CI	(0.415 , 3.349)	(0.498 , 2.606)	(-0.145 , 0.199)
-	p-value	0.758	0.758	0.757

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used

NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_AGEGRN_Age1517_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Aged between 15 and 17 years old

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
MCID increase ≥15% - GENERAL FATIGUE - Week 48	Yes	10 (18.87)	6 (12.00)	16 (18.60)
-	No	35 (66.04)	35 (70.00)	70 (81.40)
-	Missing	8 (15.09)	9 (18.00)	17 (16.50)
MCID decrease ≥15% - GENERAL FATIGUE - Week 48	Yes	10 (18.87)	9 (18.00)	19 (22.09)
-	No	35 (66.04)	32 (64.00)	67 (77.91)
-	Missing	8 (15.09)	9 (18.00)	17 (16.50)
MCID decrease ≥15% - GENERAL FATIGUE - Week 72	Yes	11 (20.75)	9 (18.00)	20 (23.26)
-	No	34 (64.15)	32 (64.00)	66 (76.74)
-	Missing	8 (15.09)	9 (18.00)	17 (16.50)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	10 (18.87)	8 (16.00)	18 (20.93)
-	No	35 (66.04)	33 (66.00)	68 (79.07)
-	Missing	8 (15.09)	9 (18.00)	17 (16.50)
MCID decrease ≥15% - SLEEP/REST FATIGUE - Week 72	Yes	10 (18.87)	8 (16.00)	18 (20.93)
-	No	35 (66.04)	33 (66.00)	68 (79.07)
-	Missing	8 (15.09)	9 (18.00)	17 (16.50)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_AGEGRN_Age1517_responsRate

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Aged between 15 and 17 years old

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
GENERAL FATIGUE-Week 48	Yes	49 (92.45)	42 (84.00)	91 (88.35)
-	No	4 (7.55)	8 (16.00)	12 (11.65)
GENERAL FATIGUE-Week 72	Yes	45 (84.91)	33 (66.00)	78 (75.73)
-	No	8 (15.09)	17 (34.00)	25 (24.27)
GENERAL FATIGUE-Week 96	Yes	38 (71.70)	31 (62.00)	69 (66.99)
-	No	15 (28.30)	19 (38.00)	34 (33.01)
SLEEP/REST FATIGUE-Week 72	Yes	45 (84.91)	33 (66.00)	78 (75.73)
-	No	8 (15.09)	17 (34.00)	25 (24.27)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Female_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigure Scale (Participant) - Female

	Result	OR	RR	ARR
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.723	0.779	-0.058
-	95% CI	(0.25 , 2.087)	(0.345 , 1.762)	(-0.247 , 0.131)
-	p-value	0.548	0.549	0.547
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	1.74	1.531	0.098
-	95% CI	(0.593 , 5.106)	(0.664 , 3.532)	(-0.09 , 0.285)
-	p-value	0.313	0.318	0.306

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Female_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Female

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	8 (16.00)	10 (21.74)	18 (23.38)
-	No	31 (62.00)	28 (60.87)	59 (76.62)
-	Missing	11 (22.00)	8 (17.39)	19 (19.79)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	11 (22.00)	7 (15.22)	18 (23.38)
-	No	28 (56.00)	31 (67.39)	59 (76.62)
-	Missing	11 (22.00)	8 (17.39)	19 (19.79)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Female_responsRate

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Female

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
COGNITIVE FATIGUE-Week 96	Yes	37 (74.00)	28 (60.87)	65 (67.71)
-	No	13 (26.00)	18 (39.13)	31 (32.29)
GENERAL FATIGUE-Week 96	Yes	37 (74.00)	28 (60.87)	65 (67.71)
-	No	13 (26.00)	18 (39.13)	31 (32.29)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Male_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigure Scale (Participant) - Male

	Result	OR	RR	ARR
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	3.214	2.824	0.114
-	95% CI	(0.298 , 34.644)	(0.326 , 24.429)	(-0.103 , 0.331)
-	p-value	0.336	0.346	0.302
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Effect measure	0.933	0.941	-0.007
-	95% CI	(0.115 , 7.553)	(0.15 , 5.91)	(-0.23 , 0.216)
-	p-value	0.948	0.948	0.948

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Male_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Male

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
MCID decrease ≥15% - COGNITIVE FATIGUE - Week 96	Yes	3 (14.29)	1 (5.56)	4 (12.12)
-	No	14 (66.67)	15 (83.33)	29 (87.88)
-	Missing	4 (19.05)	2 (11.11)	6 (15.38)
MCID decrease ≥15% - GENERAL FATIGUE - Week 96	Yes	2 (9.52)	2 (11.11)	4 (12.12)
-	No	15 (71.43)	14 (77.78)	29 (87.88)
-	Missing	4 (19.05)	2 (11.11)	6 (15.38)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_SEX_Male_responsRate

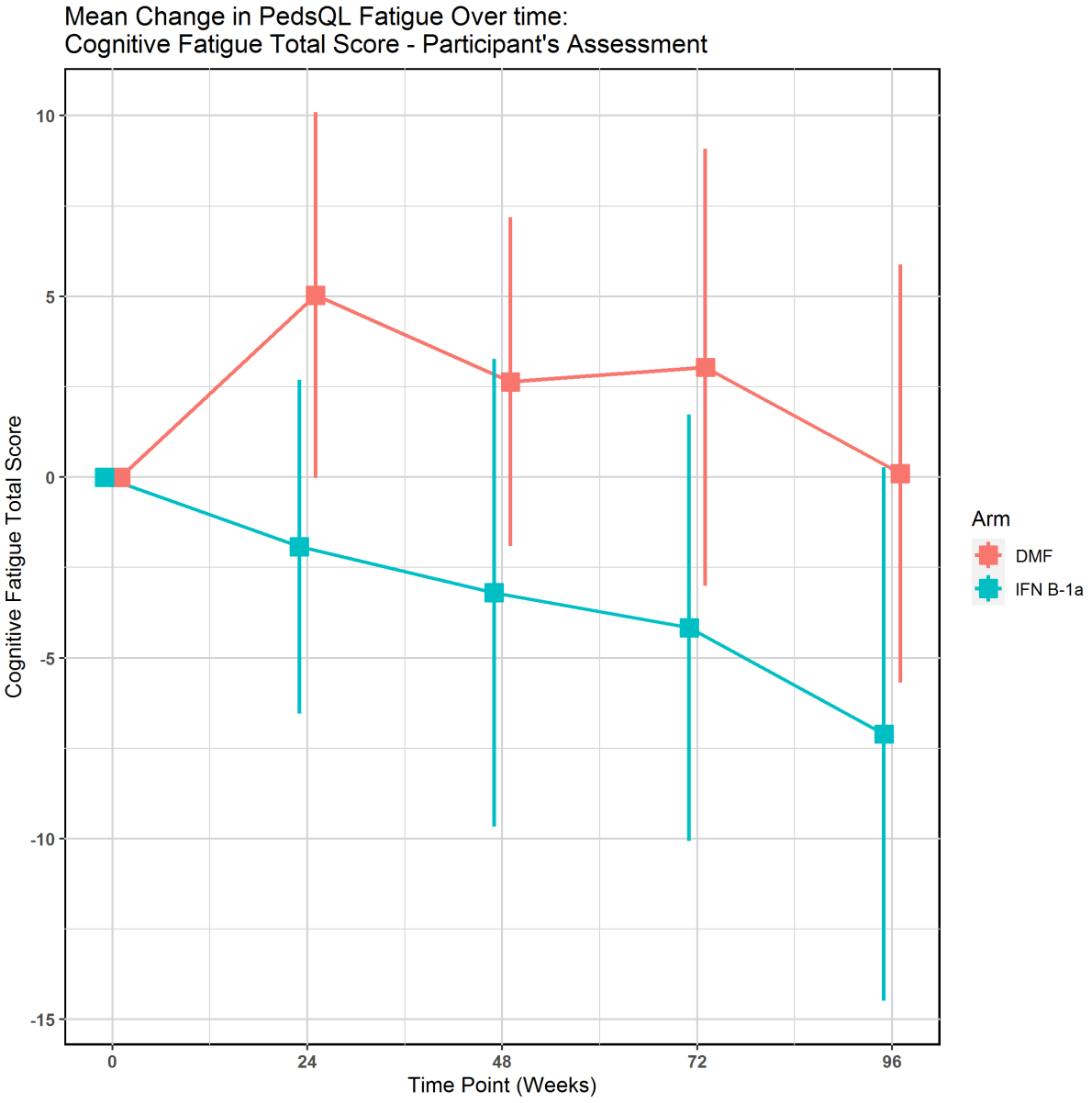
Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - Male

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
COGNITIVE FATIGUE-Week 96	Yes	17 (80.95)	10 (55.56)	27 (69.23)
-	No	4 (19.05)	8 (44.44)	12 (30.77)
GENERAL FATIGUE-Week 96	Yes	17 (80.95)	10 (55.56)	27 (69.23)
-	No	4 (19.05)	8 (44.44)	12 (30.77)

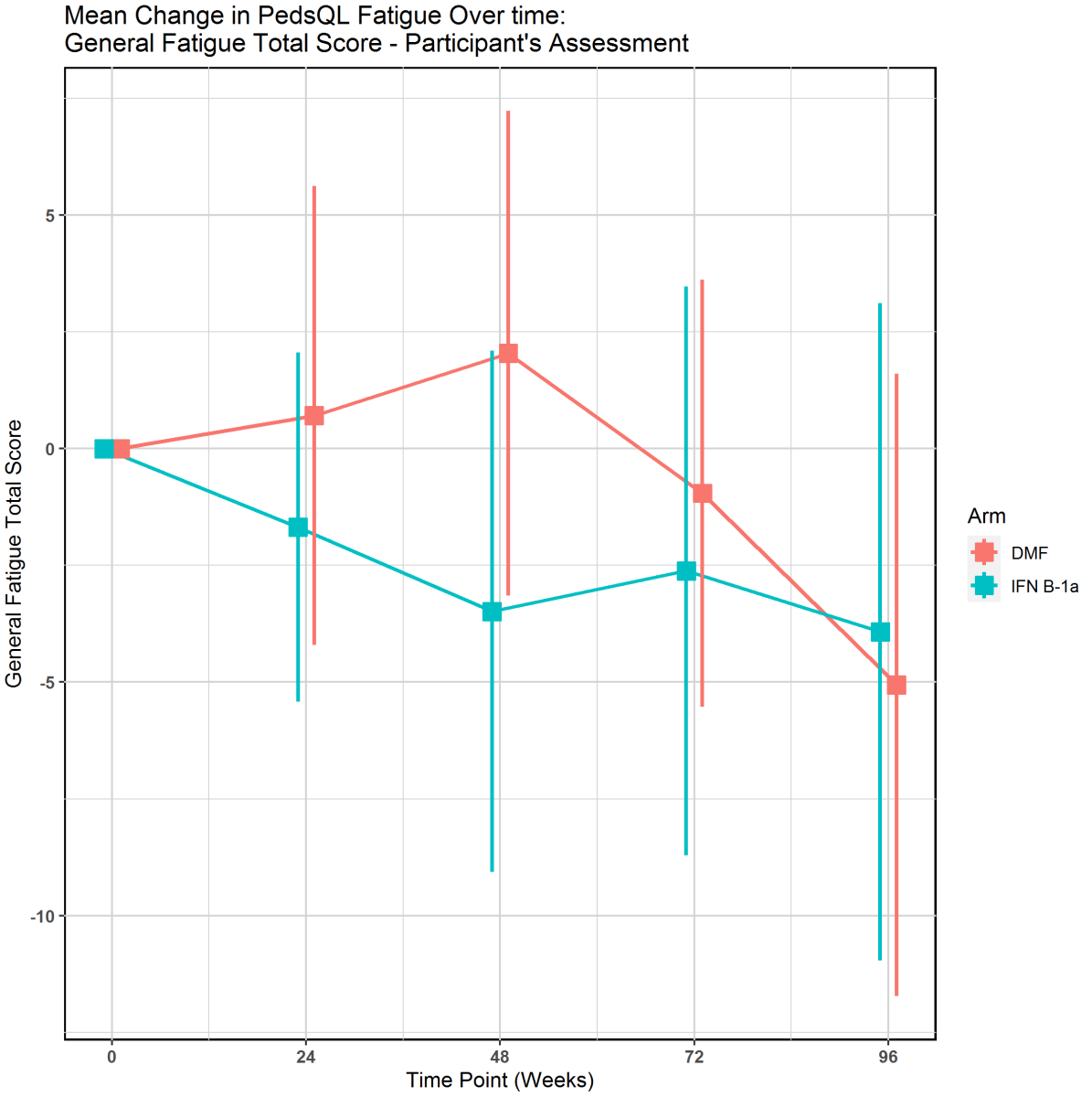
NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation

Graphics

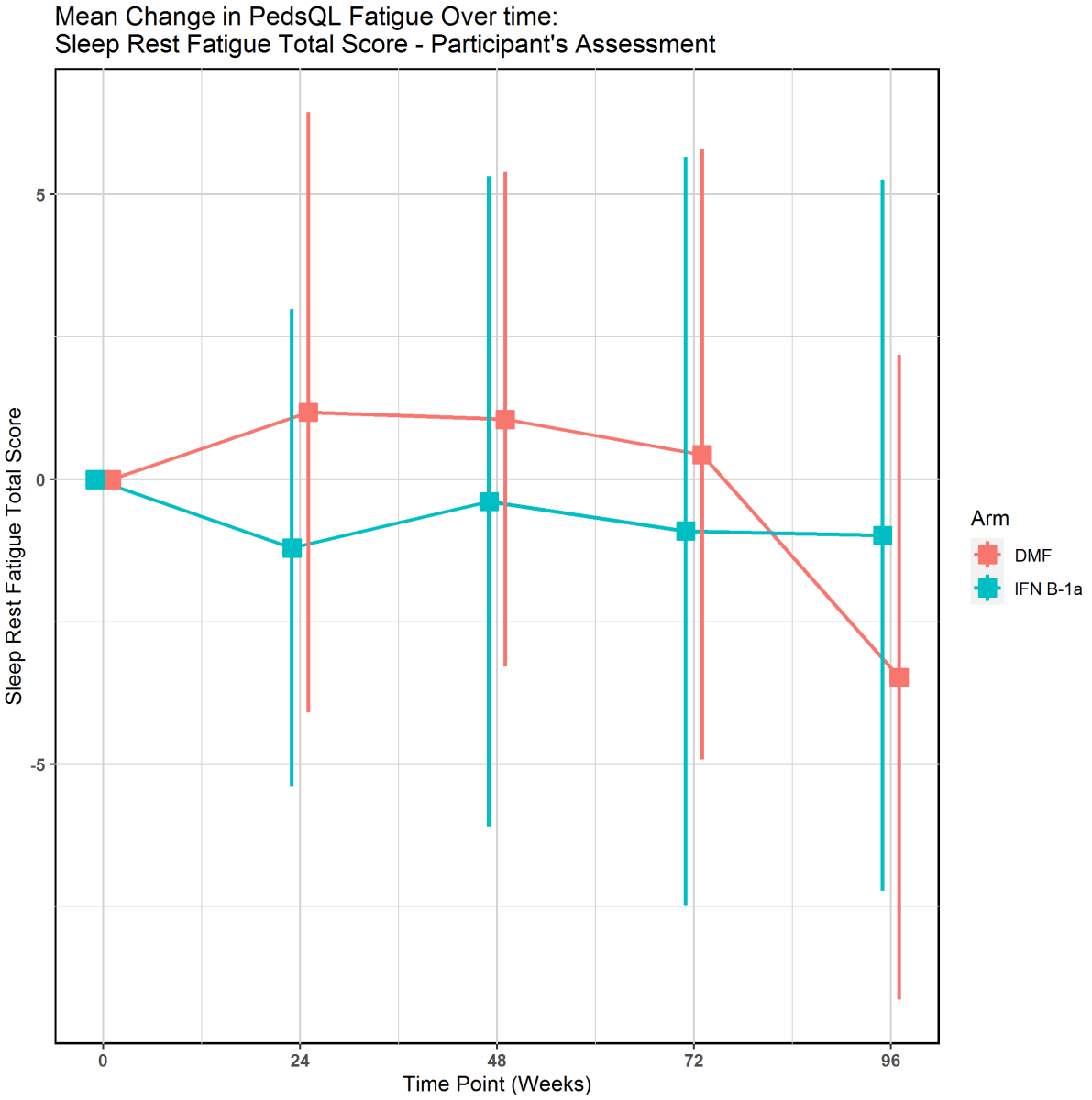
Change from baseline Cognitive Fatigue Total Score Participant's Assessment



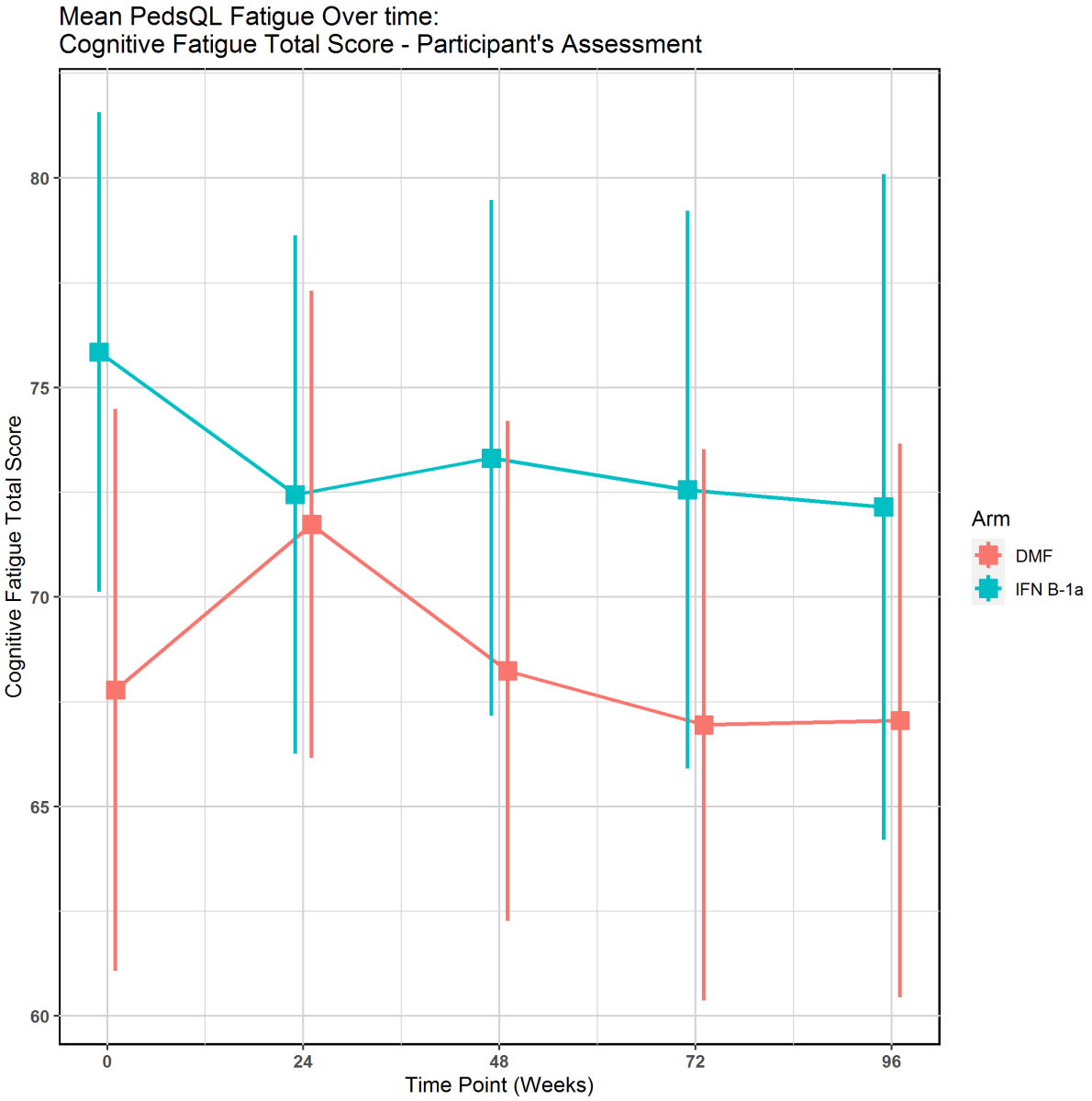
Change from baselineGeneral Fatigue Total Score Participant's Assessment



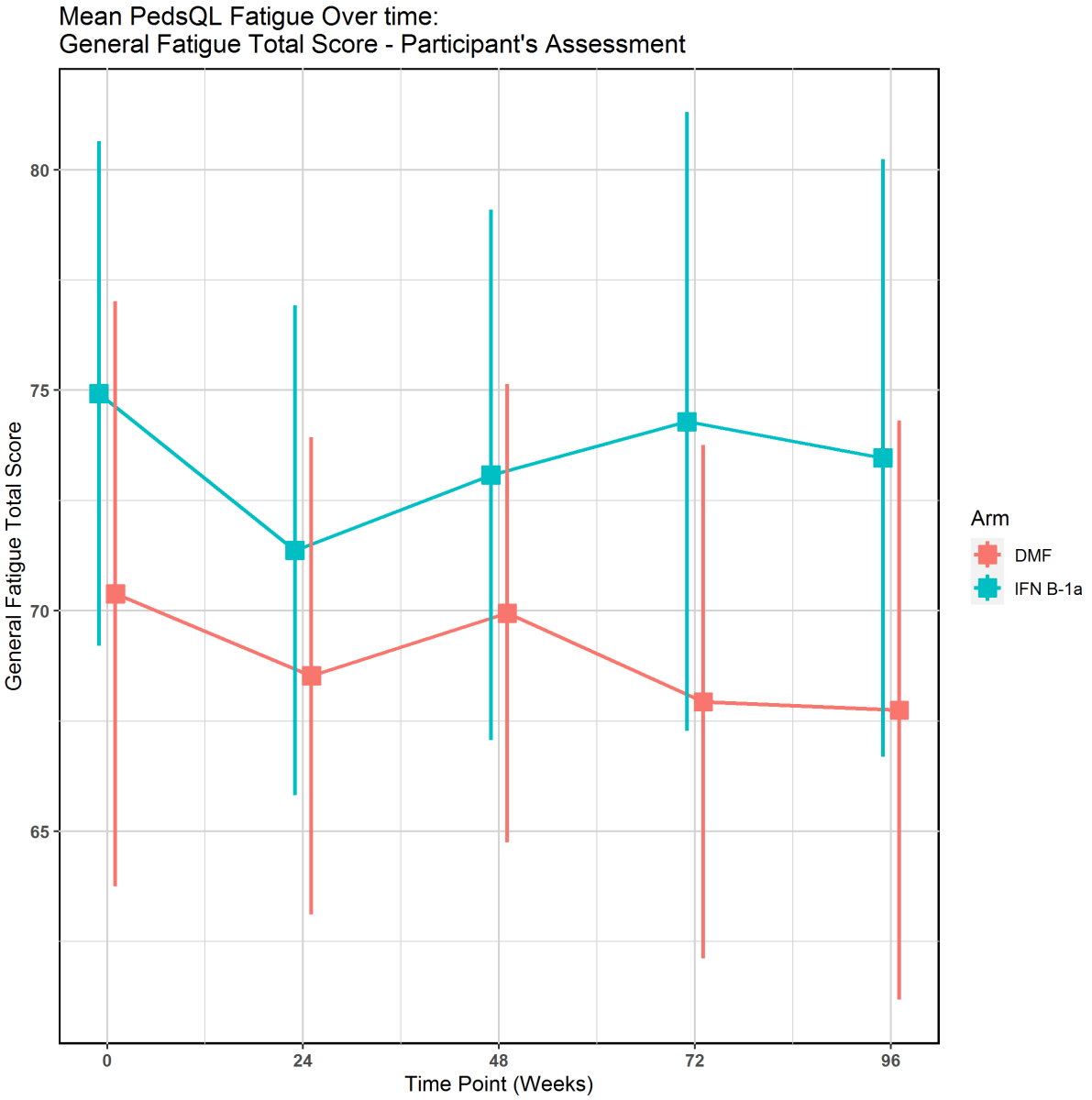
Change from baselineSleep Rest Fatigue Total Score Participant's Assessment



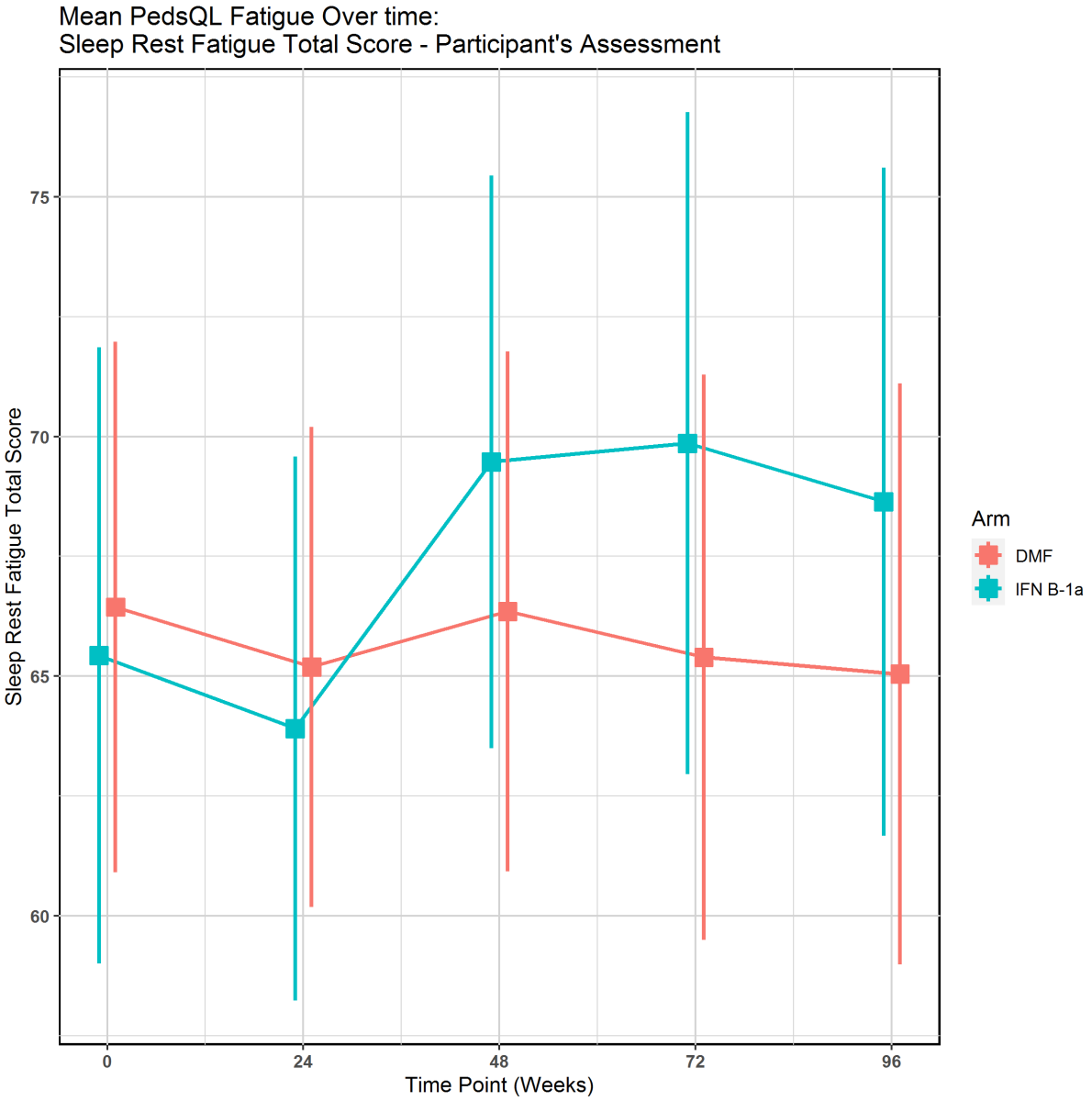
Cognitive Fatigue Total Score Participant's Assessment



General Fatigue Total Score Participant's Assessment



Sleep Rest Fatigue Total Score Participant's Assessment



EDSS

109MS306_table40_CHG_DESCRIBE (CHG FROM BL)

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135)

	DMF(N=71)	IFN B-1a (N=64)	Total (N=135)
Week 12 change from baseline			
n (%)	69 (97)	61(95)	130 (96)
Mean (SD)	0.12 (0.714)	0.12 (0.734)	0.12 (0.721)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.0	-2.0, 2.5	-2.0, 3.0
Week 24 change from baseline			
n (%)	66 (93)	58(91)	124 (92)
Mean (SD)	0.20 (0.953)	0.20 (1.162)	0.20 (1.051)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.00	0.00, 0.25
Min, Max	-2.0, 3.0	-2.0, 5.5	-2.0, 5.5
Week 36 change from baseline			
n (%)	66 (93)	56(88)	122 (90)
Mean (SD)	0.02 (0.762)	0.16 (0.915)	0.09 (0.835)
Median	0.00	0.00	0.00

	DMF(N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.5	-2.0, 2.5	-2.0, 2.5
Week 48 change from baseline			
n (%)	63 (89)	49(77)	112 (83)
Mean (SD)	0.13 (0.971)	0.11 (0.752)	0.12 (0.878)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.50	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.0	-2.0, 3.0	-2.0, 3.0

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622.sas date: 26JAN2022

	DMF(N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Week 60 change from baseline			
n (%)	62 (87)	47(73)	109 (81)
Mean (SD)	-0.12 (0.862)	0.23 (1.117)	0.03 (0.991)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-2.0, 2.0	-1.5, 5.0	-2.0, 5.0
Week 72 change from baseline			
n (%)	60 (85)	41(64)	101 (75)
Mean (SD)	0.05 (0.847)	0.02 (0.873)	0.04 (0.853)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.5	-2.0, 2.5	-2.0, 2.5
Week 84 change from baseline			
n (%)	56 (79)	39(61)	95 (70)
Mean (SD)	-0.08 (0.867)	0.21 (1.286)	0.04 (1.063)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.5, 3.0	-2.0, 6.0	-2.5, 6.0
Week 96 change from baseline			

	DMF(N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
n (%)	54 (76)	39(61)	93 (69)
Mean (SD)	-0.02 (1.090)	0.14 (0.794)	0.05 (0.975)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-5.0, 3.5	-2.0, 2.5	-5.0, 3.5

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622.sas date: 26JAN2022

109MS306_table40_CHG_DESCRIBE

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135)

	DMF(N=71)	IFN B-1a (N=64)	Total (N=135)
Baseline			
n (%)	71 (100)	64(100)	135 (100)
Mean (SD)	1.15 (1.061)	1.16 (0.967)	1.16 (1.014)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 2.00
Min, Max	0.0, 5.0	0.0, 4.0	0.0, 5.0
Week 12			
n (%)	69 (97)	61(95)	130 (96)
Mean (SD)	1.27 (1.205)	1.22 (1.039)	1.25 (1.126)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 24			
n (%)	66 (93)	58(91)	124 (92)
Mean (SD)	1.40 (1.351)	1.28 (1.445)	1.35 (1.391)
Median	1.00	1.00	1.00

	DMF(N=71)	IFN B-1a (N=64)	Total (N=135)
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sasdate: 26JAN2022

	DMF(N=71)	IFN B-1a (N=64)	Total (N=135)
Week 36			
n (%)	66 (93)	56(88)	122 (90)
Mean (SD)	1.20 (1.274)	1.24 (1.206)	1.22 (1.238)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 48			
n (%)	63 (89)	49(77)	112 (83)
Mean (SD)	1.31 (1.369)	1.20 (1.141)	1.26 (1.270)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 60			
n (%)	62 (87)	47(73)	109 (81)
Mean (SD)	1.06 (1.263)	1.33 (1.431)	1.18 (1.338)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sasdate: 26JAN2022

	DMF(N=71)	IFN B-1a (N=64)	Total (N=135)
Week 72			
n (%)	60 (85)	41(64)	101 (75)
Mean (SD)	1.26 (1.367)	1.13 (1.006)	1.21 (1.229)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 84			
n (%)	56 (79)	39(61)	95 (70)
Mean (SD)	1.11 (1.334)	1.35 (1.226)	1.21 (1.289)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.75	1.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.0	0.0, 7.0
Week 96			
n (%)	54 (76)	39(61)	93 (69)
Mean (SD)	1.19 (1.195)	1.24 (1.135)	1.22 (1.164)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 5.5	0.0, 4.0	0.0, 5.5

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sasdate: 26JAN2022

109MS306_table40_CHG_HEDGESCI

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135)

Summary of EDSS Score by Visit - ITT Population

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12 Weeks	0	-0.344	0.345
24 Weeks	0.006	-0.347	0.359
36 Weeks	-0.165	-0.522	0.192
48 Weeks	0.017	-0.357	0.390
60 Weeks	-0.362	-0.744	0.020
72 Weeks	0.03	-0.367	0.427
84 Weeks	-0.27	-0.680	0.141
96 Weeks	-0.163	-0.576	0.249

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T40/109MS306_table40_CHG_HEDGESCI.sas date: 16FEB2022

109MS306_table40_CHG_LSMEANS

Table 40: Summary of EDSS Score by Visit – ITT Population, Aged 13 years and older (n=135)

Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135)

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
12	n (%)	69 (97)	61 (95)
	Lsmean (SE)	00.11 (0.094)	00.11 (0.100)
	Lsmean_95 % CI	(-0.072, 00.301)	(-0.091, 00.306)
	Diffrence (95% CI)	0.0068 (-0.243, 0.257)	
	SE_Difference	0.1263	
	p-value	0.9571	
24	n (%)	66 (93)	58 (91)
	Lsmean (SE)	00.19 (0.143)	00.18 (0.155)
	Lsmean_95 % CI	(-0.090, 00.477)	(-0.131, 00.481)
	Diffrence (95% CI)	0.018 (-0.360, 0.397)	
	SE_Difference	0.1913	
	p-value	0.9233	
36	n (%)	66 (93)	56 (88)
	Lsmean (SE)	00.01 (0.114)	00.14 (0.127)
	Lsmean_95 % CI	(-0.212, 00.238)	(-0.114, 00.389)
	Diffrence (95% CI)	-0.12 (-0.427, 0.178)	
	SE_Difference	0.1527	

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
	p-value	0.4152	
48	n (%)	63 (89)	49 (77)
	Lsmean (SE)	00.11 (0.125)	00.08 (0.140)
	Lsmean_95 % CI	(-0.139, 00.357)	(-0.193, 00.363)
	Diffrence (95% CI)	0.024 (-0.310, 0.359)	
	SE_Difference	0.1687	
	p-value	0.8849	
60	n (%)	62 (87)	47 (73)
	Lsmean (SE)	-0.07 (0.136)	00.29 (0.159)
	Lsmean_95 % CI	(-0.342, 00.197)	(-0.029, 00.602)
	Diffrence (95% CI)	-0.36 (-0.736, 0.0191)	
	SE_Difference	0.1904	
	p-value	0.0625	
72	n (%)	60 (85)	41 (64)
	Lsmean (SE)	00.03 (0.121)	-0.01 (0.148)
	Lsmean_95 % CI	(-0.208, 00.275)	(-0.303, 00.283)
	Diffrence (95% CI)	0.044 (-0.301, 0.389)	
	SE_Difference	0.1738	
	p-value	0.8014	

TIME POINTS	STATISTICS	DMF (N=71)	IFN B-1a (N=64)
84	n (%)	56 (79)	39 (61)
	Lsmean (SE)	-0.10 (0.148)	00.16 (0.185)
	Lsmean_95 % CI	(-0.399, 00.191)	(-0.211, 00.522)
	Diffrence (95% CI)	-0.26 (-0.692, 0.173)	
	SE_Difference	0.2178	
	p-value	0.2367	
96	n (%)	54 (76)	39 (61)
	Lsmean (SE)	-0.01 (0.135)	00.12 (0.166)
	Lsmean_95 % CI	(-0.273, 00.262)	(-0.212, 00.449)
	Diffrence (95% CI)	-0.12 (-0.517, 0.269)	
	SE_Difference	0.1977	
	p-value	0.5324	

Sub groups

Krankheitsschübe

109MS306_Table38_TTE_DESCRIBE_edsseq0

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0

	DMF (N=21)	IFN B-1A (N=19)	Total (N=40)
Number of subjects who relapsed	6 (29)	7 (37)	13 (33)
Number of relapse-free subjects (a)	15 (71)	12 (63)	27 (68)
Time to first relapse (weeks) (b)			
10th percentile	40.1	4.1	23.3
25th percentile	48.4	73.0	73.0
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	2 (9.8)	3 (15.8)	5 (12.6)
24 weeks, 95% CI	(2.5, 33.8)	(5.4, 41.3)	(5.4, 27.6)
48 weeks, n (%)	4 (19.8)	3 (15.8)	7 (17.7)
48 weeks, 95% CI	(7.9, 44.6)	(5.4, 41.3)	(8.9, 33.6)
72 weeks, n (%)	5 (25.1)	4 (21.8)	9 (23.3)
72 weeks, 95% CI	(11.3, 50.3)	(8.8, 48.3)	(12.8, 40.1)
96 weeks, n (%)	6 (30.9)	7 (40.9)	13 (35.7)
96 weeks, 95% CI	(15.1, 56.5)	(21.8, 67.7)	(22.4, 53.8)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented

NOTE 2. Numbers in parentheses are percentages

NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.

In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.

(a) Subjects who did not have a relapse, regardless of time in the study

(b) Based on Kaplan-Meier product limit method

(c) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior, divided by 3), age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value)

(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study

Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban040622.sas date: 13APR2022

	DMF (N=21)	IFN B-1A (N=19)	Total (N=40)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	18 (90.2)	16 (84.2)	34 (87.4)
24 weeks, 95% CI	(66.2, 97.5)	(58.7, 94.6)	(72.4, 94.6)
48 weeks, n (%)	15 (80.2)	16 (84.2)	30 (82.3)
48 weeks, 95% CI	(55.4, 92.1)	(58.7, 94.6)	(66.4, 91.1)
72 weeks, n (%)	13 (74.9)	13 (78.2)	26 (76.7)
72 weeks, 95% CI	(49.7, 88.7)	(51.7, 91.2)	(59.9, 87.2)
96 weeks, n (%)	8 (69.1)	5 (59.1)	13 (64.3)
96 weeks, 95% CI	(43.5, 84.9)	(32.3, 78.2)	(46.2, 77.6)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.896		
95% CI (c)(d)	(0.287, 2.795)		
p-value (c)(d)	0.8501		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented

NOTE 2. Numbers in parentheses are percentages

NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.

In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.

(a) Subjects who did not have a relapse, regardless of time in the study

(b) Based on Kaplan-Meier product limit method

(c) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior, divided by 3), age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value)

(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study

Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban040622.sas date: 13APR2022

109MS306_Table38_TTE_DESCRIBE_edssgt0

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0

	DMF (N=50)	IFN B-1A (N=45)	Total (N=95)
Number of subjects who relapsed	14 (28)	22 (49)	36 (38)
Number of relapse-free subjects (a)	36 (72)	23 (51)	59 (62)
Time to first relapse (weeks) (b)			
10th percentile	21.3	8.7	10.9
25th percentile	52.9	22.9	30.4
50th percentile (95% CI)	NA	92.3 (25.6, NA)	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA
Estimated n (%), 95% CI of subjects who relapsed at (b)			
24 weeks, n (%)	5 (10.4)	13 (31.2)	18 (20.0)
24 weeks, 95% CI	(4.5, 23.2)	(19.4, 47.7)	(13.1, 29.8)
48 weeks, n (%)	10 (20.8)	16 (38.9)	26 (29.2)
48 weeks, 95% CI	(11.8, 35.3)	(25.9, 55.6)	(20.9, 39.8)
72 weeks, n (%)	13 (27.4)	18 (44.5)	31 (35.3)
72 weeks, 95% CI	(16.9, 42.5)	(30.7, 61.2)	(26.3, 46.3)
96 weeks, n (%)	14 (29.6)	22 (56.7)	36 (41.6)
96 weeks, 95% CI	(18.7, 44.9)	(41.6, 72.8)	(32.0, 52.8)

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.

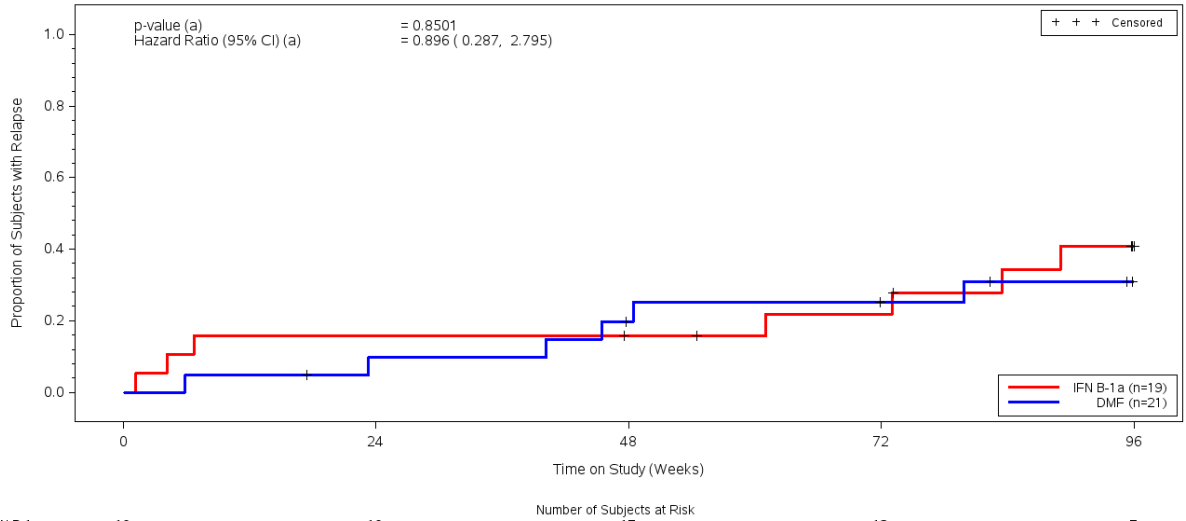
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior, divided by 3), age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value)
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban040622.sas date: 13APR2022

	DMF (N=50)	IFN B-1A (N=45)	Total (N=95)
Estimated n (%), 95% CI of subjects relapse-free at (b)			
24 weeks, n (%)	43 (89.6)	27 (68.8)	70 (80.0)
24 weeks, 95% CI	(76.8, 95.5)	(52.3, 80.6)	(70.2, 86.9)
48 weeks, n (%)	37 (79.2)	23 (61.1)	60 (70.8)
48 weeks, 95% CI	(64.7, 88.2)	(44.4, 74.1)	(60.2, 79.1)
72 weeks, n (%)	33 (72.6)	19 (55.5)	52 (64.7)
72 weeks, 95% CI	(57.5, 83.1)	(38.8, 69.3)	(53.7, 73.7)
96 weeks, n (%)	22 (70.4)	10 (43.3)	32 (58.4)
96 weeks, 95% CI	(55.1, 81.3)	(27.2, 58.4)	(47.2, 68.0)
Hazard ratio (DMF/IFN B-1a) (c)(d)	0.341		
95% CI (c)(d)	(0.167, 0.694)		
p-value (c)(d)	0.0030		

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
NOTE 3. For subjects who relapsed or were relapse-free, n represents the number of people at that timepoint who are at risk based on real observations.
The % is estimated from Kaplan-Meier and the moment you have censoring or no event, the % is not able to be estimated and thus represented with an NA.
In instances where there is an estimate at a previous timepoint, but not at the current timepoint, the n and % are carried forward.
(a) Subjects who did not have a relapse, regardless of time in the study
(b) Based on Kaplan-Meier product limit method
(c) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior, divided by 3), age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value)
(d) One subject in the DMF group was excluded due to missing number of relapses prior to the study
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-ef-tt-relapse_n=135_subgroups_ban040622.sas date: 13APR2022

109MS306_Table38_TTE_KMPLOT_edsseq0

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for EDSS equal to 0



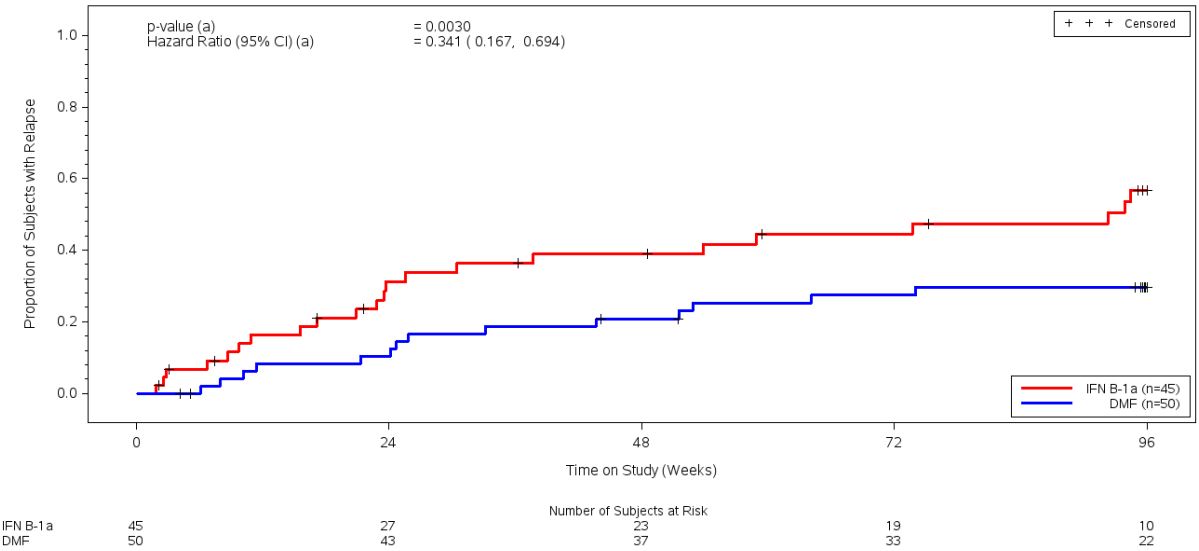
Number of Subjects at Risk

IFN B-1a	19	16	15	13	5
DMF	21	18	15	13	8

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2: Analysis from Kaplan-Meier product-limit method. One subject in the DMF group was excluded due to missing number of relapses prior to the study.
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS.
For age subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban040622.sas DATE: 15APR2022

109MS306_Table38_TTE_KMPLOT_edssgt0

Table 38: Analysis of time to first relapse - ITT Population, Aged 13 years and older (n=135) - KM Plot
Subgroup analysis for EDSS greater than 0



Number of Subjects at Risk

IFN B-1a	45	27	23	19	10
DMF	50	43	37	33	22

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented
NOTE 2: Analysis from Kaplan-Meier product-limit method. One subject in the DMF group was excluded due to missing number of relapses prior to the study.
(a) Based on Cox proportional hazards model, adjusted for baseline relapse rate (# of relapses in 3 years prior to study, divided by 3), age group and baseline EDSS.
For age subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table38_t-eff-relapse_kmplot_n=135_subgroups_ban040622.sas DATE: 15APR2022

109MS306_Table39_TTE_DESCRIBE_edsseq0

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Week 0-48			
Number of subjects with relapse	4 (19)	3 (16)	7 (18)
Number of subjects with relapses of			
0	17 (81)	16 (84)	33 (83)
1	4 (19)	2 (11)	6 (15)
2	0	1 (5)	1 (3)
3	0	0	0
>= 4	0	0	0
Total number of relapses	4	4	8
Total number of subject-years followed	17.99	17.16	35.15
Unadjusted annualized relapse rate (a)	0.222	0.233	0.228
Adjusted annualized relapse rate (b) (c)	<0.001	<0.001	
(95% CI) (b) (c)	(<0.001, <0.001)	(<0.001, <0.001)	
p-value (b) (c)	<0.0001	<0.0001	
Rate ratio (compared to IFN B-1a) (b) (c)	1.207		
(95% CI) (b) (c)	(0.271, 5.367)		
p-value (b) (c)	NA		
Subject relapse rate (e)			
n	21	19	40
Mean (SD)	0.517 (1.6705)	0.269 (0.6964)	0.399 (1.2925)
Median	0.000	0.000	0.000

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Q1, Q3	0.000, 0.000	0.000, 0.000	0.000, 0.000
Min, Max	0.00, 7.61	0.00, 2.66	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Week 48-96			
Number of subjects with relapse	2 (10)	5 (26)	7 (18)
Number of subjects with relapses of			
0	16 (76)	11 (58)	27 (68)
1	2 (10)	5 (26)	7 (18)
2	0	0	0
3	0	0	0
>= 4	0	0	0
Total number of relapses	2	5	7
Total number of subject-years followed	15.58	12.57	28.15
Unadjusted annualized relapse rate (a)	0.128	0.398	0.249
Adjusted annualized relapse rate (b) (c)	0.098	0.357	
(95% CI) (b) (c)	(0.020, 0.488)	(0.110, 1.160)	
p-value (b) (c)	0.0046	0.0866	
Rate ratio (compared to IFN B-1a) (b) (c)	0.274		
(95% CI) (b) (c)	(0.049, 1.547)		
p-value (b) (c)	0.1200		
Subject relapse rate (e)			
n	18	16	34
Mean (SD)	0.137 (0.4027)	1.794 (6.0341)	0.917 (4.1640)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.087	0.000, 0.000
Min, Max	0.00, 1.38	0.00, 24.35	0.00, 24.35

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Week 0-96			
Number of subjects with relapse	6 (29)	7 (37)	13 (33)
Number of subjects with relapses of			
0	15 (71)	12 (63)	27 (68)
1	6 (29)	5 (26)	11 (28)
2	0	2 (11)	2 (5)
3	0	0	0
>= 4	0	0	0
Total number of relapses	6	9	15
Total number of subject-years followed	33.57	29.73	63.29
Unadjusted annualized relapse rate (a)	0.179	0.303	0.237
Adjusted annualized relapse rate (b) (c)	0.112	0.173	
(95% CI) (b) (c)	(0.035, 0.357)	(0.055, 0.543)	
p-value (b) (c)	0.0002	0.0026	
Rate ratio (compared to IFN B-1a) (b) (c)	0.649		
(95% CI) (b) (c)	(0.225, 1.874)		
p-value (b) (c)	0.4199		
Relative risk (compared to IFN B-1a) (c) (d)	0.952		
(95% CI) (c) (d)	(0.393, 2.303)		
p-value (c) (d)	0.9128		
Subject relapse rate (e)			
n	21	19	40
Mean (SD)	0.495 (1.6479)	0.435 (0.7751)	0.467 (1.2926)
Median	0.000	0.000	0.000

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Q1, Q3	0.000, 0.543	0.000, 0.543	0.000, 0.543
Min, Max	0.00, 7.61	0.00, 2.66	0.00, 7.61

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

109MS306_Table39_TTE_DESCRIBE_edssgt0

Table 39: Summary of annualized relapse rate - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Week 0-48			
Number of subjects with relapse	10 (20)	16 (36)	26 (27)
Number of subjects with relapses of			
0	40 (80)	29 (64)	69 (73)
1	7 (14)	11 (24)	18 (19)
2	3 (6)	3 (7)	6 (6)
3	0	1 (2)	1 (1)
>= 4	0	1 (2)	1 (1)
Total number of relapses	13	25	38
Total number of subject-years followed	43.93	35.26	79.19
Unadjusted annualized relapse rate (a)	0.296	0.709	0.480
Adjusted annualized relapse rate (b) (c)	0.298	0.805	
(95% CI) (b) (c)	(0.152, 0.585)	(0.483, 1.340)	
p-value (b) (c)	0.0004	0.4036	
Rate ratio (compared to IFN B-1a) (b) (c)	0.370		
(95% CI) (b) (c)	(0.166, 0.828)		
p-value (b) (c)	0.0163		
Subject relapse rate (e)			
n	50	45	95
Mean (SD)	0.303 (0.6573)	0.836 (1.5538)	0.556 (1.1945)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.084	0.000, 1.084

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Min, Max	0.00, 2.17	0.00, 7.45	0.00, 7.45

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Week 48-96			
Number of subjects with relapse	9 (18)	13 (29)	22 (23)
Number of subjects with relapses of			
0	37 (74)	20 (44)	57 (60)
1	6 (12)	9 (20)	15 (16)
2	2 (4)	3 (7)	5 (5)
3	1 (2)	1 (2)	2 (2)
>= 4	0	0	0
Total number of relapses	13	18	31
Total number of subject-years followed	38.59	26.05	64.64
Unadjusted annualized relapse rate (a)	0.337	0.691	0.480
Adjusted annualized relapse rate (b) (c)	0.203	0.668	
(95% CI) (b) (c)	(0.086, 0.481)	(0.323, 1.378)	
p-value (b) (c)	0.0003	0.2743	
Rate ratio (compared to IFN B-1a) (b) (c)	0.304		
(95% CI) (b) (c)	(0.113, 0.819)		
p-value (b) (c)	0.0139		
Subject relapse rate (e)			
n	46	33	79
Mean (SD)	0.440 (1.0366)	1.197 (3.1123)	0.756 (2.1761)
Median	0.000	0.000	0.000
Q1, Q3	0.000, 0.000	0.000, 1.097	0.000, 1.087
Min, Max	0.00, 4.84	0.00, 17.39	0.00, 17.39

NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.

And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Week 0-96			
Number of subjects with relapse	14 (28)	22 (49)	36 (38)
Number of subjects with relapses of			
0	36 (72)	23 (51)	59 (62)
1	6 (12)	11 (24)	17 (18)
2	5 (10)	6 (13)	11 (12)
3	2 (4)	3 (7)	5 (5)
>= 4	1 (2)	2 (4)	3 (3)
Total number of relapses	26	43	69
Total number of subject-years followed	82.52	61.31	143.83
Unadjusted annualized relapse rate (a)	0.315	0.701	0.480
Adjusted annualized relapse rate (b) (c)	0.264	0.795	
(95% CI) (b) (c)	(0.144, 0.484)	(0.487, 1.296)	
p-value (b) (c)	<0.0001	0.3571	
Rate ratio (compared to IFN B-1a) (b) (c)	0.332		
(95% CI) (b) (c)	(0.161, 0.685)		
p-value (b) (c)	0.0034		
Relative risk (compared to IFN B-1a) (c) (d)	0.719		
(95% CI) (c) (d)	(0.465, 1.113)		
p-value (c) (d)	0.1392		
Subject relapse rate (e)			
n	50	45	95
Mean (SD)	0.361 (0.6749)	0.907 (1.4816)	0.620 (1.1576)
Median	0.000	0.000	0.000

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Q1, Q3	0.000, 0.543	0.000, 1.358	0.000, 1.085
Min, Max	0.00, 2.20	0.00, 7.45	0.00, 7.45

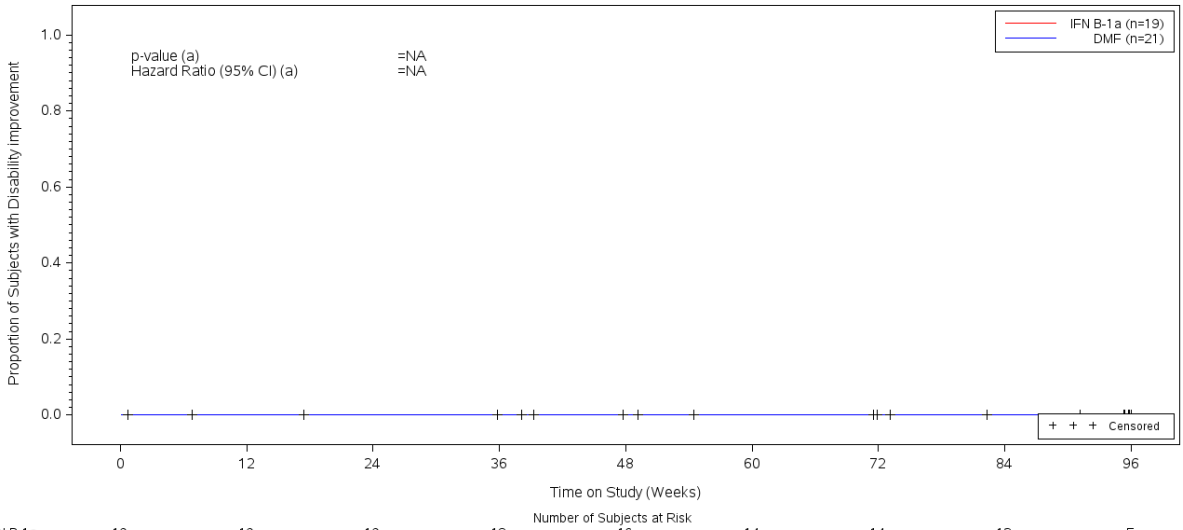
NOTE 1. Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm are presented
NOTE 2. Numbers in parentheses are percentages
(a) Total number of relapses that occurred during the study divided by the total number of suject-years followed in the study
(b) Estimated from a negative binomial regression model, adjusted for the baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
Baseline relapse rate is calculated as the number of relapses in three years prior to study entry divided by 3.
And when there is censoring or no event, the rate and CI are not able to be estimated and thus represented with an NA.
(c) One subject in the DMF group was excluded due to missing number of relapses prior to the study
(d) Estimated from log-binomial model, adjusted for baseline relapse rate, age group, baseline EDSS (except for EDSS=0 subgroup since all patients have same EDSS value.
(e) Number of relapses for each subject divided by the number of years followed in the study for that subject
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table39_t-ef-arr_n=135_subgroups_ban050922.sas date: 09MAY2022

Behinderung

Behinderungsverbesserung

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_edsseq0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for EDSS equal to 0



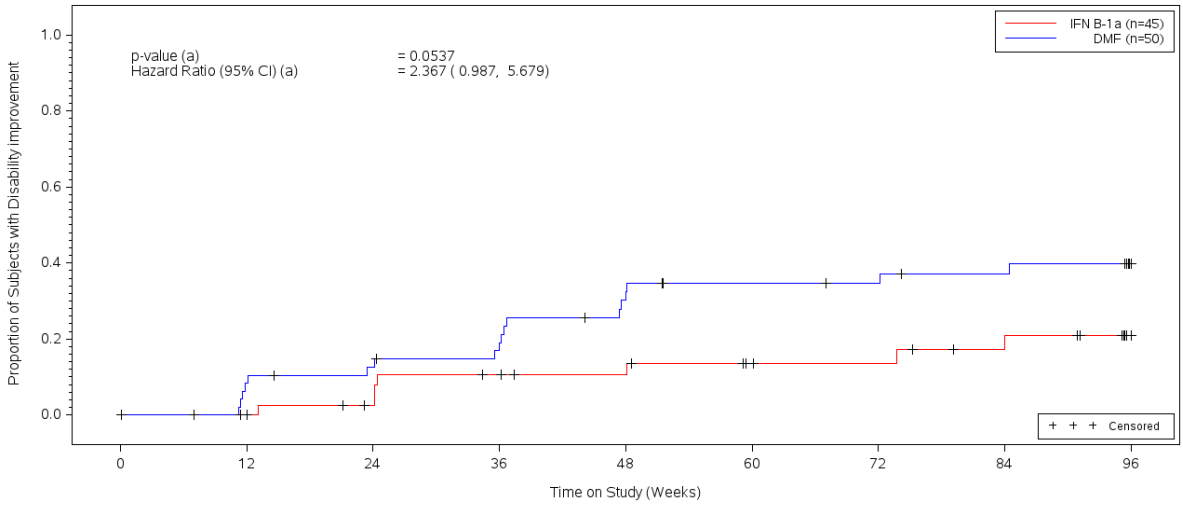
Number of Subjects at Risk

IFN B-1a	19	19	19	18	16	14	14	13	5
DMF	21	19	18	18	17	17	15	14	7

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Plot uses Kaplan-Meier product-limit method. Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group. For AGE subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban04APR2022.TXT 29APR2022

109MS306_Table51_TTE_improvement_12WKS_KMPLOT_edssgt0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12 weeks - ITT population, Aged 13 years and older (n=135)
Subgroup analysis for EDSS greater than 0



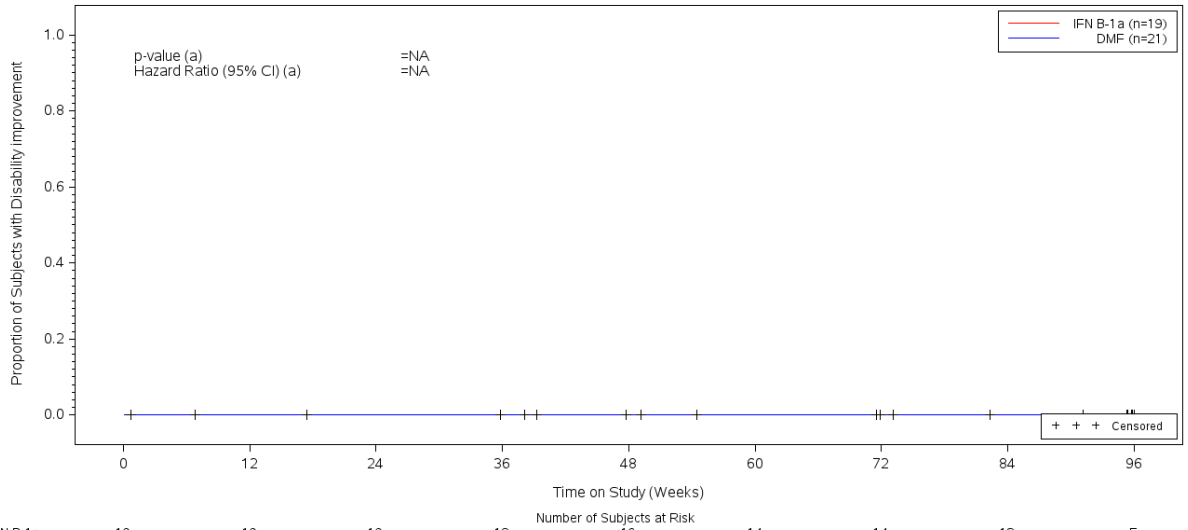
Number of Subjects at Risk

IFN B-1a	45	39	34	31	29	25	25	21	4
DMF	50	43	40	36	29	27	25	24	7

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Plot uses Kaplan-Meier product-limit method. Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group. For AGE subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban04.sas 29APR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_edsseq0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for EDSS equal to 0



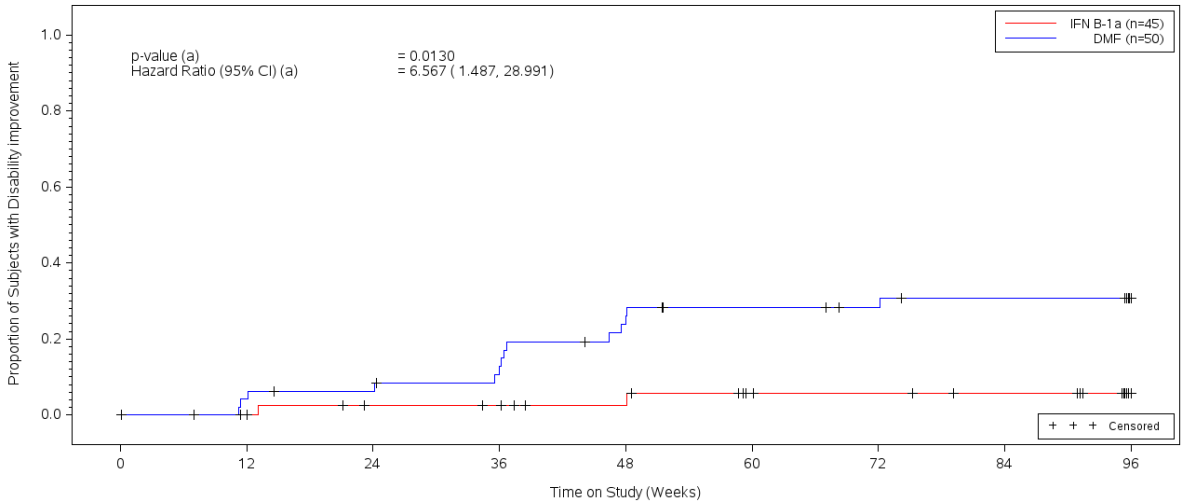
Number of Subjects at Risk

IFN B-1a	19	19	19	18	16	14	14	13	5
DMF	21	19	18	18	17	17	15	14	7

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Plot uses Kaplan-Meier product-limit method. Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group. For AGE subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban04.sas DATE: 29APR2022

109MS306_Table51_TTE_improvement_24WKS_KMPLOT_edssgt0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 24 weeks - ITT population, Aged 13 years and older (n=135)
Analysis for EDSS greater than 0



Number of Subjects at Risk

IFN B-1a	45	39	36	34	31	26	26	24	5
DMF	50	45	43	39	32	30	27	26	9

NOTE 1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup and >=10 events in at least one subgroup in at least one arm are presented.
NOTE 2: Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
NOTE 3: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Plot uses Kaplan-Meier product-limit method. Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group. For AGE subgroup analyses, we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/output/programs/109MS306_table51_tt_kmplot_disability_improvement_n=135_subgroups_ban04.sas 29APR2022

109MS306_Table51_TTE_improvement_DESCRIBE_edsseq0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	0	0	0
Number of subjects without confirmed improvement of disability (a)	21 (100)	19 (100)	40 (100)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score

from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	0 (0.0)	(NA)	0 (0.0)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	0 (0.0)	(NA)	0 (0.0)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
84 weeks, 95% CI	NA	NA	NA
96 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
96 weeks, 95% CI	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	19 (NA)	(NA)	38 (NA)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	18 (NA)	(NA)	37 (NA)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	18 (NA)	18 (NA)	36 (NA)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	17 (NA)	16 (NA)	33 (NA)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	17 (NA)	14 (NA)	31 (NA)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	15 (NA)	14 (NA)	29 (NA)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	14 (NA)	13 (NA)	27 (NA)
84 weeks, 95% CI	NA	NA	NA
96 weeks, n (%)	7 (NA)	5 (NA)	12 (NA)
96 weeks, 95% CI	NA	NA	NA
Hazard ratio (DMF vs IFN B-1a) (c)	NA		
95% CI (c)	(NA, NA)		
p-value (c)	NA		
Relative risk (DMF vs IFN B-1a) (d)	NA		
(95% CI) (d)	(NA, NA)		
p-value (d)	NA		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=21)	**IFN B-1a (N=19)**	**Total (N=40)**
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	0	0	0
Number of subjects without confirmed improvement of disability (a)	21 (100)	19 (100)	40 (100)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	NA	NA	NA
25th percentile	NA	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.

(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	0 (0.0)	(NA)	0 (0.0)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	0 (0.0)	(NA)	0 (0.0)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
84 weeks, 95% CI	NA	NA	NA
96 weeks, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
96 weeks, 95% CI	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	19 (NA)	(NA)	38 (NA)
12 weeks, 95% CI	NA	NA	NA
24 weeks, n (%)	18 (NA)	(NA)	37 (NA)
24 weeks, 95% CI	NA	NA	NA
36 weeks, n (%)	18 (NA)	18 (NA)	36 (NA)
36 weeks, 95% CI	NA	NA	NA
48 weeks, n (%)	17 (NA)	16 (NA)	33 (NA)
48 weeks, 95% CI	NA	NA	NA
60 weeks, n (%)	17 (NA)	14 (NA)	31 (NA)
60 weeks, 95% CI	NA	NA	NA
72 weeks, n (%)	15 (NA)	14 (NA)	29 (NA)
72 weeks, 95% CI	NA	NA	NA
84 weeks, n (%)	14 (NA)	13 (NA)	27 (NA)
84 weeks, 95% CI	NA	NA	NA
96 weeks, n (%)	7 (NA)	5 (NA)	12 (NA)
96 weeks, 95% CI	NA	NA	NA
Hazard ratio (DMF vs IFN B-1a) (c)	NA		
95% CI (c)	(NA, NA)		
p-value (c)	NA		
Relative risk (DMF vs IFN B-1a) (d)	NA		
(95% CI) (d)	(NA, NA)		
p-value (d)	NA		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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109MS306_Table51_TTE_improvement_DESCRIBE_edssgt0

Table 51: Time to confirmed disability improvement, measured by a decrease in EDSS score, sustained for 12, 24 weeks - ITT population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 12 WEEKS			
Number of subjects with confirmed improvement of disability (a)	18 (36)	7 (16)	25 (26)
Number of subjects without confirmed improvement of disability (a)	32 (64)	38 (84)	70 (74)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	12.1	24.4	24.1
25th percentile	36.7	NA	48.1
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score

from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table51_main_edss_disability_improvement_n=135_subgroups_ban051222.sas date: 12MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	5 (10.4)	0 (0.0)	5 (5.7)
12 weeks, 95% CI	(4.5, 23.2)	NA	(2.4, 13.1)
24 weeks, n (%)	7 (14.7)	3 (8.0)	10 (11.6)
24 weeks, 95% CI	(7.3, 28.4)	(2.6, 22.7)	(6.4, 20.5)
36 weeks, n (%)	10 (21.2)	4 (10.7)	14 (16.5)
36 weeks, 95% CI	(12.0, 35.9)	(4.1, 26.0)	(10.1, 26.3)
48 weeks, n (%)	16 (34.6)	5 (13.7)	21 (25.4)
48 weeks, 95% CI	(22.8, 50.2)	(5.9, 29.8)	(17.3, 36.3)
60 weeks, n (%)	16 (34.6)	5 (13.7)	21 (25.4)
60 weeks, 95% CI	(22.8, 50.2)	(5.9, 29.8)	(17.3, 36.3)
72 weeks, n (%)	17 (37.2)	5 (13.7)	22 (26.9)
72 weeks, 95% CI	(24.9, 52.9)	(5.9, 29.8)	(18.5, 38.0)
84 weeks, n (%)	17 (37.2)	7 (20.9)	24 (29.9)
84 weeks, 95% CI	(24.9, 52.9)	(10.4, 39.3)	(21.1, 41.4)
96 weeks, n (%)	18 (39.8)	7 (20.9)	25 (31.5)
96 weeks, 95% CI	(27.1, 55.6)	(10.4, 39.3)	(22.4, 43.1)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	43 (89.6)	39 (NA)	82 (94.3)
12 weeks, 95% CI	(76.8, 95.5)	NA	(86.9, 97.6)
24 weeks, n (%)	40 (85.3)	34 (92.0)	74 (88.4)
24 weeks, 95% CI	(71.6, 92.7)	(77.3, 97.4)	(79.5, 93.6)
36 weeks, n (%)	36 (78.8)	31 (89.3)	67 (83.5)
36 weeks, 95% CI	(64.1, 88.0)	(74.0, 95.9)	(73.7, 89.9)
48 weeks, n (%)	29 (65.4)	29 (86.3)	58 (74.6)
48 weeks, 95% CI	(49.8, 77.2)	(70.2, 94.1)	(63.7, 82.7)
60 weeks, n (%)	27 (65.4)	25 (86.3)	52 (74.6)
60 weeks, 95% CI	(49.8, 77.2)	(70.2, 94.1)	(63.7, 82.7)
72 weeks, n (%)	25 (62.8)	25 (86.3)	50 (73.1)
72 weeks, 95% CI	(47.1, 75.1)	(70.2, 94.1)	(62.0, 81.5)
84 weeks, n (%)	24 (62.8)	21 (79.1)	45 (70.1)
84 weeks, 95% CI	(47.1, 75.1)	(60.7, 89.6)	(58.6, 78.9)
96 weeks, n (%)	7 (60.2)	4 (79.1)	11 (68.5)
96 weeks, 95% CI	(44.4, 72.9)	(60.7, 89.6)	(56.9, 77.6)
Hazard ratio (DMF vs IFN B-1a) (c)	2.367		
95% CI (c)	(0.987, 5.679)		
p-value (c)	0.0537		
Relative risk (DMF vs IFN B-1a) (d)	2.333		
(95% CI) (d)	(1.080, 5.038)		
p-value (d)	0.0310		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
CONFIRMED DISABILITY IMPROVEMENT SUSTAINED FOR 24 WEEKS			
Number of subjects with confirmed improvement of disability (a)	14 (28)	2 (4)	16 (17)
Number of subjects without confirmed improvement of disability (a)	36 (72)	43 (96)	79 (83)
Time to confirmed improvement of disability (weeks) (b)			
10th percentile	35.6	NA	36.4
25th percentile	48.0	NA	NA
50th percentile (95% CI)	NA	NA	NA
75th percentile	NA	NA	NA
90th percentile	NA	NA	NA

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.

(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Estimated n (%), 95% CI of subjects with confirmed improvement of disability at (b)			
12 weeks, n (%)	3 (6.3)	0 (0.0)	3 (3.4)
12 weeks, 95% CI	(2.1, 18.1)	NA	(1.1, 10.2)
24 weeks, n (%)	4 (8.4)	1 (2.6)	5 (5.7)
24 weeks, 95% CI	(3.2, 20.8)	(0.4, 16.8)	(2.4, 13.2)
36 weeks, n (%)	7 (14.9)	1 (2.6)	8 (9.4)
36 weeks, 95% CI	(7.4, 28.8)	(0.4, 16.8)	(4.8, 18.0)
48 weeks, n (%)	13 (28.3)	2 (5.6)	15 (18.4)
48 weeks, 95% CI	(17.5, 43.7)	(1.4, 20.7)	(11.5, 28.7)
60 weeks, n (%)	13 (28.3)	2 (5.6)	15 (18.4)
60 weeks, 95% CI	(17.5, 43.7)	(1.4, 20.7)	(11.5, 28.7)
72 weeks, n (%)	14 (30.8)	2 (5.6)	16 (19.9)
72 weeks, 95% CI	(19.5, 46.5)	(1.4, 20.7)	(12.6, 30.5)
84 weeks, n (%)	14 (30.8)	2 (5.6)	16 (19.9)
84 weeks, 95% CI	(19.5, 46.5)	(1.4, 20.7)	(12.6, 30.5)
96 weeks, n (%)	14 (30.8)	2 (5.6)	16 (19.9)
96 weeks, 95% CI	(19.5, 46.5)	(1.4, 20.7)	(12.6, 30.5)

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.

(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Estimated n (%), 95% CI of subjects without confirmed improvement of disability at (b)			
12 weeks, n (%)	45 (93.7)	39 (NA)	84 (96.6)
12 weeks, 95% CI	(81.9, 97.9)	NA	(89.8, 98.9)
24 weeks, n (%)	43 (91.6)	36 (97.4)	79 (94.3)
24 weeks, 95% CI	(79.2, 96.8)	(83.2, 99.6)	(86.8, 97.6)
36 weeks, n (%)	39 (85.1)	34 (97.4)	73 (90.6)
36 weeks, 95% CI	(71.2, 92.6)	(83.2, 99.6)	(82.0, 95.2)
48 weeks, n (%)	32 (71.7)	31 (94.4)	63 (81.6)
48 weeks, 95% CI	(56.3, 82.5)	(79.3, 98.6)	(71.3, 88.5)
60 weeks, n (%)	30 (71.7)	26 (94.4)	56 (81.6)
60 weeks, 95% CI	(56.3, 82.5)	(79.3, 98.6)	(71.3, 88.5)
72 weeks, n (%)	27 (69.2)	26 (94.4)	53 (80.1)
72 weeks, 95% CI	(53.5, 80.5)	(79.3, 98.6)	(69.5, 87.4)
84 weeks, n (%)	26 (69.2)	24 (94.4)	50 (80.1)
84 weeks, 95% CI	(53.5, 80.5)	(79.3, 98.6)	(69.5, 87.4)
96 weeks, n (%)	9 (69.2)	5 (94.4)	14 (80.1)
96 weeks, 95% CI	(53.5, 80.5)	(79.3, 98.6)	(69.5, 87.4)
Hazard ratio (DMF vs IFN B-1a) (c)	6.567		
95% CI (c)	(1.487, 28.991)		
p-value (c)	0.0130		
Relative risk (DMF vs IFN B-1a) (d)	6.374		
(95% CI) (d)	(1.540, 26.38)		
p-value (d)	0.0106		

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and >=10 events in at least one subgroup in at least one arm are presented.
NOTE2: For subjects who improved or without improvement, n is # of people at timepoint at risk based on real observations. % estimated from KM and when have censoring or no event, % is not able to be estimated and represented with NA. When an estimate is at previous timepoint, but not at current timepoint, n and % are carried forward.
(a) Disability improvement is defined as at least a one-point decrease in the EDSS score from a baseline EDSS of 0 to 5, or at least a 0.5 point decrease in the EDSS score from a baseline EDSS of 5.5, sustained for 12 or 24 weeks. Sustained improvement can start where a relapse is occurring but is confirmed only in a relapse-free period.
(b) Time to disability improvement and estimated proportion of subjects with disability improvement are based on Kaplan-Meier product limit method.
(c) Hazard ratio (HR), 95% CI and p-value are based on Cox proportional hazards model, adjusted for baseline EDSS score and age group.
(d) Relative risk (RR), 95% CI and p-value are based on log-binomial model, adjusted for baseline EDSS score and age group. When model does not converge, RR is NA.
In AGE subgroup analyses for HR and RR , we did NOT include age as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
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EDSS-Wert

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_EDSSBL_EQZERO

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF(N=21)	IFN B-1a (N=19)	Total (N=40)
Week 12 change from baseline			
n (%)	21 (100)	19(100)	40 (100)
Mean (SD)	0.50 (0.775)	0.37 (0.761)	0.44 (0.761)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 2.0	0.0, 3.0
Week 24 change from baseline			
n (%)	18 (86)	19(100)	37 (93)
Mean (SD)	0.67 (0.985)	0.16 (0.501)	0.41 (0.807)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 3.0	0.0, 2.0	0.0, 3.0
Week 36 change from baseline			
n (%)	19 (90)	19(100)	38 (95)
Mean (SD)	0.32 (0.691)	0.34 (0.708)	0.33 (0.690)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 2.5	0.0, 2.0	0.0, 2.5
Week 48 change from baseline			
n (%)	18 (86)	16(84)	34 (85)
Mean (SD)	0.67 (0.970)	0.25 (0.775)	0.47 (0.896)
Median	0.00	0.00	0.00

	DMF(N=21)	**IFN B-1a (N=19)**	**Total (N=40)**
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 05APR2022

	DMF(N=21)	IFN B-1a (N=19)	Total (N=40)
Week 60 change from baseline			
n (%)	18 (86)	15(79)	33 (83)
Mean (SD)	0.53 (0.737)	0.23 (0.623)	0.39 (0.693)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 2.0
Week 72 change from baseline			
n (%)	17 (81)	13(68)	30 (75)
Mean (SD)	0.29 (0.588)	0.35 (0.851)	0.32 (0.701)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 2.0	0.0, 2.5	0.0, 2.5
Week 84 change from baseline			
n (%)	16 (76)	12(63)	28 (70)
Mean (SD)	0.31 (0.793)	1.04 (1.738)	0.63 (1.310)
Median	0.00	0.50	0.00
Q1, Q3	0.00, 0.00	0.00, 1.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 6.0	0.0, 6.0
Week 96 change from baseline			
n (%)	15 (71)	13(68)	28 (70)
Mean (SD)	0.47 (0.972)	0.42 (0.862)	0.45 (0.906)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.50
Min, Max	0.0, 3.5	0.0, 2.5	0.0, 3.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 05APR2022

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_EDSSBL_GTZERO

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF(N=50)	IFN B-1a (N=45)	Total (N=95)
Week 12 change from baseline			
n (%)	48 (96)	42(93)	90 (95)
Mean (SD)	-0.04 (0.626)	0.01 (0.703)	-0.02 (0.660)
Median	0.00	0.00	0.00
Q1, Q3	-0.25, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 2.0	-2.0, 2.5	-2.0, 2.5
Week 24 change from baseline			
n (%)	48 (96)	39(87)	87 (92)
Mean (SD)	0.03 (0.890)	0.22 (1.380)	0.11 (1.133)
Median	0.00	0.00	0.00
Q1, Q3	-0.25, 0.50	0.00, 0.00	0.00, 0.50
Min, Max	-2.0, 2.5	-2.0, 5.5	-2.0, 5.5
Week 36 change from baseline			
n (%)	47 (94)	37(82)	84 (88)
Mean (SD)	-0.10 (0.764)	0.07 (1.001)	-0.02 (0.874)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-2.0, 2.0	-2.0, 2.5	-2.0, 2.5
Week 48 change from baseline			
n (%)	45 (90)	33(73)	78 (82)
Mean (SD)	-0.09 (0.894)	0.05 (0.743)	-0.03 (0.831)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-1.5, 2.5	-2.0, 2.0	-2.0, 2.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 05APR2022

	DMF(N=50)	IFN B-1a (N=45)	Total (N=95)
Week 60 change from baseline			
n (%)	44 (88)	32(71)	76 (80)
Mean (SD)	-0.39 (0.769)	0.23 (1.295)	-0.13 (1.062)
Median	-0.25	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-1.00, 0.00
Min, Max	-2.0, 2.0	-1.5, 5.0	-2.0, 5.0
Week 72 change from baseline			
n (%)	43 (86)	28(62)	71 (75)
Mean (SD)	-0.05 (0.918)	-0.13 (0.857)	-0.08 (0.889)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.50	0.00, 0.00	-0.50, 0.00
Min, Max	-2.0, 2.5	-2.0, 2.0	-2.0, 2.5
Week 84 change from baseline			
n (%)	40 (80)	27(60)	67 (71)
Mean (SD)	-0.24 (0.855)	-0.17 (0.820)	-0.21 (0.836)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	-0.50, 0.00	-0.50, 0.00
Min, Max	-2.5, 2.0	-2.0, 2.0	-2.5, 2.0
Week 96 change from baseline			
n (%)	39 (78)	26(58)	65 (68)
Mean (SD)	-0.21 (1.087)	0.00 (0.735)	-0.12 (0.960)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-5.0, 2.5	-2.0, 2.0	-5.0, 2.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 05APR2022

109MS306_table40_CHG_DESCRIBE_EDSSBL_EQZERO

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF(N=21)	IFN B-1a (N=19)	Total (N=40)
Baseline			
n (%)	21 (100)	19(100)	40 (100)
Mean (SD)	0.00 (0.000)	0.00 (0.000)	0.00 (0.000)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 0.0	0.0, 0.0	0.0, 0.0
Week 12			
n (%)	21 (100)	19(100)	40 (100)
Mean (SD)	0.50 (0.775)	0.37 (0.761)	0.44 (0.761)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 2.0	0.0, 3.0
Week 24			
n (%)	18 (86)	19(100)	37 (93)
Mean (SD)	0.67 (0.985)	0.16 (0.501)	0.41 (0.807)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 3.0	0.0, 2.0	0.0, 3.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

	DMF(N=21)	IFN B-1a (N=19)	Total (N=40)
Week 36			
n (%)	19 (90)	19(100)	38 (95)
Mean (SD)	0.32 (0.691)	0.34 (0.708)	0.33 (0.690)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 2.5	0.0, 2.0	0.0, 2.5
Week 48			
n (%)	18 (86)	16(84)	34 (85)
Mean (SD)	0.67 (0.970)	0.25 (0.775)	0.47 (0.896)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0
Week 60			
n (%)	18 (86)	15(79)	33 (83)
Mean (SD)	0.53 (0.737)	0.23 (0.623)	0.39 (0.693)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 1.00
Min, Max	0.0, 2.0	0.0, 2.0	0.0, 2.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

	DMF(N=21)	IFN B-1a (N=19)	Total (N=40)
Week 72			
n (%)	17 (81)	13(68)	30 (75)
Mean (SD)	0.29 (0.588)	0.35 (0.851)	0.32 (0.701)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	0.0, 2.0	0.0, 2.5	0.0, 2.5
Week 84			
n (%)	16 (76)	12(63)	28 (70)
Mean (SD)	0.31 (0.793)	1.04 (1.738)	0.63 (1.310)
Median	0.00	0.50	0.00
Q1, Q3	0.00, 0.00	0.00, 1.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 6.0	0.0, 6.0
Week 96			
n (%)	15 (71)	13(68)	28 (70)
Mean (SD)	0.47 (0.972)	0.42 (0.862)	0.45 (0.906)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.50
Min, Max	0.0, 3.5	0.0, 2.5	0.0, 3.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

109MS306_table40_CHG_DESCRIBE_EDSSBL_GTZERO

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF(N=50)	IFN B-1a (N=45)	Total (N=95)
Baseline			
n (%)	50 (100)	45(100)	95 (100)
Mean (SD)	1.64 (0.892)	1.64 (0.720)	1.64 (0.811)
Median	1.50	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	1.0, 5.0	1.0, 4.0	1.0, 5.0
Week 12			
n (%)	48 (96)	42(93)	90 (95)
Mean (SD)	1.60 (1.211)	1.61 (0.914)	1.61 (1.077)
Median	1.25	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 24			
n (%)	48 (96)	39(87)	87 (92)
Mean (SD)	1.68 (1.374)	1.83 (1.439)	1.75 (1.397)
Median	1.00	1.50	1.50
Q1, Q3	1.00, 2.25	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

	DMF(N=50)	IFN B-1a (N=45)	Total (N=95)
Week 36			
n (%)	47 (94)	37(82)	84 (88)
Mean (SD)	1.56 (1.284)	1.70 (1.151)	1.63 (1.222)
Median	1.50	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 48			
n (%)	45 (90)	33(73)	78 (82)
Mean (SD)	1.57 (1.429)	1.67 (0.997)	1.61 (1.258)
Median	1.50	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 60			
n (%)	44 (88)	32(71)	76 (80)
Mean (SD)	1.28 (1.370)	1.84 (1.417)	1.52 (1.408)
Median	1.00	1.50	1.25
Q1, Q3	0.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

	DMF(N=50)	IFN B-1a (N=45)	Total (N=95)
Week 72			
n (%)	43 (86)	28(62)	71 (75)
Mean (SD)	1.64 (1.403)	1.50 (0.861)	1.58 (1.213)
Median	1.50	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 84			
n (%)	40 (80)	27(60)	67 (71)
Mean (SD)	1.43 (1.380)	1.48 (0.925)	1.45 (1.210)
Median	1.00	1.50	1.00
Q1, Q3	0.50, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 96			
n (%)	39 (78)	26(58)	65 (68)
Mean (SD)	1.47 (1.164)	1.65 (1.037)	1.55 (1.110)
Median	1.50	1.50	1.50
Q1, Q3	1.00, 2.00	1.00, 2.00	1.00, 2.00
Min, Max	0.0, 5.5	0.0, 4.0	0.0, 5.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 05APR2022

109MS306_table40_CHG_HEDGESCI_EDSSBL_EQZERO

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	0.074	-0.498	0.646
24	0.254	-0.346	0.855
36	-0.083	-0.681	0.515
48	0.179	-0.459	0.817
60	0.098	-0.542	0.738
72	-0.146	-0.816	0.524
84	-0.249	-0.942	0.444
96	0.008	-0.677	0.693

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_HEDGESCI_SubGr.sas date: 05APR2022

109MS306_table40_CHG_HEDGESCI_EDSSBL_GTZERO

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	-0.085	-0.482	0.312
24	-0.091	-0.495	0.313
36	-0.164	-0.579	0.251
48	-0.186	-0.617	0.245
60	-0.371	-0.810	0.068
72	0.054	-0.400	0.508
84	-0.152	-0.617	0.313
96	-0.099	-0.573	0.374

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_HEDGESCI_SubGr.sas date: 05APR2022

109MS306_table40_CHG_LSMEANS_EDSSBL_EQZERO

Table 40: Summary of EDSS Score by Visit ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

TIME POINTS		DMF(N=21)	IFN B-1a (N=19)
12	n (%)	21 (100)	19 (100)
	Lsmean (SE)	0.50 (0.168)	0.37 (0.176)
	Lsmean_95 % CI	(0.161, 0.839)	(0.012, 0.725)
	Diffrence (95% CI)	0.13 (-0.361, 0.624)	
	SE_Difference	0.2432	
	p-value	0.5917	
24	n (%)	18 (86)	19 (100)
	Lsmean (SE)	0.67 (0.183)	0.16 (0.178)
	Lsmean_95 % CI	(0.296, 1.038)	(-0.203, 0.519)
	Diffrence (95% CI)	0.51 (-0.0088, 1.026)	
	SE_Difference	0.2549	
	p-value	0.0538	
36	n (%)	19 (90)	19 (100)
	Lsmean (SE)	0.32 (0.161)	0.34 (0.161)
	Lsmean_95 % CI	(-0.010, 0.641)	(0.016, 0.668)
	Diffrence (95% CI)	-0.026 (-0.487, 0.434)	
	SE_Difference	0.2271	
	p-value	0.9084	
48	n (%)	18 (86)	16 (84)
	Lsmean (SE)	0.67 (0.208)	0.25 (0.221)
	Lsmean_95 % CI	(0.242, 1.091)	(-0.200, 0.700)
	Diffrence (95% CI)	0.42 (-0.202, 1.035)	
	SE_Difference	0.3037	
	p-value	0.1796	

TIME POINTS		DMF(N=21)	IFN B-1a (N=19)
60	n (%)	18 (86)	15 (79)
	Lsmean (SE)	0.53 (0.162)	0.23 (0.178)
	Lsmean_95 % CI	(0.197, 0.858)	(-0.129, 0.596)
	Diffrence (95% CI)	0.29 (-0.196, 0.785)	
	SE_Difference	0.2405	
	p-value	0.2300	
72	n (%)	17 (81)	13 (68)
	Lsmean (SE)	0.29 (0.173)	0.35 (0.198)
	Lsmean_95 % CI	(-0.060, 0.648)	(-0.059, 0.751)
	Diffrence (95% CI)	-0.052 (-0.590, 0.486)	
	SE_Difference	0.2626	
	p-value	0.8443	
84	n (%)	16 (76)	12 (63)
	Lsmean (SE)	0.31 (0.320)	1.04 (0.370)
	Lsmean_95 % CI	(-0.346, 0.971)	(0.282, 1.802)
	Diffrence (95% CI)	-0.73 (-1.735, 0.276)	
	SE_Difference	0.4892	
	p-value	0.1481	
96	n (%)	15 (71)	13 (68)
	Lsmean (SE)	0.47 (0.238)	0.42 (0.256)
	Lsmean_95 % CI	(-0.023, 0.957)	(-0.103, 0.949)
	Diffrence (95% CI)	0.044 (-0.675, 0.763)	
	SE_Difference	0.3498	
	p-value	0.9018	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.

Note3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable).
Note4: Treatment group, age group and baseline EDSS score were as covariates.
Note5: For age sugroup analyses, we did NOT include AGE as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 14MAY2022

109MS306_table40_CHG_LSMEANS_EDSSBL_GTZERO

Table 40: Summary of EDSS Score by Visit ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

TIME POINTS		DMF(N=50)	IFN B-1a (N=45)
12	n (%)	48 (96)	42 (93)
	Lsmean (SE)	-0.04 (0.096)	0.01 (0.102)
	Lsmean_95 % CI	(-0.232, 0.148)	(-0.191, 0.215)
	Diffrence (95% CI)	-0.054 (-0.332, 0.225)	
	SE_Difference	0.1400	
	p-value	0.7030	
24	n (%)	48 (96)	39 (87)
	Lsmean (SE)	0.03 (0.164)	0.22 (0.182)
	Lsmean_95 % CI	(-0.295, 0.357)	(-0.144, 0.579)
	Diffrence (95% CI)	-0.19 (-0.673, 0.300)	
	SE_Difference	0.2448	
	p-value	0.4478	
36	n (%)	47 (94)	37 (82)
	Lsmean (SE)	-0.10 (0.128)	0.07 (0.144)
	Lsmean_95 % CI	(-0.350, 0.158)	(-0.219, 0.354)
	Diffrence (95% CI)	-0.16 (-0.546, 0.220)	
	SE_Difference	0.1925	
	p-value	0.3987	
48	n (%)	45 (90)	33 (73)
	Lsmean (SE)	-0.09 (0.124)	0.05 (0.145)
	Lsmean_95 % CI	(-0.336, 0.159)	(-0.244, 0.335)
	Diffrence (95% CI)	-0.13 (-0.515, 0.246)	
	SE_Difference	0.1911	
	p-value	0.4841	

TIME POINTS		DMF(N=50)	IFN B-1a (N=45)
60	n (%)	44 (88)	32 (71)
	Lsmean (SE)	-0.39 (0.154)	0.23 (0.181)
	Lsmean_95 % CI	(-0.694, -0.079)	(-0.126, 0.595)
	Diffrence (95% CI)	-0.62 (-1.094, -0.147)	
	SE_Difference	0.2376	
	p-value	0.0109	
72	n (%)	43 (86)	28 (62)
	Lsmean (SE)	-0.05 (0.136)	-0.13 (0.169)
	Lsmean_95 % CI	(-0.319, 0.226)	(-0.462, 0.212)
	Diffrence (95% CI)	0.078 (-0.355, 0.512)	
	SE_Difference	0.2172	
	p-value	0.7190	
84	n (%)	40 (80)	27 (60)
	Lsmean (SE)	-0.24 (0.133)	-0.17 (0.162)
	Lsmean_95 % CI	(-0.503, 0.028)	(-0.490, 0.157)
	Diffrence (95% CI)	-0.071 (-0.489, 0.348)	
	SE_Difference	0.2095	
	p-value	0.7364	
96	n (%)	39 (78)	26 (58)
	Lsmean (SE)	-0.21 (0.154)	0.00 (0.189)
	Lsmean_95 % CI	(-0.513, 0.103)	(-0.377, 0.377)
	Diffrence (95% CI)	-0.21 (-0.692, 0.282)	
	SE_Difference	0.2437	
	p-value	0.4031	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.

Note3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable).
Note4: Treatment group, age group and baseline EDSS score were as covariates.
Note5: For age sugroup analyses, we did NOT include AGE as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 14MAY2022

BVMT-R

MCID

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having a MCID of 15% of the total score when comparing each timepoint to basline score by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
Trial 2 Week 48 >=15% increase from baseline	Effect measure	1.458	1.250	0.091
	95% CI	(0.264, 8.048)	(0.453, 3.449)	(-0.318, 0.500)
	p-value	0.6651	0.6665	0.6632
Trial 3 Week 48 >=15% increase from baseline	Effect measure	0.656	0.750	-0.091
	95% CI	(0.108, 4.003)	(0.217, 2.597)	(-0.478, 0.296)
	p-value	0.6480	0.6498	0.6456

NOTE1: To create YES/NO event variables, we calculated timepoint score minus basline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table52_MCID_15PCT_EFFECTMEASURES_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having a MCID of 15% of the total score when comparing each timepoint to basline score by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
Trial 2 Week 48 >=15% increase from baseline	Effect measure	0.415	0.552	-0.190
	95% CI	(0.131, 1.310)	(0.251, 1.214)	(-0.433, 0.053)
	p-value	0.1337	0.1392	0.1257
Trial 3 Week 48 >=15% increase from baseline	Effect measure	0.179	0.289	-0.328
	95% CI	(0.049, 0.662)	(0.106, 0.787)	(-0.555, -0.101)
	p-value	0.0099	0.0152	0.0046

NOTE1: To create YES/NO event variables, we calculated timepoint score minus basline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS equal to 0

	Event (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
BVMT Trial 2 Week 48 >=15% increase from baseline				
	Yes	5 (24)	4 (21)	9 (23)
	No	6 (29)	7 (37)	13 (33)
	Missing	10 (48)	8 (42)	18 (45)
BVMT Trial 3 Week 48 >=15% increase from baseline				
	Yes	3 (14)	4 (21)	7 (18)
	No	8 (38)	7 (37)	15 (38)
	Missing	10 (48)	8 (42)	18 (45)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table52_MCID_15pct_NPERCENT_EVENT_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS greater than 0

	Event (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
BVMT Trial 2 Week 48 >=15% increase from baseline				
	Yes	7 (14)	11 (24)	18 (19)
	No	23 (46)	15 (33)	38 (40)
	Missing	20 (40)	19 (42)	39 (41)
BVMT Trial 3 Week 48 >=15% increase from baseline				
	Yes	4 (8)	12 (27)	16 (17)
	No	26 (52)	14 (31)	40 (42)
	Missing	20 (40)	19 (42)	39 (41)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for EDSS equal to 0

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
BVMT Trial 1 scale Week 0				
	Yes	11 (52)	11 (58)	22 (55)
	No	10 (48)	8 (42)	18 (45)
BVMT Trial 1 scale Week 48				
	Yes	14 (67)	14 (74)	28 (70)
	No	7 (33)	5 (26)	12 (30)
BVMT Trial 1 scale Week 96				
	Yes	16 (76)	14 (74)	30 (75)
	No	5 (24)	5 (26)	10 (25)
BVMT Trial 2 scale Week 0				
	Yes	11 (52)	11 (58)	22 (55)
	No	10 (48)	8 (42)	18 (45)
BVMT Trial 2 scale Week 48				
	Yes	14 (67)	14 (74)	28 (70)

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
	No	7 (33)	5 (26)	12 (30)
BVMT Trial 2 scale Week 96				
	Yes	16 (76)	14 (74)	30 (75)
	No	5 (24)	5 (26)	10 (25)
BVMT Trial 3 scale Week 0				
	Yes	11 (52)	11 (58)	22 (55)
	No	10 (48)	8 (42)	18 (45)
BVMT Trial 3 scale Week 48				
	Yes	14 (67)	14 (74)	28 (70)
	No	7 (33)	5 (26)	12 (30)
BVMT Trial 3 scale Week 96				
	Yes	16 (76)	14 (74)	30 (75)
	No	5 (24)	5 (26)	10 (25)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table52_MCID_15PCT_NPERCENT_RESPONSE_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit-ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for EDSS greater than 0

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
BVMT Trial 1 scale Week 0				
	Yes	30 (60)	26 (58)	56 (59)
	No	20 (40)	19 (42)	39 (41)
BVMT Trial 1 scale Week 48				
	Yes	36 (72)	30 (67)	66 (69)
	No	14 (28)	15 (33)	29 (31)
BVMT Trial 1 scale Week 96				
	Yes	35 (70)	26 (58)	61 (64)
	No	15 (30)	19 (42)	34 (36)
BVMT Trial 2 scale Week 0				
	Yes	30 (60)	26 (58)	56 (59)
	No	20 (40)	19 (42)	39 (41)
BVMT Trial 2 scale Week 48				
	Yes	36 (72)	30 (67)	66 (69)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
	No	14 (28)	15 (33)	29 (31)
BVMT Trial 2 scale Week 96				
	Yes	35 (70)	26 (58)	61 (64)
	No	15 (30)	19 (42)	34 (36)
BVMT Trial 3 scale Week 0				
	Yes	30 (60)	26 (58)	56 (59)
	No	20 (40)	19 (42)	39 (41)
BVMT Trial 3 scale Week 48				
	Yes	36 (72)	30 (67)	66 (69)
	No	14 (28)	15 (33)	29 (31)
BVMT Trial 3 scale Week 96				
	Yes	35 (70)	26 (58)	61 (64)
	No	15 (30)	19 (42)	34 (36)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table52_t-ef-bvmt-sum-byvst_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_EQZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	10 (48)	11 (58)	21 (53)
Mean (SD)	1.1 (2.42)	1.5 (2.73)	1.3 (2.53)
Median	1.0	2.0	1.0
Q1, Q3	0.0, 2.0	-1.0, 4.0	0.0, 3.0
Min, Max	-4, 5	-3, 6	-4, 6
Week 96 change from baseline			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-0.4 (2.55)	1.3 (3.06)	0.4 (2.85)
Median	-1.0	1.0	0.0
Q1, Q3	-2.0, 2.0	-0.5, 2.5	-2.0, 2.0
Min, Max	-4, 4	-3, 7	-4, 7

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	10 (48)	11 (58)	21 (53)
Mean (SD)	1.4 (3.20)	1.1 (2.88)	1.2 (2.96)
Median	1.5	1.0	1.0
Q1, Q3	-1.0, 4.0	-1.0, 3.0	-1.0, 3.0
Min, Max	-4, 6	-5, 6	-5, 6
Week 96 change from baseline			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	0.3 (2.45)	0.0 (2.51)	0.2 (2.40)
Median	-1.0	-0.5	-1.0
Q1, Q3	-1.0, 2.0	-2.0, 2.0	-1.0, 2.0
Min, Max	-2, 5	-3, 4	-3, 5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	10 (48)	11 (58)	21 (53)
Mean (SD)	0.4 (2.12)	0.8 (2.18)	0.6 (2.11)
Median	0.0	0.0	0.0
Q1, Q3	0.0, 2.0	-1.0, 3.0	0.0, 2.0
Min, Max	-4, 4	-2, 4	-4, 4
Week 96 change from baseline			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-0.1 (1.62)	-0.8 (1.75)	-0.4 (1.66)
Median	0.0	-1.0	0.0
Q1, Q3	-1.0, 1.0	-2.0, 0.5	-1.0, 1.0
Min, Max	-3, 2	-3, 2	-3, 2

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

109MS306_table52_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_GTZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 1			
Week 48 change from baseline			
n (%)	27 (54)	26 (58)	53 (56)
Mean (SD)	0.1 (2.20)	0.0 (1.60)	0.0 (1.91)
Median	0.0	0.0	0.0
Q1, Q3	-2.0, 2.0	-1.0, 1.0	-2.0, 2.0
Min, Max	-4, 4	-3, 2	-4, 4
Week 96 change from baseline			
n (%)	22 (44)	17 (38)	39 (41)
Mean (SD)	0.9 (1.91)	0.3 (2.64)	0.6 (2.24)
Median	1.0	0.0	1.0
Q1, Q3	-1.0, 2.0	-1.0, 1.0	-1.0, 2.0
Min, Max	-3, 5	-5, 5	-5, 5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 2			
Week 48 change from baseline			
n (%)	27 (54)	26 (58)	53 (56)
Mean (SD)	0.4 (1.69)	1.1 (1.87)	0.7 (1.80)
Median	0.0	1.0	1.0
Q1, Q3	-1.0, 2.0	0.0, 2.0	0.0, 2.0
Min, Max	-3, 3	-2, 5	-3, 5
Week 96 change from baseline			
n (%)	22 (44)	17 (38)	39 (41)
Mean (SD)	1.1 (1.34)	1.4 (1.97)	1.2 (1.63)
Median	1.0	1.0	1.0
Q1, Q3	0.0, 2.0	0.0, 3.0	0.0, 2.0
Min, Max	-1, 4	-1, 6	-1, 6

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 3			
Week 48 change from baseline			
n (%)	27 (54)	26 (58)	53 (56)
Mean (SD)	0.4 (1.25)	1.5 (1.88)	0.9 (1.66)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 1.0	0.0, 3.0	0.0, 2.0
Min, Max	-2, 3	-2, 7	-2, 7
Week 96 change from baseline			
n (%)	22 (44)	17 (38)	39 (41)
Mean (SD)	1.1 (2.07)	0.7 (1.26)	0.9 (1.75)
Median	1.0	1.0	1.0
Q1, Q3	-1.0, 2.0	0.0, 1.0	0.0, 2.0
Min, Max	-2, 6	-1, 3	-2, 6

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Brief Visuospatial Memory Test (BVMT-R) scores range from 0 to 12.
Note3: This is based on Change variable (CHG)
W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE(CHG FROM BL)_SubGr date: 13MAY2022

109MS306_table52_CHG_DESCRIBE_EDSSBL_EQZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	11 (52)	11 (58)	22 (55)
Mean (SD)	6.7 (2.87)	6.0 (2.05)	6.4 (2.46)
Median	6.0	7.0	6.5
Q1, Q3	5.0, 10.0	4.0, 8.0	4.0, 8.0
Min, Max	1, 10	3, 9	1, 10
Week 48			
n (%)	14 (67)	14 (74)	28 (70)
Mean (SD)	7.7 (1.68)	7.1 (2.76)	7.4 (2.27)
Median	7.5	7.5	7.5
Q1, Q3	6.0, 10.0	4.0, 9.0	6.0, 9.0
Min, Max	6, 10	3, 12	3, 12
Week 96			
n (%)	16 (76)	14 (74)	30 (75)
Mean (SD)	7.1 (2.53)	6.7 (2.81)	6.9 (2.63)
Median	8.0	6.5	7.5
Q1, Q3	6.0, 8.0	4.0, 9.0	5.0, 9.0
Min, Max	1, 12	3, 11	1, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	11 (52)	11 (58)	22 (55)
Mean (SD)	8.2 (3.54)	8.6 (1.91)	8.4 (2.79)
Median	10.0	9.0	9.0
Q1, Q3	5.0, 11.0	8.0, 10.0	8.0, 11.0
Min, Max	3, 12	4, 11	3, 12
Week 48			
n (%)	14 (67)	14 (74)	28 (70)
Mean (SD)	9.5 (1.56)	9.1 (3.05)	9.3 (2.39)
Median	9.5	10.0	10.0
Q1, Q3	9.0, 11.0	8.0, 11.0	8.5, 11.0
Min, Max	6, 12	1, 12	1, 12
Week 96			
n (%)	16 (76)	14 (74)	30 (75)
Mean (SD)	9.5 (2.28)	8.4 (2.79)	9.0 (2.55)
Median	10.0	8.5	10.0
Q1, Q3	8.5, 11.0	6.0, 11.0	7.0, 11.0
Min, Max	3, 12	5, 12	3, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	11 (52)	11 (58)	22 (55)
Mean (SD)	9.8 (1.72)	9.4 (1.80)	9.6 (1.74)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 11.0	7.0, 11.0	8.0, 11.0
Min, Max	6, 12	7, 12	6, 12
Week 48			
n (%)	14 (67)	14 (74)	28 (70)
Mean (SD)	10.1 (1.64)	9.7 (2.09)	9.9 (1.85)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 11.0	9.0, 11.0	9.0, 11.0
Min, Max	7, 12	5, 12	5, 12
Week 96			
n (%)	16 (76)	14 (74)	30 (75)
Mean (SD)	10.1 (1.63)	8.6 (2.50)	9.4 (2.18)
Median	10.5	9.0	10.0
Q1, Q3	9.0, 11.5	6.0, 11.0	8.0, 11.0
Min, Max	7, 12	5, 12	5, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

109MS306_table52_CHG_DESCRIBE_EDSSBL_GTZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 1			
Baseline			
n (%)	30 (60)	26 (58)	56 (59)
Mean (SD)	6.9 (2.42)	5.9 (2.23)	6.4 (2.36)
Median	6.5	6.0	6.0
Q1, Q3	6.0, 8.0	5.0, 7.0	5.0, 8.0
Min, Max	2, 11	2, 12	2, 12
Week 48			
n (%)	36 (72)	30 (67)	66 (69)
Mean (SD)	6.1 (2.75)	5.7 (2.38)	5.9 (2.58)
Median	6.0	5.0	5.5
Q1, Q3	4.0, 9.0	4.0, 8.0	4.0, 8.0
Min, Max	1, 11	2, 12	1, 12
Week 96			
n (%)	35 (70)	26 (58)	61 (64)
Mean (SD)	7.1 (2.66)	6.8 (2.69)	6.9 (2.65)
Median	7.0	6.5	7.0
Q1, Q3	5.0, 9.0	5.0, 8.0	5.0, 9.0
Min, Max	0, 11	3, 12	0, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 2			
Baseline			
n (%)	30 (60)	26 (58)	56 (59)
Mean (SD)	8.8 (1.95)	7.5 (2.27)	8.2 (2.19)
Median	9.0	7.5	8.0
Q1, Q3	7.0, 10.0	6.0, 9.0	6.5, 10.0
Min, Max	5, 12	3, 12	3, 12
Week 48			
n (%)	36 (72)	30 (67)	66 (69)
Mean (SD)	8.6 (2.44)	8.6 (2.75)	8.6 (2.57)
Median	9.0	9.0	9.0
Q1, Q3	7.0, 10.0	7.0, 11.0	7.0, 10.0
Min, Max	2, 12	1, 12	1, 12
Week 96			
n (%)	35 (70)	26 (58)	61 (64)
Mean (SD)	9.4 (2.27)	9.2 (2.27)	9.3 (2.25)
Median	10.0	10.0	10.0
Q1, Q3	8.0, 11.0	7.0, 11.0	8.0, 11.0
Min, Max	4, 12	6, 12	4, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Brief Visuospatial Memory Test-Revised - Trial 3			
Baseline			
n (%)	30 (60)	26 (58)	56 (59)
Mean (SD)	9.3 (2.17)	8.5 (2.25)	9.0 (2.22)
Median	10.0	9.0	9.0
Q1, Q3	7.0, 11.0	7.0, 10.0	7.0, 11.0
Min, Max	5, 12	4, 12	4, 12
Week 48			
n (%)	36 (72)	30 (67)	66 (69)
Mean (SD)	9.3 (2.41)	9.8 (2.26)	9.6 (2.34)
Median	10.0	11.0	10.0
Q1, Q3	7.0, 11.0	9.0, 11.0	8.0, 11.0
Min, Max	2, 12	4, 12	2, 12
Week 96			
n (%)	35 (70)	26 (58)	61 (64)
Mean (SD)	9.9 (1.89)	9.8 (1.77)	9.9 (1.83)
Median	10.0	10.0	10.0
Q1, Q3	8.0, 12.0	8.0, 11.0	8.0, 12.0
Min, Max	5, 12	6, 12	5, 12

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

109MS306_table52_CHG_HEDGESCI_EDSSBL_EQZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	-0.057	-0.841	0.728
	96 Weeks	-0.605	-1.483	0.273
Trial 2	48 Weeks	0.139	-0.647	0.925
	96 Weeks	0.351	-0.513	1.214
Trial 3	48 Weeks	-0.243	-1.031	0.544
	96 Weeks	0.142	-0.716	0.999

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 13MAY2022

109MS306_table52_CHG_HEDGESCI_EDSSBL_GTZERO

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
Trial 1	48 Weeks	0.144	-0.376	0.664
	96 Weeks	0.258	-0.353	0.868
Trial 2	48 Weeks	-0.304	-0.827	0.218
	96 Weeks	-0.109	-0.718	0.499
Trial 3	48 Weeks	-0.696	-1.231	-0.161
	96 Weeks	0.264	-0.346	0.875

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_HEDGESCI_SubGr.sas date: 13MAY2022

109MS306_table52_CHG_LSMEANS_TRIAL1_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1. Subgroup analysis for EDSS equal to 0

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=19)
48	n (%)	10 (48)	11 (58)
	Lsmean (SE)	1.19 (0.696)	1.20 (0.739)
	Lsmean_95 % CI	(-0.278, 2.657)	(-0.357, 2.763)
	Diffrence (95% CI)	-0.014 (-2.062, 2.035)	
	SE_Difference	0.9710	
	p-value	0.9891	
96	n (%)	9 (43)	8 (42)
	Lsmean (SE)	-0.18 (1.003)	0.92 (1.110)
	Lsmean_95 % CI	(-2.351, 1.982)	(-1.477, 3.319)
	Diffrence (95% CI)	-1.11 (-4.451, 2.241)	
	SE_Difference	1.5488	
	p-value	0.4881	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table52_CHG_LSMEANS_TRIAL1_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 1. Subgroup analysis for EDSS greater than 0

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=45)
48	n (%)	27 (54)	26 (58)
	Lsmean (SE)	0.23 (0.422)	0.00 (0.416)
	Lsmean_95 % CI	(-0.621, 1.076)	(-0.832, 0.841)
	Diffrence (95% CI)	0.22 (-0.847, 1.293)	
	SE_Difference	0.5324	
	p-value	0.6773	
96	n (%)	22 (44)	17 (38)
	Lsmean (SE)	0.73 (0.553)	-0.10 (0.638)
	Lsmean_95 % CI	(-0.393, 1.851)	(-1.396, 1.194)
	Diffrence (95% CI)	0.83 (-0.596, 2.256)	
	SE_Difference	0.7025	
	p-value	0.2454	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table52_CHG_LSMEANS_TRIAL2_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for EDSS equal to 0

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=19)
48	n (%)	10 (48)	11 (58)
	Lsmean (SE)	1.08 (0.660)	1.57 (0.700)
	Lsmean_95 % CI	(-0.314, 2.469)	(0.092, 3.045)
	Diffrence (95% CI)	-0.49 (-2.457, 1.475)	
	SE_Difference	0.9318	
	p-value	0.6050	
96	n (%)	9 (43)	8 (42)
	Lsmean (SE)	0.36 (0.754)	-0.22 (0.850)
	Lsmean_95 % CI	(-1.273, 1.984)	(-2.054, 1.617)
	Diffrence (95% CI)	0.57 (-1.915, 3.064)	
	SE_Difference	1.1523	
	p-value	0.6266	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table52_CHG_LSMEANS_TRIAL2_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 2. Subgroup analysis for EDSS greater than 0

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=45)
48	n (%)	27 (54)	26 (58)
	Lsmean (SE)	0.52 (0.393)	0.99 (0.386)
	Lsmean_95 % CI	(-0.271, 1.309)	(0.210, 1.760)
	Diffrence (95% CI)	-0.47 (-1.474, 0.541)	
	SE_Difference	0.5013	
	p-value	0.3567	
96	n (%)	22 (44)	17 (38)
	Lsmean (SE)	1.24 (0.383)	1.07 (0.443)
	Lsmean_95 % CI	(0.461, 2.018)	(0.173, 1.973)
	Diffrence (95% CI)	0.17 (-0.846, 1.179)	
	SE_Difference	0.4988	
	p-value	0.7406	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table52_CHG_LSMEANS_TRIAL3_edsseq0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for EDSS equal to 0

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=19)
48	n (%)	10 (48)	11 (58)
	Lsmean (SE)	0.50 (0.596)	0.64 (0.633)
	Lsmean_95 % CI	(-0.759, 1.757)	(-0.700, 1.972)
	Diffrence (95% CI)	-0.14 (-1.907, 1.635)	
	SE_Difference	0.8395	
	p-value	0.8730	
96	n (%)	9 (43)	8 (42)
	Lsmean (SE)	-0.09 (0.603)	-0.82 (0.679)
	Lsmean_95 % CI	(-1.396, 1.210)	(-2.283, 0.649)
	Diffrence (95% CI)	0.72 (-1.268, 2.717)	
	SE_Difference	0.9224	
	p-value	0.4464	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table52_CHG_LSMEANS_TRIAL3_edssgt0

Table 52: Summary of Brief Visuospatial Memory Test (BVMT-R) Assessments by Visit - ITT Population, Aged 13 years and older (n=135)_Brief Visuospatial Memory Test-Revised - Trial 3. Subgroup analysis for EDSS greater than 0

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=45)
48	n (%)	27 (54)	26 (58)
	Lsmean (SE)	0.42 (0.329)	1.29 (0.323)
	Lsmean_95 % CI	(-0.244, 1.078)	(0.640, 1.939)
	Diffrence (95% CI)	-0.87 (-1.703, -0.0418)	
	SE_Difference	0.4132	
	p-value	0.0399	
96	n (%)	22 (44)	17 (38)
	Lsmean (SE)	1.19 (0.354)	0.55 (0.407)
	Lsmean_95 % CI	(0.473, 1.910)	(-0.272, 1.380)
	Diffrence (95% CI)	0.64 (-0.271, 1.546)	
	SE_Difference	0.4476	
	p-value	0.1632	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T52/109MS306_table52_CHG_LSMEANS_SubGr.sas date: 19APR2022

SDMT

109MS306_table53_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_EQZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Week 48 change from baseline			
n (%)	11 (52)	11 (58)	22 (55)
Mean (SD)	1.8 (6.16)	2.6 (6.98)	2.2 (6.44)
Median	3.0	5.0	4.5
Q1, Q3	-3.0, 6.0	-4.0, 7.0	-3.0, 6.0
Min, Max	-11, 9	-11, 13	-11, 13
Week 96 change from baseline			
n (%)	10 (48)	8 (42)	18 (45)
Mean (SD)	9.7 (8.83)	1.9 (8.01)	6.2 (9.15)
Median	8.5	1.5	5.5
Q1, Q3	3.0, 13.0	-2.0, 7.0	-1.0, 12.0
Min, Max	-1, 28	-12, 14	-12, 28

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
Note3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
Note4: This is based on Change variable (CHG)
SOURCE:
W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_DESCRIBE_(CHG FROM BL)_SubGr.sas date: 13APR2022

109MS306_table53_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_GTZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Week 48 change from baseline			
n (%)	28 (56)	26 (58)	54 (57)
Mean (SD)	4.6 (7.86)	1.5 (10.33)	3.1 (9.18)
Median	4.0	3.5	4.0
Q1, Q3	0.0, 9.0	-3.0, 8.0	-1.0, 9.0
Min, Max	-9, 22	-26, 17	-26, 22
Week 96 change from baseline			
n (%)	23 (46)	18 (40)	41 (43)
Mean (SD)	6.7 (9.16)	1.4 (10.71)	4.3 (10.09)
Median	6.0	4.5	5.0
Q1, Q3	3.0, 13.0	-1.0, 9.0	1.0, 9.0
Min, Max	-19, 26	-28, 12	-28, 26

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
Note3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
Note4: This is based on Change variable (CHG)
SOURCE:
W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_DESCRIBE_(CHG FROM BL)_SubGr.sas date: 13APR2022

109MS306_table53_CHG_DESCRIBE_EDSSBL_EQZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Baseline			
n (%)	11 (52)	11 (58)	22 (55)
Mean (SD)	55.3 (10.57)	59.8 (5.34)	57.5 (8.50)
Median	51.0	61.0	60.0
Q1, Q3	49.0, 66.0	53.0, 63.0	51.0, 63.0
Min, Max	38, 71	52, 68	38, 71
Week 48			
n (%)	15 (71)	14 (74)	29 (73)
Mean (SD)	55.9 (9.87)	60.9 (9.60)	58.3 (9.90)
Median	56.0	60.5	58.0
Q1, Q3	50.0, 64.0	57.0, 69.0	52.0, 66.0
Min, Max	34, 75	37, 72	34, 75
Week 96			
n (%)	17 (81)	14 (74)	31 (78)
Mean (SD)	63.0 (9.47)	60.1 (9.83)	61.7 (9.58)
Median	61.0	60.5	61.0
Q1, Q3	56.0, 72.0	50.0, 69.0	53.0, 70.0
Min, Max	46, 79	47, 75	46, 79

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_DESCRIBE_banupdate012622.sas date: 13APR2022

109MS306_table53_CHG_DESCRIBE_EDSSBL_GTZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Baseline			
n (%)	31 (62)	26 (58)	57 (60)
Mean (SD)	57.7 (14.65)	56.2 (13.92)	57.0 (14.22)
Median	57.0	54.0	56.0
Q1, Q3	50.0, 66.0	47.0, 59.0	48.0, 63.0
Min, Max	26, 86	30, 87	26, 87
Week 48			
n (%)	37 (74)	30 (67)	67 (71)
Mean (SD)	58.1 (14.13)	56.9 (14.11)	57.6 (14.03)
Median	58.0	56.0	57.0
Q1, Q3	49.0, 67.0	52.0, 64.0	50.0, 65.0
Min, Max	28, 93	15, 86	15, 93
Week 96			
n (%)	35 (70)	26 (58)	61 (64)
Mean (SD)	59.6 (13.09)	58.4 (12.06)	59.1 (12.57)
Median	60.0	57.5	59.0
Q1, Q3	52.0, 66.0	52.0, 65.0	52.0, 65.0
Min, Max	25, 98	34, 95	25, 98

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: High symbol digit modalities test (SDMT) total score indicates better cognitive and cerebral function.
NOTE3: The SDMT scale is 0 to 110; missing SDMT scores were not imputed.
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table53_DESCRIBE_banupdate012622.sas date: 13APR2022

109MS306_table53_CHG_HEDGESCI_EDSSBL_EQZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135). Subgroup analysis for EDSSBL Score EQ Zero

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
48	-0.124	-0.961	0.712
96	0.923	-0.061	1.906

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_HEDGESCI_SubGr.sas date: 13APR2022

109MS306_table53_CHG_HEDGESCI_EDSSBL_GTZERO

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - ITT Population (n=135). Subgroup analysis for EDSSBL Score GT Zero

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
48	0.349	-0.189	0.887
96	0.534	-0.094	1.162

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_HEDGESCI_SubGr.sas date: 13APR2022

109MS306_table53_CHG_LSMEANS_edsseq0

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0

TIME POINTS	STATISTICS	DMF(N=21)	IFN B-1a (N=19)
48	n (%)	11 (52)	11 (58)
	Lsmean (SE)	0.93 (1.912)	3.13 (2.089)
	Lsmean_95 % CI	(-3.090, 4.946)	(-1.259, 7.518)
	Diffrence (95% CI)	-2.20 (-8.101, 3.699)	
	SE_Difference	2.8081	
	p-value	0.4433	
96	n (%)	10 (48)	8 (42)
	Lsmean (SE)	8.79 (2.768)	3.04 (3.240)
	Lsmean_95 % CI	(2.855, 14.729)	(-3.907, 9.992)
	Diffrence (95% CI)	5.75 (-3.590, 15.089)	
	SE_Difference	4.3544	
	p-value	0.2079	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_LSMEANS_SubGr.sas date: 19APR2022

109MS306_table53_CHG_LSMEANS_edssgt0

Table 53: Summary of Symbol Digit Modalities Test (SDMT) Scores by Visit - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0

TIME POINTS	STATISTICS	DMF(N=50)	IFN B-1a (N=45)
48	n (%)	28 (56)	26 (58)
	Lsmean (SE)	4.80 (1.935)	1.56 (1.919)
	Lsmean_95 % CI	(0.909, 8.681)	(-2.295, 5.413)
	Diffrence (95% CI)	3.24 (-1.619, 8.092)	
	SE_Difference	2.4174	
	p-value	0.1867	
96	n (%)	23 (46)	18 (40)
	Lsmean (SE)	8.83 (2.313)	4.19 (2.659)
	Lsmean_95 % CI	(4.145, 13.520)	(-1.200, 9.576)
	Diffrence (95% CI)	4.64 (-1.183, 10.472)	
	SE_Difference	2.8761	
	p-value	0.1148	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T53/109MS306_table53_CHG_LSMEANS_SubGr.sas date: 19APR2022

PedsQL Fatigue

Parents

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_EDSSBL_EQZERO

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score EQ Zero. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	10 (48)	17 (89)	27 (68)
Mean (SD)	4.2 (15.71)	-6.4 (16.93)	-2.5 (16.99)
Median	2.1	-4.2	0.0
Q1,Q3	-4.2, 16.7	-16.7, 8.3	-12.5, 12.5
Min, Max	-21, 29	-46, 13	-46, 29
Week 48			
n (%)	9 (43)	14 (74)	23 (58)
Mean (SD)	6.5 (17.07)	-7.1 (18.01)	-1.8 (18.54)
Median	0.0	-4.2	0.0
Q1,Q3	0.0, 16.7	-20.8, 4.2	-12.5, 8.3
Min, Max	-21, 33	-42, 29	-42, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	8 (38)	8 (42)	16 (40)
Mean (SD)	-0.5 (18.29)	-5.7 (28.69)	-3.1 (23.40)
Median	-2.1	-8.3	-2.1
Q1,Q3	-12.5, 8.3	-22.9, 2.1	-18.8, 2.1
Min, Max	-25, 33	-42, 54	-42, 54
Week 96			
n (%)	7 (33)	7 (37)	14 (35)
Mean (SD)	-5.4 (6.68)	-3.6 (24.47)	-4.5 (17.25)
Median	-4.2	0.0	-2.1
Q1,Q3	-12.5, 0.0	-20.8, 12.5	-12.5, 0.0
Min, Max	-17, 0	-46, 29	-46, 29

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score EQ Zero. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	10 (48)	17 (89)	27 (68)
Mean (SD)	2.1 (17.60)	3.7 (19.54)	3.1 (18.51)
Median	-2.1	8.3	4.2
Q1,Q3	-4.2, 4.2	-12.5, 12.5	-12.5, 12.5
Min, Max	-21, 42	-33, 46	-33, 46
Week 48			
n (%)	9 (43)	14 (74)	23 (58)
Mean (SD)	4.6 (16.33)	-0.3 (17.64)	1.6 (16.94)
Median	0.0	2.1	0.0
Q1,Q3	-8.3, 8.3	-12.5, 8.3	-8.3, 8.3
Min, Max	-13, 33	-29, 38	-29, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	8 (38)	8 (42)	16 (40)
Mean (SD)	1.0 (10.85)	0.0 (19.42)	0.5 (15.21)
Median	0.0	-2.1	0.0
Q1,Q3	-6.3, 6.3	-10.4, 16.7	-6.3, 12.5
Min, Max	-13, 21	-33, 25	-33, 25
Week 96			
n (%)	7 (33)	7 (37)	14 (35)
Mean (SD)	0.6 (18.54)	2.4 (29.15)	1.5 (23.49)
Median	0.0	12.5	0.0
Q1,Q3	-12.5, 12.5	-20.8, 16.7	-12.5, 16.7
Min, Max	-25, 33	-42, 46	-42, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score EQ Zero. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	10 (48)	17 (89)	27 (68)
Mean (SD)	5.8 (13.21)	-3.7 (17.79)	-0.2 (16.65)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 16.7	-4.2, 0.0	-4.2, 4.2
Min, Max	-8, 33	-50, 29	-50, 33
Week 48			
n (%)	9 (43)	14 (74)	23 (58)
Mean (SD)	7.4 (15.14)	0.9 (19.76)	3.4 (18.02)
Median	0.0	4.2	4.2
Q1,Q3	0.0, 16.7	0.0, 8.3	0.0, 8.3
Min, Max	-8, 33	-50, 33	-50, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	8 (38)	8 (42)	16 (40)
Mean (SD)	5.7 (10.90)	0.0 (36.19)	2.9 (25.99)
Median	0.0	-2.1	0.0
Q1,Q3	0.0, 12.5	-27.1, 22.9	-4.2, 12.5
Min, Max	-4, 25	-46, 58	-46, 58
Week 96			
n (%)	7 (33)	7 (37)	14 (35)
Mean (SD)	-1.8 (2.23)	1.2 (30.31)	-0.3 (20.70)
Median	0.0	4.2	0.0
Q1,Q3	-4.2, 0.0	-20.8, 33.3	-4.2, 4.2
Min, Max	-4, 0	-50, 33	-50, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_EDSSBL_GTZERO

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score GT Zero. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	30 (60)	32 (71)	62 (65)
Mean (SD)	-3.8 (16.09)	-3.5 (17.81)	-3.6 (16.86)
Median	-4.2	-4.2	-4.2
Q1,Q3	-16.7, 4.2	-10.4, 0.0	-12.5, 4.2
Min, Max	-38, 29	-50, 38	-50, 38
Week 48			
n (%)	26 (52)	22 (49)	48 (51)
Mean (SD)	3.8 (16.34)	-12.3 (23.59)	-3.6 (21.36)
Median	4.2	-6.3	-2.1
Q1,Q3	-8.3, 12.5	-20.8, 4.2	-12.5, 8.3
Min, Max	-29, 38	-71, 25	-71, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	23 (46)	17 (38)	40 (42)
Mean (SD)	2.0 (19.98)	-6.1 (14.37)	-1.5 (18.07)
Median	0.0	-8.3	-4.2
Q1,Q3	-12.5, 20.8	-12.5, 0.0	-12.5, 14.6
Min, Max	-38, 33	-38, 21	-38, 33
Week 96			
n (%)	13 (26)	12 (27)	25 (26)
Mean (SD)	-2.2 (17.48)	-4.5 (20.37)	-3.3 (18.56)
Median	-4.2	-2.1	-4.2
Q1,Q3	-12.5, 4.2	-18.8, 6.3	-16.7, 4.2
Min, Max	-29, 38	-38, 38	-38, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score GT Zero. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	30 (60)	32 (71)	62 (65)
Mean (SD)	0.4 (19.03)	-0.8 (19.44)	-0.2 (19.09)
Median	0.0	0.0	0.0
Q1,Q3	-16.7, 8.3	-12.5, 8.3	-12.5, 8.3
Min, Max	-29, 46	-38, 46	-38, 46
Week 48			
n (%)	26 (52)	22 (49)	48 (51)
Mean (SD)	0.8 (20.55)	-4.0 (23.90)	-1.4 (22.04)
Median	2.1	-2.1	0.0
Q1,Q3	-8.3, 8.3	-12.5, 8.3	-10.4, 8.3
Min, Max	-33, 50	-63, 50	-63, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	23 (46)	17 (38)	40 (42)
Mean (SD)	-1.4 (20.16)	-4.7 (19.03)	-2.8 (19.51)
Median	0.0	0.0	0.0
Q1,Q3	-16.7, 12.5	-25.0, 8.3	-18.8, 12.5
Min, Max	-42, 38	-33, 25	-42, 38
Week 96			
n (%)	13 (26)	12 (27)	25 (26)
Mean (SD)	-0.6 (23.87)	-5.6 (18.58)	-3.0 (21.20)
Median	0.0	-2.1	0.0
Q1,Q3	-16.7, 4.2	-14.6, 8.3	-16.7, 8.3
Min, Max	-29, 46	-42, 21	-42, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

Table 42.44: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline. Subgroup analysis for EDSSBL Score GT Zero. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	30 (60)	32 (71)	62 (65)
Mean (SD)	1.8 (20.92)	-2.5 (18.51)	-0.4 (19.67)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 8.3	-14.6, 6.3	-12.5, 8.3
Min, Max	-42, 54	-50, 46	-50, 54
Week 48			
n (%)	26 (52)	22 (49)	48 (51)
Mean (SD)	3.2 (15.47)	-3.0 (19.75)	0.4 (17.64)
Median	0.0	-2.1	0.0
Q1,Q3	-4.2, 8.3	-16.7, 8.3	-12.5, 8.3
Min, Max	-21, 46	-38, 46	-38, 46

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	23 (46)	17 (38)	40 (42)
Mean (SD)	-1.6 (17.89)	-1.5 (19.60)	-1.6 (18.39)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 4.2	-8.3, 8.3	-8.3, 6.3
Min, Max	-46, 38	-38, 38	-46, 38
Week 96			
n (%)	13 (26)	12 (27)	25 (26)
Mean (SD)	2.9 (14.07)	-9.0 (17.12)	-2.8 (16.44)
Median	4.2	-4.2	0.0
Q1,Q3	-4.2, 8.3	-25.0, 4.2	-12.5, 8.3
Min, Max	-25, 33	-38, 13	-38, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note3: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE (CHG From BL)_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_DESCRIBE_EDSSBL_EQZERO

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. General Fatigue

	IFN B-1a (N= 19)	DMF (N= 21)	Total (N= 40)
Baseline			
n (%)	17 (89)	12 (57)	29 (73)
Mean (SD)	72.8 (20.20)	74.0 (18.81)	73.3 (19.30)
Median	79.2	70.8	75.0
Q1,Q3	58.3, 83.3	58.3, 93.8	58.3, 87.5
Min, Max	38, 100	50, 100	38, 100
Week 24			
n (%)	18 (95)	16 (76)	34 (85)
Mean (SD)	65.7 (20.79)	71.4 (25.22)	68.4 (22.80)
Median	62.5	77.1	70.8
Q1,Q3	54.2, 83.3	50.0, 95.8	50.0, 87.5
Min, Max	21, 100	29, 100	21, 100
Week 48			
n (%)	15 (79)	15 (71)	30 (75)
Mean (SD)	66.7 (19.09)	77.2 (24.29)	71.9 (22.13)
Median	70.8	87.5	75.0
Q1,Q3	45.8, 79.2	58.3, 100.0	54.2, 91.7
Min, Max	38, 96	29, 100	29, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 19)	**DMF (N= 21)**	**Total (N= 40)**
Week 72			
n (%)	9 (47)	13 (62)	22 (55)
Mean (SD)	73.1 (19.33)	75.6 (22.23)	74.6 (20.65)
Median	75.0	83.3	81.3
Q1,Q3	58.3, 87.5	75.0, 87.5	58.3, 87.5
Min, Max	42, 100	25, 100	25, 100
Week 96			
n (%)	8 (42)	11 (52)	19 (48)
Mean (SD)	75.0 (18.50)	69.7 (23.50)	71.9 (21.15)
Median	72.9	70.8	70.8
Q1,Q3	60.4, 91.7	45.8, 91.7	54.2, 91.7
Min, Max	50, 100	38, 100	38, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Sleep/Rest Fatigue

	IFN B-1a (N= 19)	DMF (N= 21)	Total (N= 40)
Baseline			
n (%)	17 (89)	12 (57)	29 (73)
Mean (SD)	63.7 (23.19)	71.9 (19.06)	67.1 (21.60)
Median	66.7	68.8	66.7
Q1,Q3	50.0, 83.3	58.3, 89.6	58.3, 83.3
Min, Max	13, 100	46, 100	13, 100
Week 24			
n (%)	18 (95)	16 (76)	34 (85)
Mean (SD)	66.0 (23.01)	64.1 (27.42)	65.1 (24.81)
Median	75.0	62.5	64.6
Q1,Q3	50.0, 87.5	47.9, 87.5	50.0, 87.5
Min, Max	25, 96	8, 100	8, 100
Week 48			
n (%)	15 (79)	15 (71)	30 (75)
Mean (SD)	63.1 (22.10)	71.1 (26.75)	67.1 (24.45)
Median	66.7	79.2	70.8
Q1,Q3	41.7, 79.2	54.2, 91.7	45.8, 87.5
Min, Max	25, 96	17, 100	17, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 19)	**DMF (N= 21)**	**Total (N= 40)**
Week 72			
n (%)	9 (47)	12 (57)	21 (53)
Mean (SD)	70.8 (20.73)	70.8 (23.50)	70.8 (21.81)
Median	70.8	75.0	70.8
Q1,Q3	58.3, 83.3	50.0, 89.6	58.3, 87.5
Min, Max	33, 100	33, 100	33, 100
Week 96			
n (%)	8 (42)	11 (52)	19 (48)
Mean (SD)	66.7 (22.27)	70.8 (27.95)	69.1 (25.13)
Median	66.7	79.2	70.8
Q1,Q3	56.3, 83.3	37.5, 95.8	45.8, 91.7
Min, Max	25, 96	33, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Cognitive Fatigue

	IFN B-1a (N= 19)	DMF (N= 21)	Total (N= 40)
Baseline			
n (%)	17 (89)	12 (57)	29 (73)
Mean (SD)	75.5 (26.31)	72.9 (28.89)	74.4 (26.93)
Median	83.3	75.0	83.3
Q1,Q3	58.3, 95.8	52.1, 100.0	54.2, 100.0
Min, Max	0, 100	13, 100	0, 100
Week 24			
n (%)	18 (95)	16 (76)	34 (85)
Mean (SD)	73.1 (20.87)	73.2 (28.67)	73.2 (24.45)
Median	70.8	77.1	70.8
Q1,Q3	54.2, 95.8	52.1, 100.0	54.2, 100.0
Min, Max	29, 100	21, 100	21, 100
Week 48			
n (%)	15 (79)	15 (71)	30 (75)
Mean (SD)	75.3 (21.96)	74.7 (25.61)	75.0 (23.44)
Median	70.8	79.2	77.1
Q1,Q3	58.3, 100.0	50.0, 100.0	54.2, 100.0
Min, Max	33, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 19)	**DMF (N= 21)**	**Total (N= 40)**
Week 72			
n (%)	9 (47)	13 (62)	22 (55)
Mean (SD)	75.0 (22.34)	81.1 (23.18)	78.6 (22.50)
Median	75.0	91.7	87.5
Q1,Q3	54.2, 100.0	66.7, 100.0	58.3, 100.0
Min, Max	50, 100	33, 100	33, 100
Week 96			
n (%)	8 (42)	11 (52)	19 (48)
Mean (SD)	70.3 (26.01)	70.8 (28.32)	70.6 (26.62)
Median	70.8	75.0	75.0
Q1,Q3	47.9, 95.8	54.2, 100.0	50.0, 100.0
Min, Max	33, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_DESCRIBE_EDSSBL_GTZERO

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. General Fatigue

	IFN B-1a (N= 45)	DMF (N= 50)	Total (N= 95)
Baseline			
n (%)	35 (78)	38 (76)	73 (77)
Mean (SD)	72.0 (23.82)	67.4 (26.28)	69.6 (25.06)
Median	79.2	68.8	70.8
Q1,Q3	58.3, 91.7	54.2, 91.7	58.3, 91.7
Min, Max	13, 100	0, 100	0, 100
Week 24			
n (%)	40 (89)	40 (80)	80 (84)
Mean (SD)	67.3 (25.45)	69.6 (20.15)	68.4 (22.84)
Median	70.8	70.8	70.8
Q1,Q3	50.0, 89.6	58.3, 87.5	52.1, 87.5
Min, Max	13, 100	21, 100	13, 100
Week 48			
n (%)	28 (62)	36 (72)	64 (67)
Mean (SD)	67.4 (25.31)	70.1 (22.88)	68.9 (23.81)
Median	70.8	72.9	72.9
Q1,Q3	58.3, 85.4	52.1, 90.8	56.3, 90.8
Min, Max	8, 100	25, 100	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 45)	**DMF (N= 50)**	**Total (N= 95)**
Week 72			
n (%)	20 (44)	30 (60)	50 (53)
Mean (SD)	70.8 (27.47)	70.8 (21.47)	70.8 (23.78)
Median	77.1	75.0	75.0
Q1,Q3	62.5, 91.7	54.2, 87.5	54.2, 87.5
Min, Max	8, 100	29, 100	8, 100
Week 96			
n (%)	14 (31)	17 (34)	31 (33)
Mean (SD)	74.1 (20.94)	69.6 (23.97)	71.6 (22.40)
Median	75.0	70.8	70.8
Q1,Q3	62.5, 91.7	54.2, 87.5	54.2, 87.5
Min, Max	29, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Sleep/Rest Fatigue

	IFN B-1a (N= 45)	DMF (N= 50)	Total (N= 95)
Baseline			
n (%)	35 (78)	38 (76)	73 (77)
Mean (SD)	68.3 (25.31)	65.7 (25.66)	67.0 (25.35)
Median	66.7	66.7	66.7
Q1,Q3	45.8, 91.7	50.0, 87.5	50.0, 91.7
Min, Max	17, 100	0, 100	0, 100
Week 24			
n (%)	40 (89)	40 (80)	80 (84)
Mean (SD)	68.6 (26.32)	68.9 (20.57)	68.8 (23.47)
Median	66.7	70.8	70.8
Q1,Q3	47.9, 93.8	61.3, 82.3	52.1, 87.5
Min, Max	21, 100	8, 100	8, 100
Week 48			
n (%)	28 (62)	36 (72)	64 (67)
Mean (SD)	71.9 (20.87)	67.9 (23.40)	69.7 (22.24)
Median	72.9	72.9	72.9
Q1,Q3	58.3, 89.6	52.1, 83.3	56.3, 87.5
Min, Max	29, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 45)	**DMF (N= 50)**	**Total (N= 95)**
Week 72			
n (%)	20 (44)	30 (60)	50 (53)
Mean (SD)	72.3 (22.83)	65.7 (24.11)	68.3 (23.60)
Median	70.8	66.7	68.8
Q1,Q3	60.4, 89.6	54.2, 83.3	58.3, 87.5
Min, Max	17, 100	13, 100	13, 100
Week 96			
n (%)	14 (31)	17 (34)	31 (33)
Mean (SD)	69.9 (23.01)	70.1 (17.00)	70.0 (19.59)
Median	68.8	75.0	70.8
Q1,Q3	54.2, 87.5	58.3, 75.0	58.3, 79.2
Min, Max	25, 100	29, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Cognitive Fatigue

	IFN B-1a (N= 45)	DMF (N= 50)	Total (N= 95)
Baseline			
n (%)	35 (78)	38 (76)	73 (77)
Mean (SD)	77.3 (19.00)	70.3 (28.33)	73.6 (24.40)
Median	75.0	81.3	75.0
Q1,Q3	62.5, 95.8	45.8, 95.8	54.2, 95.8
Min, Max	46, 100	0, 100	0, 100
Week 24			
n (%)	40 (89)	40 (80)	80 (84)
Mean (SD)	74.4 (24.97)	75.0 (22.00)	74.7 (23.39)
Median	79.2	79.2	79.2
Q1,Q3	54.2, 100.0	61.3, 95.8	58.3, 97.9
Min, Max	4, 100	25, 100	4, 100
Week 48			
n (%)	28 (62)	36 (72)	64 (67)
Mean (SD)	77.1 (21.57)	72.8 (23.07)	74.7 (22.36)
Median	83.3	77.1	79.2
Q1,Q3	58.3, 97.9	58.3, 91.7	58.3, 95.8
Min, Max	29, 100	4, 100	4, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	IFN B-1a (N= 45)	**DMF (N= 50)**	**Total (N= 95)**
Week 72			
n (%)	20 (44)	30 (60)	50 (53)
Mean (SD)	78.1 (18.63)	68.2 (20.95)	72.2 (20.45)
Median	83.3	64.6	75.0
Q1,Q3	62.5, 93.8	50.0, 87.5	58.3, 87.5
Min, Max	42, 100	33, 100	33, 100
Week 96			
n (%)	14 (31)	17 (34)	31 (33)
Mean (SD)	77.1 (18.40)	68.9 (28.61)	72.6 (24.50)
Median	77.1	66.7	75.0
Q1,Q3	62.5, 95.8	58.3, 95.8	62.5, 95.8
Min, Max	42, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_DESCRIBE_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_HEDGESCI_EDSSBL_EQZERO

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.584	-0.214	1.381
	48	0.359	-0.485	1.204
	72	0.214	-0.769	1.198
	96	-0.139	-1.188	0.911
GENERAL FATIGUE	24	0.639	-0.162	1.439
	48	0.772	-0.098	1.641
	72	0.216	-0.767	1.200
	96	-0.1	-1.148	0.949
SLEEP/REST FATIGUE	24	-0.084	-0.866	0.697
	48	0.287	-0.555	1.129
	72	0.066	-0.914	1.047
	96	-0.073	-1.121	0.975

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_HEDGESCI_EDSSBL_GTZERO

Table 42.44: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.217	-0.283	0.717
	48	0.351	-0.221	0.923
	72	-0.009	-0.635	0.618
	96	0.764	-0.051	1.579
GENERAL FATIGUE	24	-0.014	-0.512	0.484
	48	0.806	0.214	1.397
	72	0.455	-0.180	1.091
	96	0.12	-0.665	0.905
SLEEP/REST FATIGUE	24	0.062	-0.436	0.560
	48	0.216	-0.354	0.785
	72	0.163	-0.465	0.791
	96	0.229	-0.559	1.016

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table42_44_CHG_LSMEANS_edsseq0

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	10 (48)	17 (89)
Lsmean (SE)	04.40 (5.242)	-8.02 (4.654)
Lsmean_95 % CI	(-6.442, 15.246)	(-17.65, 01.609)
Diffrence (95% CI)	12.42 (-1.374, 26.216)	
SE_Difference	6.6686	
p-value	0.0753	
Week 48		
n (%)	9 (43)	14 (74)
Lsmean (SE)	06.46 (5.649)	-9.55 (5.083)
Lsmean_95 % CI	(-5.361, 18.284)	(-20.19, 01.084)
Diffrence (95% CI)	16.02 (0.483, 31.549)	
SE_Difference	7.4214	
p-value	0.0439	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	8 (38)	8 (42)
Lsmean (SE)	-0.67 (8.041)	-4.68 (8.201)
Lsmean_95 % CI	(-18.19, 16.846)	(-22.55, 13.189)
Diffrence (95% CI)	4.01 (-21.031, 29.041)	
SE_Difference	1.4905	
p-value	0.7335	
Week 96		
n (%)	7 (33)	7 (37)
Lsmean (SE)	-4.53 (6.835)	-4.39 (6.835)
Lsmean_95 % CI	(-19.76, 10.695)	(-19.62, 10.834)
Diffrence (95% CI)	-0.14 (-21.787, 21.509)	
SE_Difference	9.7156	
p-value	0.9889	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	10 (48)	17 (89)
Lsmean (SE)	04.60 (6.068)	03.32 (5.222)
Lsmean_95 % CI	(-7.955, 17.151)	(-7.480, 14.126)
Diffrence (95% CI)	1.27 (-14.405, 16.954)	
SE_Difference	7.5795	
p-value	0.8679	
Week 48		
n (%)	9 (43)	14 (74)
Lsmean (SE)	05.77 (5.436)	-3.72 (4.734)
Lsmean_95 % CI	(-5.608, 17.145)	(-13.63, 06.192)
Diffrence (95% CI)	9.49 (-5.210, 24.182)	
SE_Difference	7.0213	
p-value	0.1926	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	8 (38)	8 (42)
Lsmean (SE)	01.67 (5.500)	-0.56 (5.570)
Lsmean_95 % CI	(-10.31, 13.655)	(-12.69, 11.580)
Diffrence (95% CI)	2.23 (-14.818, 19.271)	
SE_Difference	7.8227	
p-value	0.7808	
Week 96		
n (%)	7 (33)	7 (37)
Lsmean (SE)	03.78 (9.582)	-0.80 (9.582)
Lsmean_95 % CI	(-17.58, 25.127)	(-22.15, 20.552)
Diffrence (95% CI)	4.57 (-26.507, 35.657)	
SE_Difference	3.9495	
p-value	0.7497	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	10 (48)	17 (89)
Lsmean (SE)	05.76 (4.495)	-5.17 (3.993)
Lsmean_95 % CI	(-3.540, 15.058)	(-13.43, 03.088)
Diffrence (95% CI)	10.93 (-1.050, 22.913)	
SE_Difference	5.7919	
p-value	0.0718	
Week 48		
n (%)	9 (43)	14 (74)
Lsmean (SE)	06.97 (5.101)	-0.78 (4.558)
Lsmean_95 % CI	(-3.708, 17.646)	(-10.32, 08.764)
Diffrence (95% CI)	7.75 (-6.324, 21.814)	
SE_Difference	6.7217	
p-value	0.2635	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	8 (38)	8 (42)
Lsmean (SE)	05.32 (7.511)	00.10 (7.631)
Lsmean_95 % CI	(-11.05, 21.682)	(-16.52, 16.732)
Diffrence (95% CI)	5.21 (-18.122, 28.545)	
SE_Difference	0.7090	
p-value	0.6353	
Week 96		
n (%)	7 (33)	7 (37)
Lsmean (SE)	-0.52 (7.613)	-0.07 (7.613)
Lsmean_95 % CI	(-17.48, 16.442)	(-17.04, 16.889)
Diffrence (95% CI)	-0.45 (-24.582, 23.687)	
SE_Difference	0.8316	
p-value	0.9679	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table42_44_CHG_LSMEANS_edssgt0

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	30 (60)	32 (71)
Lsmean (SE)	-8.40 (3.348)	-6.54 (2.987)
Lsmean_95 % CI	(-15.10, -1.699)	(-12.52, -0.566)
Diffrence (95% CI)	-1.86 (-9.725, 6.013)	
SE_Difference	3.9311	
p-value	0.6386	
Week 48		
n (%)	26 (52)	22 (49)
Lsmean (SE)	00.40 (4.962)	-12.2 (4.518)
Lsmean_95 % CI	(-9.605, 10.396)	(-21.33, -3.117)
Diffrence (95% CI)	12.62 (0.925, 24.314)	
SE_Difference	5.8026	
p-value	0.0351	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	23 (46)	17 (38)
Lsmean (SE)	04.26 (3.977)	-1.46 (4.374)
Lsmean_95 % CI	(-3.803, 12.330)	(-10.33, 07.416)
Diffrence (95% CI)	5.72 (-5.013, 16.451)	
SE_Difference	5.2916	
p-value	0.2870	
Week 96		
n (%)	13 (26)	12 (27)
Lsmean (SE)	-0.21 (4.651)	00.20 (5.001)
Lsmean_95 % CI	(-9.883, 09.460)	(-10.20, 10.604)
Diffrence (95% CI)	-0.42 (-13.857, 13.025)	
SE_Difference	6.4631	
p-value	0.9493	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	30 (60)	32 (71)
Lsmean (SE)	-1.28 (3.815)	-2.03 (3.396)
Lsmean_95 % CI	(-8.919, 06.356)	(-8.831, 04.764)
Diffrence (95% CI)	0.75 (-8.210, 9.714)	
SE_Difference	4.4771	
p-value	0.8672	
Week 48		
n (%)	26 (52)	22 (49)
Lsmean (SE)	-3.89 (5.100)	-4.34 (4.601)
Lsmean_95 % CI	(-14.17, 06.389)	(-13.62, 04.928)
Diffrence (95% CI)	0.46 (-11.501, 12.411)	
SE_Difference	5.9322	
p-value	0.9392	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	23 (46)	17 (38)
Lsmean (SE)	00.66 (4.251)	-0.57 (4.636)
Lsmean_95 % CI	(-7.964, 09.279)	(-9.970, 08.834)
Diffrence (95% CI)	1.23 (-10.126, 12.578)	
SE_Difference	5.5973	
p-value	0.8279	
Week 96		
n (%)	13 (26)	12 (27)
Lsmean (SE)	00.51 (4.769)	-3.43 (5.091)
Lsmean_95 % CI	(-9.409, 10.429)	(-14.02, 07.153)
Diffrence (95% CI)	3.94 (-9.763, 17.650)	
SE_Difference	6.5909	
p-value	0.5560	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 42: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Cognitive Fatigue

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 24		
n (%)	30 (60)	32 (71)
Lsmean (SE)	01.23 (4.042)	-1.63 (3.608)
Lsmean_95 % CI	(-6.863, 09.317)	(-8.851, 05.592)
Diffrence (95% CI)	2.86 (-6.707, 12.420)	
SE_Difference	4.7777	
p-value	0.5523	
Week 48		
n (%)	26 (52)	22 (49)
Lsmean (SE)	01.05 (4.342)	-1.88 (3.858)
Lsmean_95 % CI	(-7.704, 09.796)	(-9.650, 05.899)
Diffrence (95% CI)	2.92 (-7.327, 13.170)	
SE_Difference	5.0850	
p-value	0.5686	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	23 (46)	17 (38)
Lsmean (SE)	01.07 (3.717)	04.78 (3.985)
Lsmean_95 % CI	(-6.466, 08.612)	(-3.299, 12.867)
Diffrence (95% CI)	-3.71 (-13.704, 6.281)	
SE_Difference	4.9268	
p-value	0.4562	
Week 96		
n (%)	13 (26)	12 (27)
Lsmean (SE)	03.31 (4.507)	-4.61 (4.817)
Lsmean_95 % CI	(-6.065, 12.681)	(-14.63, 05.405)
Diffrence (95% CI)	7.92 (-5.671, 21.513)	
SE_Difference	6.5358	
p-value	0.2390	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T42_44/109MS306_table42_44_CHG_LSMEANS_SubGr.sas date: 18APR2022

Participants

MCID

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_eq0_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigure Scale (Participant) – EDSS=0

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	0.571	0.6	-0.044
-	95% CI	(0.047 , 6.999)	(0.06 , 5.988)	(-0.237 , 0.148)
-	p-value	0.662	0.663	0.651

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE6: Only ≥10 events in either treatment arm are shown in this table

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_eq0_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - EDSS=0

	Event (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	1 (4.76)	2 (10.53)	3 (9.09)
-	No	14 (66.67)	16 (84.21)	30 (90.91)
-	Missing	6 (28.57)	1 (5.26)	7 (17.50)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Only ≥10 events in either treatment arm are shown in this table

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_eq0_responsRate

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - EDSS=0

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
COGNITIVE FATIGUE-Week 96	Yes	15 (71.43)	13 (68.42)	28 (70.00)
-	No	6 (28.57)	6 (31.58)	12 (30.00)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Only ≥10 events in either treatment arm are shown in this table

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_gt0_effectmeasures

Effect Measure of PedsQL Multidimensional Fatigure Scale (Participant) – EDSS>0

	Result	OR	RR	ARR
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Effect measure	5.484	4.39	0.188
-	95% CI	(1.113 , 27.008)	(1.029 , 18.729)	(0.037 , 0.34)
-	p-value	0.036	0.046	0.015

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Statistics include effect measures, effect measures, p values, and 95% confidence intervals (CI).Effect measures: odds ratio (OR), risk raitios (RR) and absolute risk reductions (ARR)
NOTE4: When there are zero cells, OR, RR, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE5: When there are zero cells, ARR, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE6: Only ≥10 events in either treatment arm are shown in this table

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_gt0_NPERCENT

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) – EDSS>0

	Event (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
MCID increase ≥15% - COGNITIVE FATIGUE - Week 96	Yes	10 (20.00)	2 (4.44)	12 (15.58)
-	No	31 (62.00)	34 (75.56)	65 (84.42)
-	Missing	9 (18.00)	9 (20.00)	18 (18.95)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Only ≥10 events in either treatment arm are shown in this table

109MS306_CSRTab41_43Related_PedsQLFatigueParticipant_Baseline_EDSS_gt0_responsRate

Summary statistics PedsQL Multidimensional Fatigure Scale (Participant) - EDSS>0

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
COGNITIVE FATIGUE-Week 96	Yes	39 (78.00)	25 (55.56)	64 (67.37)
-	No	11 (22.00)	20 (44.44)	31 (32.63)

NOTE1: Scale of the measure is 0 to 100.Patients' data that were non-missing at baseline but missing at follow-up points are imputed as NOT having MCID increase/decrease ≥15%
NOTE2: Patients whose data were missing at both baseline and follow-up points are excluded from the calculation
NOTE3: Only ≥10 events in either treatment arm are shown in this table

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_EQZERO

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score EQ Zero. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-3.3 (10.35)	-3.2 (15.36)	-3.3 (13.12)
Median	0.0	-2.1	0.0
Q1,Q3	-12.5, 4.2	-12.5, 12.5	-12.5, 4.2
Min, Max	-21, 13	-29, 25	-29, 25
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	-1.2 (14.84)	-0.5 (14.78)	-0.8 (14.57)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 4.2	-12.5, 8.3	-12.5, 4.2
Min, Max	-25, 38	-25, 29	-25, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	-10.9 (9.25)	-2.4 (20.91)	-6.5 (16.64)
Median	-12.5	-4.2	-8.3
Q1,Q3	-16.7, -4.2	-16.7, 8.3	-16.7, 4.2
Min, Max	-25, 8	-29, 50	-29, 50
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-6.9 (15.92)	-8.7 (23.04)	-7.8 (19.56)
Median	-4.2	-12.5	-8.3
Q1,Q3	-20.8, 4.2	-25.0, 0.0	-25.0, 4.2
Min, Max	-33, 21	-46, 38	-46, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score EQ Zero. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-4.2 (18.23)	-3.2 (17.77)	-3.7 (17.70)
Median	-4.2	2.1	0.0
Q1,Q3	-16.7, 8.3	-12.5, 8.3	-12.5, 8.3
Min, Max	-46, 29	-38, 17	-46, 29
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	0.9 (13.98)	0.2 (16.26)	0.5 (15.07)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-4.2, 12.5	-8.3, 10.4
Min, Max	-17, 33	-46, 25	-46, 33

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	0.0 (15.02)	1.3 (16.65)	0.7 (15.60)
Median	0.0	4.2	0.0
Q1,Q3	-8.3, 8.3	-12.5, 12.5	-12.5, 12.5
Min, Max	-25, 25	-25, 29	-25, 29
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-4.2 (19.62)	0.6 (19.38)	-1.7 (19.25)
Median	-2.1	0.0	0.0
Q1,Q3	-10.4, 4.2	-12.5, 12.5	-12.5, 8.3
Min, Max	-42, 33	-29, 38	-42, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score EQ Zero. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	1.4 (9.27)	-0.5 (16.29)	0.4 (13.40)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 8.3	-8.3, 4.2	-4.2, 8.3
Min, Max	-13, 17	-38, 33	-38, 33
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	0.6 (14.79)	-0.2 (27.99)	0.1 (22.83)
Median	-2.1	0.0	-2.1
Q1,Q3	-8.3, 8.3	-16.7, 16.7	-8.3, 12.5
Min, Max	-21, 33	-58, 63	-58, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	-1.9 (16.72)	0.3 (18.23)	-0.8 (17.22)
Median	-4.2	0.0	-4.2
Q1,Q3	-8.3, 0.0	-12.5, 16.7	-12.5, 12.5
Min, Max	-21, 38	-29, 33	-29, 38
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-5.6 (13.10)	-4.8 (20.75)	-5.2 (17.15)
Median	-4.2	0.0	-4.2
Q1,Q3	-16.7, 0.0	-12.5, 8.3	-16.7, 8.3
Min, Max	-25, 21	-54, 17	-54, 21

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_GTZERO

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score GT Zero. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	38 (76)	34 (76)	72 (76)
Mean (SD)	2.3 (19.92)	-0.9 (12.47)	0.8 (16.78)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-8.3, 4.2	-8.3, 6.3
Min, Max	-29, 75	-29, 29	-29, 75
Week 48			
n (%)	35 (70)	25 (56)	60 (63)
Mean (SD)	3.3 (19.25)	-5.7 (20.23)	-0.4 (20.00)
Median	4.2	0.0	2.1
Q1,Q3	-12.5, 16.7	-16.7, 8.3	-12.5, 12.5
Min, Max	-29, 63	-58, 25	-58, 63

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	35 (70)	21 (47)	56 (59)
Mean (SD)	2.7 (16.14)	-2.8 (15.83)	0.7 (16.10)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 12.5	-12.5, 8.3	-8.3, 12.5
Min, Max	-33, 46	-29, 21	-33, 46
Week 96			
n (%)	30 (60)	21 (47)	51 (54)
Mean (SD)	-4.3 (23.40)	-1.0 (18.16)	-2.9 (21.27)
Median	-2.1	0.0	0.0
Q1,Q3	-16.7, 8.3	-12.5, 16.7	-16.7, 8.3
Min, Max	-71, 42	-38, 33	-71, 42

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score GT Zero. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	38 (76)	34 (76)	72 (76)
Mean (SD)	3.3 (19.26)	-0.1 (13.59)	1.7 (16.79)
Median	2.1	0.0	0.0
Q1,Q3	-4.2, 8.3	-8.3, 8.3	-4.2, 8.3
Min, Max	-33, 79	-42, 25	-42, 79
Week 48			
n (%)	35 (70)	25 (56)	60 (63)
Mean (SD)	1.1 (15.72)	-0.8 (20.34)	0.3 (17.65)
Median	0.0	-4.2	0.0
Q1,Q3	-8.3, 8.3	-16.7, 8.3	-8.3, 8.3
Min, Max	-29, 42	-38, 50	-38, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	35 (70)	21 (47)	56 (59)
Mean (SD)	0.6 (19.76)	-2.4 (20.86)	-0.5 (20.04)
Median	-4.2	0.0	-2.1
Q1,Q3	-12.5, 12.5	-16.7, 8.3	-12.5, 12.5
Min, Max	-46, 58	-46, 42	-46, 58
Week 96			
n (%)	30 (60)	21 (47)	51 (54)
Mean (SD)	-3.2 (17.87)	-2.0 (17.31)	-2.7 (17.48)
Median	-2.1	-4.2	-4.2
Q1,Q3	-12.5, 8.3	-8.3, 12.5	-12.5, 8.3
Min, Max	-58, 25	-54, 25	-58, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135), Change from Baseline; Subgroup analysis for EDSSBL Score GT Zero. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	38 (76)	34 (76)	72 (76)
Mean (SD)	6.5 (20.82)	-2.7 (16.91)	2.1 (19.49)
Median	4.2	0.0	0.0
Q1,Q3	-4.2, 12.5	-8.3, 4.2	-8.3, 10.4
Min, Max	-21, 100	-50, 38	-50, 100
Week 48			
n (%)	35 (70)	25 (56)	60 (63)
Mean (SD)	3.5 (16.37)	-5.3 (14.41)	-0.2 (16.06)
Median	0.0	-4.2	-4.2
Q1,Q3	-8.3, 16.7	-12.5, 0.0	-10.4, 12.5
Min, Max	-29, 58	-33, 33	-33, 58

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	35 (70)	21 (47)	56 (59)
Mean (SD)	4.9 (22.11)	-7.1 (16.20)	0.4 (20.78)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 16.7	-12.5, 0.0	-12.5, 12.5
Min, Max	-25, 100	-46, 17	-46, 100
Week 96			
n (%)	30 (60)	21 (47)	51 (54)
Mean (SD)	2.4 (20.08)	-8.5 (21.75)	-2.1 (21.27)
Median	0.0	-4.2	0.0
Q1,Q3	-12.5, 20.8	-20.8, 0.0	-16.7, 8.3
Min, Max	-29, 50	-42, 46	-42, 50

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

109MS306_table41_43_CHG_DESCRIBE_EDSSBL_EQZERO

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-3.3 (10.35)	-3.2 (15.36)	-3.3 (13.12)
Median	0.0	-2.1	0.0
Q1,Q3	-12.5, 4.2	-12.5, 12.5	-12.5, 4.2
Min, Max	-21, 13	-29, 25	-29, 25
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	-1.2 (14.84)	-0.5 (14.78)	-0.8 (14.57)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 4.2	-12.5, 8.3	-12.5, 4.2
Min, Max	-25, 38	-25, 29	-25, 38

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	-10.9 (9.25)	-2.4 (20.91)	-6.5 (16.64)
Median	-12.5	-4.2	-8.3
Q1,Q3	-16.7, -4.2	-16.7, 8.3	-16.7, 4.2
Min, Max	-25, 8	-29, 50	-29, 50
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-6.9 (15.92)	-8.7 (23.04)	-7.8 (19.56)
Median	-4.2	-12.5	-8.3
Q1,Q3	-20.8, 4.2	-25.0, 0.0	-25.0, 4.2
Min, Max	-33, 21	-46, 38	-46, 38

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-4.2 (18.23)	-3.2 (17.77)	-3.7 (17.70)
Median	-4.2	2.1	0.0
Q1,Q3	-16.7, 8.3	-12.5, 8.3	-12.5, 8.3
Min, Max	-46, 29	-38, 17	-46, 29
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	0.9 (13.98)	0.2 (16.26)	0.5 (15.07)
Median	0.0	0.0	0.0
Q1,Q3	-8.3, 8.3	-4.2, 12.5	-8.3, 10.4
Min, Max	-17, 33	-46, 25	-46, 33

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	0.0 (15.02)	1.3 (16.65)	0.7 (15.60)
Median	0.0	4.2	0.0
Q1,Q3	-8.3, 8.3	-12.5, 12.5	-12.5, 12.5
Min, Max	-25, 25	-25, 29	-25, 29
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-4.2 (19.62)	0.6 (19.38)	-1.7 (19.25)
Median	-2.1	0.0	0.0
Q1,Q3	-10.4, 4.2	-12.5, 12.5	-12.5, 8.3
Min, Max	-42, 33	-29, 38	-42, 38

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	1.4 (9.27)	-0.5 (16.29)	0.4 (13.40)
Median	0.0	0.0	0.0
Q1,Q3	-4.2, 8.3	-8.3, 4.2	-4.2, 8.3
Min, Max	-13, 17	-38, 33	-38, 33
Week 48			
n (%)	14 (67)	18 (95)	32 (80)
Mean (SD)	0.6 (14.79)	-0.2 (27.99)	0.1 (22.83)
Median	-2.1	0.0	-2.1
Q1,Q3	-8.3, 8.3	-16.7, 16.7	-8.3, 12.5
Min, Max	-21, 33	-58, 63	-58, 63

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	13 (62)	14 (74)	27 (68)
Mean (SD)	-1.9 (16.72)	0.3 (18.23)	-0.8 (17.22)
Median	-4.2	0.0	-4.2
Q1,Q3	-8.3, 0.0	-12.5, 16.7	-12.5, 12.5
Min, Max	-21, 38	-29, 33	-29, 38
Week 96			
n (%)	12 (57)	13 (68)	25 (63)
Mean (SD)	-5.6 (13.10)	-4.8 (20.75)	-5.2 (17.15)
Median	-4.2	0.0	-4.2
Q1,Q3	-16.7, 0.0	-12.5, 8.3	-16.7, 8.3
Min, Max	-25, 21	-54, 17	-54, 21

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

109MS306_table41_43_CHG_DESCRIBE_EDSSBL_GTZERO

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	41 (82)	36 (80)	77 (81)
Mean (SD)	67.9 (26.32)	75.6 (21.71)	71.5 (24.43)
Median	75.0	79.2	79.2
Q1,Q3	58.3, 87.5	70.8, 91.7	62.5, 91.7
Min, Max	0, 96	8, 100	0, 100
Week 24			
n (%)	44 (88)	43 (96)	87 (92)
Mean (SD)	70.0 (21.78)	72.4 (22.66)	71.2 (22.12)
Median	72.9	75.0	75.0
Q1,Q3	58.3, 85.4	58.3, 87.5	58.3, 87.5
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	42 (84)	33 (73)	75 (79)
Mean (SD)	69.3 (20.07)	73.6 (23.65)	71.2 (21.67)
Median	70.8	79.2	70.8
Q1,Q3	50.0, 83.3	62.5, 91.7	58.3, 91.7
Min, Max	25, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	27 (60)	69 (73)
Mean (SD)	69.9 (21.65)	74.5 (24.52)	71.7 (22.75)
Median	70.8	79.2	75.0
Q1,Q3	54.2, 87.5	66.7, 91.7	58.3, 91.7
Min, Max	29, 100	17, 100	17, 100
Week 96			
n (%)	39 (78)	25 (56)	64 (67)
Mean (SD)	68.3 (24.10)	77.2 (20.91)	71.7 (23.15)
Median	66.7	75.0	70.8
Q1,Q3	54.2, 91.7	62.5, 95.8	56.3, 93.8
Min, Max	0, 100	21, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	41 (82)	36 (80)	77 (81)
Mean (SD)	64.1 (21.35)	66.3 (26.42)	65.2 (23.71)
Median	62.5	68.8	66.7
Q1,Q3	50.0, 83.3	43.8, 93.8	50.0, 87.5
Min, Max	13, 96	21, 100	13, 100
Week 24			
n (%)	44 (88)	43 (96)	87 (92)
Mean (SD)	65.9 (20.20)	65.7 (23.65)	65.8 (21.85)
Median	62.5	66.7	62.5
Q1,Q3	52.1, 81.3	54.2, 83.3	54.2, 83.3
Min, Max	21, 100	8, 100	8, 100
Week 48			
n (%)	42 (84)	33 (73)	75 (79)
Mean (SD)	65.0 (22.87)	73.2 (21.60)	68.6 (22.55)
Median	66.7	70.8	70.8
Q1,Q3	45.8, 83.3	58.3, 91.7	54.2, 91.7
Min, Max	13, 100	21, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	27 (60)	69 (73)
Mean (SD)	64.4 (23.32)	70.8 (24.41)	66.9 (23.78)
Median	68.8	75.0	70.8
Q1,Q3	50.0, 79.2	54.2, 87.5	54.2, 87.5
Min, Max	13, 100	8, 100	8, 100
Week 96			
n (%)	39 (78)	25 (56)	64 (67)
Mean (SD)	65.3 (21.15)	70.7 (22.68)	67.4 (21.74)
Median	66.7	79.2	70.8
Q1,Q3	50.0, 83.3	58.3, 87.5	50.0, 87.5
Min, Max	25, 100	8, 100	8, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

Table 41.43: Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	41 (82)	36 (80)	77 (81)
Mean (SD)	64.2 (24.74)	78.8 (21.00)	71.0 (24.06)
Median	66.7	83.3	75.0
Q1,Q3	50.0, 83.3	64.6, 95.8	54.2, 91.7
Min, Max	0, 100	21, 100	0, 100
Week 24			
n (%)	44 (88)	43 (96)	87 (92)
Mean (SD)	70.6 (22.57)	73.8 (25.38)	72.2 (23.92)
Median	75.0	79.2	75.0
Q1,Q3	58.3, 87.5	58.3, 95.8	58.3, 91.7
Min, Max	13, 100	0, 100	0, 100
Week 48			
n (%)	42 (84)	33 (73)	75 (79)
Mean (SD)	66.5 (22.71)	75.5 (20.54)	70.4 (22.10)
Median	64.6	75.0	75.0
Q1,Q3	50.0, 83.3	66.7, 91.7	54.2, 91.7
Min, Max	13, 100	29, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	27 (60)	69 (73)
Mean (SD)	65.9 (24.32)	72.5 (22.24)	68.5 (23.59)
Median	70.8	75.0	70.8
Q1,Q3	45.8, 83.3	50.0, 91.7	50.0, 87.5
Min, Max	13, 100	29, 100	13, 100
Week 96			
n (%)	39 (78)	25 (56)	64 (67)
Mean (SD)	66.3 (25.12)	74.7 (24.88)	69.6 (25.16)
Median	66.7	75.0	72.9
Q1,Q3	45.8, 87.5	62.5, 100.0	50.0, 91.7
Min, Max	17, 100	13, 100	13, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_DESCRIBE_SubGr .sas date: 07APR2022

109MS306_table41_43_CHG_HEDGESCI_EDSSBL_EQZERO

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.136	-0.550	0.822
	48	0.036	-0.663	0.734
	72	-0.127	-0.882	0.629
	96	-0.043	-0.827	0.742
GENERAL FATIGUE	24	-0.007	-0.692	0.678
	48	-0.049	-0.748	0.649
	72	-0.52	-1.288	0.249
	96	0.086	-0.699	0.871
SLEEP/REST FATIGUE	24	-0.052	-0.737	0.634
	48	0.043	-0.655	0.742
	72	-0.082	-0.838	0.673
	96	-0.247	-1.034	0.541

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table41_43_CHG_HEDGESCI_EDSSBL_GTZERO

Table 41.43: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
COGNITIVE FATIGUE	24	0.48	0.011	0.950
	48	0.564	0.040	1.087
	72	0.598	0.045	1.150
	96	0.524	-0.043	1.092
GENERAL FATIGUE	24	0.188	-0.276	0.652
	48	0.458	-0.062	0.978
	72	0.344	-0.201	0.889
	96	-0.155	-0.713	0.404
SLEEP/REST FATIGUE	24	0.203	-0.261	0.667
	48	0.11	-0.404	0.623
	72	0.148	-0.394	0.689
	96	-0.069	-0.626	0.489

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43/109MS306_table41_43_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table41_43_CHG_LSMEANS_edsseq0

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS equal to 0. General Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	-1.88 (3.649)	-2.16 (3.599)
Lsmean_95 % CI	(-9.339, 05.586)	(-9.525, 05.197)
Diffrence (95% CI)	0.29 (-9.119, 9.694)	
SE_Difference	4.5991	
p-value	0.9506	
Week 48		
n (%)	14 (67)	18 (95)
Lsmean (SE)	-0.44 (4.065)	-0.47 (3.944)
Lsmean_95 % CI	(-8.768, 07.887)	(-8.546, 07.613)
Diffrence (95% CI)	0.027 (-10.484, 10.537)	
SE_Difference	5.1312	
p-value	0.9959	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	13 (62)	14 (74)
Lsmean (SE)	-9.16 (4.438)	00.59 (4.551)
Lsmean_95 % CI	(-18.34, 00.018)	(-8.829, 10.000)
Diffrence (95% CI)	-9.75 (-22.003, 2.506)	
SE_Difference	5.9238	
p-value	0.1134	
Week 96		
n (%)	12 (57)	13 (68)
Lsmean (SE)	-6.30 (5.874)	-6.79 (6.036)
Lsmean_95 % CI	(-18.52, 05.911)	(-19.35, 05.760)
Diffrence (95% CI)	0.49 (-16.061, 17.037)	
SE_Difference	7.9577	
p-value	0.9517	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS equal to 0. Sleep/Rest Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	01.53 (4.728)	-0.72 (4.484)
Lsmean_95 % CI	(-8.137, 11.204)	(-9.887, 08.454)
Diffrence (95% CI)	2.25 (-9.806, 14.307)	
SE_Difference	5.8948	
p-value	0.7054	
Week 48		
n (%)	14 (67)	18 (95)
Lsmean (SE)	03.86 (4.351)	00.62 (4.055)
Lsmean_95 % CI	(-5.057, 12.768)	(-7.684, 08.930)
Diffrence (95% CI)	3.23 (-7.886, 14.351)	
SE_Difference	5.4279	
p-value	0.5563	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	13 (62)	14 (74)
Lsmean (SE)	04.58 (3.960)	05.16 (3.954)
Lsmean_95 % CI	(-3.615, 12.769)	(-3.024, 13.336)
Diffrence (95% CI)	-0.58 (-11.362, 10.204)	
SE_Difference	5.2124	
p-value	0.9126	
Week 96		
n (%)	12 (57)	13 (68)
Lsmean (SE)	-0.84 (5.999)	02.13 (5.840)
Lsmean_95 % CI	(-13.31, 11.638)	(-10.01, 14.280)
Diffrence (95% CI)	-2.97 (-19.522, 13.578)	
SE_Difference	7.9581	
p-value	0.7125	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS equal to 0. Cognitive Fatigue

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	02.18 (3.827)	-0.59 (3.789)
Lsmean_95 % CI	(-5.646, 10.007)	(-8.345, 07.156)
Diffrence (95% CI)	2.77 (-7.237, 12.787)	
SE_Difference	4.8951	
p-value	0.5752	
Week 48		
n (%)	14 (67)	18 (95)
Lsmean (SE)	04.93 (5.837)	01.88 (5.668)
Lsmean_95 % CI	(-7.023, 16.891)	(-9.729, 13.492)
Diffrence (95% CI)	3.05 (-12.219, 18.324)	
SE_Difference	7.4550	
p-value	0.6853	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	13 (62)	14 (74)
Lsmean (SE)	00.43 (4.617)	02.54 (4.697)
Lsmean_95 % CI	(-9.126, 09.977)	(-7.176, 12.256)
Diffrence (95% CI)	-2.11 (-14.870, 10.641)	
SE_Difference	6.1659	
p-value	0.7348	
Week 96		
n (%)	12 (57)	13 (68)
Lsmean (SE)	-3.67 (4.989)	-2.30 (5.056)
Lsmean_95 % CI	(-14.04, 06.709)	(-12.81, 08.217)
Diffrence (95% CI)	-1.37 (-15.381, 12.642)	
SE_Difference	6.7375	
p-value	0.8409	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

109MS306_table41_43_CHG_LSMEANS_edssgt0

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS greater than 0. General Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	38 (76)	34 (76)
Lsmean (SE)	01.52 (2.856)	01.19 (2.820)
Lsmean_95 % CI	(-4.184, 07.215)	(-4.440, 06.816)
Diffrence (95% CI)	0.33 (-6.888, 7.543)	
SE_Difference	3.6160	
p-value	0.9281	
Week 48		
n (%)	35 (70)	25 (56)
Lsmean (SE)	01.83 (3.737)	-2.40 (3.830)
Lsmean_95 % CI	(-5.660, 09.313)	(-10.07, 05.275)
Diffrence (95% CI)	4.22 (-5.362, 13.809)	
SE_Difference	4.7849	
p-value	0.3812	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	35 (70)	21 (47)
Lsmean (SE)	05.02 (2.612)	02.86 (3.116)
Lsmean_95 % CI	(-0.219, 10.262)	(-3.396, 09.110)
Diffrence (95% CI)	2.16 (-5.162, 9.492)	
SE_Difference	3.6513	
p-value	0.5558	
Week 96		
n (%)	30 (60)	21 (47)
Lsmean (SE)	-4.71 (3.994)	01.85 (4.678)
Lsmean_95 % CI	(-12.75, 03.320)	(-7.560, 11.262)
Diffrence (95% CI)	-6.57 (-17.523, 4.391)	
SE_Difference	5.4465	
p-value	0.2340	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS greater than 0. Sleep/Rest Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	38 (76)	34 (76)
Lsmean (SE)	04.26 (2.838)	01.85 (2.777)
Lsmean_95 % CI	(-1.405, 09.922)	(-3.694, 07.391)
Diffrence (95% CI)	2.41 (-4.650, 9.469)	
SE_Difference	3.5378	
p-value	0.4981	
Week 48		
n (%)	35 (70)	25 (56)
Lsmean (SE)	-1.97 (3.559)	-0.04 (3.646)
Lsmean_95 % CI	(-9.099, 05.159)	(-7.340, 07.269)
Diffrence (95% CI)	-1.93 (-11.025, 7.156)	
SE_Difference	4.5381	
p-value	0.6715	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	35 (70)	21 (47)
Lsmean (SE)	-0.20 (3.844)	-0.19 (4.587)
Lsmean_95 % CI	(-7.913, 07.514)	(-9.395, 09.016)
Diffrence (95% CI)	-0.010 (-10.748, 10.728)	
SE_Difference	5.3513	
p-value	0.9985	
Week 96		
n (%)	30 (60)	21 (47)
Lsmean (SE)	-4.84 (3.333)	-1.41 (3.904)
Lsmean_95 % CI	(-11.54, 01.868)	(-9.263, 06.444)
Diffrence (95% CI)	-3.43 (-12.556, 5.701)	
SE_Difference	4.5376	
p-value	0.4538	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

Table 41.43: Analysis of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135); Subgroup analysis for EDSS greater than 0. Cognitive Fatigue

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	38 (76)	34 (76)
Lsmean (SE)	07.43 (3.342)	02.29 (3.367)
Lsmean_95 % CI	(00.759, 14.096)	(-4.431, 09.005)
Diffrence (95% CI)	5.14 (-3.519, 13.800)	
SE_Difference	4.3395	
p-value	0.2403	
Week 48		
n (%)	35 (70)	25 (56)
Lsmean (SE)	01.79 (3.160)	-2.25 (3.327)
Lsmean_95 % CI	(-4.541, 08.120)	(-8.919, 04.410)
Diffrence (95% CI)	4.04 (-4.349, 12.438)	
SE_Difference	4.1900	
p-value	0.3386	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	35 (70)	21 (47)
Lsmean (SE)	04.85 (3.683)	-0.35 (4.550)
Lsmean_95 % CI	(-2.540, 12.240)	(-9.476, 08.784)
Diffrence (95% CI)	5.20 (-5.576, 15.968)	
SE_Difference	5.3680	
p-value	0.3376	
Week 96		
n (%)	30 (60)	21 (47)
Lsmean (SE)	01.73 (4.145)	-2.66 (5.104)
Lsmean_95 % CI	(-6.606, 10.070)	(-12.93, 07.606)
Diffrence (95% CI)	4.39 (-7.668, 16.457)	
SE_Difference	5.9961	
p-value	0.4672	

NOTE1: Only results for subgroups that fulfill the criteria of >=10 patients in every arm and subgroup are presented.
NOTE2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T41_43\109MS306_table41_43_CHG_LSMEANS_SubGr_ban041322.sas date: 18APR2022

PedsQL QoL

Parents

MCID 15%

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_edsseq0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD for having a MCID of 15% total score when comparing each timepoint to baseline score by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	0.688	0.773	-0.080
	95% CI	(0.131, 3.610)	(0.242, 2.465)	(-0.428, 0.267)
	p-value	0.6579	0.6631	0.6511
EMOTIONAL scale Week 48 >=15% increase from baseline	Effect measure	2.813	2.318	0.155
	95% CI	(0.387, 20.458)	(0.459, 11.720)	(-0.149, 0.460)
	p-value	0.3071	0.3092	0.3182

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15 (coded as YES). Scales are 0 to 100, so 15% = 15)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a

NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_edssgt0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD for having a MCID of 15% total score when comparing each timepoint to baseline score by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	0.323	0.400	-0.171
	95% CI	(0.090, 1.153)	(0.138, 1.155)	(-0.354, 0.012)
	p-value	0.0817	0.0904	0.0664
EMOTIONAL scale Week 48 >=15% increase from baseline	Effect measure	4.103	3.241	0.192
	95% CI	(1.022, 16.473)	(0.973, 10.796)	(0.019, 0.365)
	p-value	0.0466	0.0555	0.0298

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15 (coded as YES). Scales are 0 to 100, so 15% = 15)
NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_edsseq0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS equal to 0

	EVENT	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	3 (14)	6 (32)	9 (23)
	No	8 (38)	11 (58)	19 (48)
	Missing	10 (48)	2 (11)	12 (30)
EMOTIONAL scale Week 48 >=15% increase from baseline				
	Yes	3 (14)	2 (11)	5 (13)
	No	8 (38)	15 (79)	23 (58)
	Missing	10 (48)	2 (11)	12 (30)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_edssgt0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS greater than 0

	EVENT	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	4 (8)	10 (22)	14 (15)
	No	31 (62)	25 (56)	56 (59)
	Missing	15 (30)	10 (22)	25 (26)
EMOTIONAL scale Week 48 >=15% increase from baseline				
	Yes	10 (20)	3 (7)	13 (14)
	No	26 (52)	32 (71)	58 (61)
	Missing	14 (28)	10 (22)	24 (25)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_edsseq0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) for having non-missing responses at baseline and each timepoint by study arm. Subgroup analysis for edsseq0

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
PHYSICAL scale Week 0				
	Yes	11 (52)	17 (89)	28 (70)
	No	10 (48)	2 (11)	12 (30)
PHYSICAL scale Week 24				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
PHYSICAL scale Week 48				
	Yes	15 (71)	15 (79)	30 (75)
	No	6 (29)	4 (21)	10 (25)
PHYSICAL scale Week 72				
	Yes	14 (67)	9 (47)	23 (58)
	No	7 (33)	10 (53)	17 (43)
PHYSICAL scale Week 96				
	Yes	11 (52)	8 (42)	19 (48)
	No	10 (48)	11 (58)	21 (53)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
EMOTIONAL scale Week 0				
	Yes	11 (52)	17 (89)	28 (70)
	No	10 (48)	2 (11)	12 (30)
EMOTIONAL scale Week 24				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
EMOTIONAL scale Week 48				
	Yes	15 (71)	15 (79)	30 (75)
	No	6 (29)	4 (21)	10 (25)
EMOTIONAL scale Week 72				
	Yes	14 (67)	9 (47)	23 (58)
	No	7 (33)	10 (53)	17 (43)
EMOTIONAL scale Week 96				
	Yes	11 (52)	8 (42)	19 (48)
	No	10 (48)	11 (58)	21 (53)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
SOCIAL scale Week 0				
	Yes	11 (52)	17 (89)	28 (70)
	No	10 (48)	2 (11)	12 (30)
SOCIAL scale Week 24				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
SOCIAL scale Week 48				
	Yes	15 (71)	15 (79)	30 (75)
	No	6 (29)	4 (21)	10 (25)
SOCIAL scale Week 72				
	Yes	14 (67)	9 (47)	23 (58)
	No	7 (33)	10 (53)	17 (43)
SOCIAL scale Week 96				
	Yes	11 (52)	8 (42)	19 (48)
	No	10 (48)	11 (58)	21 (53)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
SCHOOL scale Week 0				
	Yes	11 (52)	17 (89)	28 (70)
	No	10 (48)	2 (11)	12 (30)
SCHOOL scale Week 24				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
SCHOOL scale Week 48				
	Yes	15 (71)	15 (79)	30 (75)
	No	6 (29)	4 (21)	10 (25)
SCHOOL scale Week 72				
	Yes	14 (67)	9 (47)	23 (58)
	No	7 (33)	10 (53)	17 (43)
SCHOOL scale Week 96				
	Yes	11 (52)	8 (42)	19 (48)
	No	10 (48)	11 (58)	21 (53)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_edssgt0

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) for having non-missing responses at baseline and each timepoint by study arm. Subgroup analysis for edssgt0

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
PHYSICAL scale Week 0				
	Yes	36 (72)	35 (78)	71 (75)
	No	14 (28)	10 (22)	24 (25)
PHYSICAL scale Week 24				
	Yes	40 (80)	40 (89)	80 (84)
	No	10 (20)	5 (11)	15 (16)
PHYSICAL scale Week 48				
	Yes	37 (74)	28 (62)	65 (68)
	No	13 (26)	17 (38)	30 (32)
PHYSICAL scale Week 72				
	Yes	32 (64)	20 (44)	52 (55)
	No	18 (36)	25 (56)	43 (45)
PHYSICAL scale Week 96				
	Yes	18 (36)	14 (31)	32 (34)
	No	32 (64)	31 (69)	63 (66)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
EMOTIONAL scale Week 0				
	Yes	36 (72)	35 (78)	71 (75)
	No	14 (28)	10 (22)	24 (25)
EMOTIONAL scale Week 24				
	Yes	39 (78)	40 (89)	79 (83)
	No	11 (22)	5 (11)	16 (17)
EMOTIONAL scale Week 48				
	Yes	37 (74)	28 (62)	65 (68)
	No	13 (26)	17 (38)	30 (32)
EMOTIONAL scale Week 72				
	Yes	32 (64)	20 (44)	52 (55)
	No	18 (36)	25 (56)	43 (45)
EMOTIONAL scale Week 96				
	Yes	18 (36)	14 (31)	32 (34)
	No	32 (64)	31 (69)	63 (66)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
SOCIAL scale Week 0				
	Yes	36 (72)	35 (78)	71 (75)
	No	14 (28)	10 (22)	24 (25)
SOCIAL scale Week 24				
	Yes	40 (80)	40 (89)	80 (84)
	No	10 (20)	5 (11)	15 (16)
SOCIAL scale Week 48				
	Yes	37 (74)	28 (62)	65 (68)
	No	13 (26)	17 (38)	30 (32)
SOCIAL scale Week 72				
	Yes	32 (64)	20 (44)	52 (55)
	No	18 (36)	25 (56)	43 (45)
SOCIAL scale Week 96				
	Yes	18 (36)	14 (31)	32 (34)
	No	32 (64)	31 (69)	63 (66)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
SCHOOL scale Week 0				
	Yes	35 (70)	35 (78)	70 (74)
	No	15 (30)	10 (22)	25 (26)
SCHOOL scale Week 24				
	Yes	40 (80)	38 (84)	78 (82)
	No	10 (20)	7 (16)	17 (18)
SCHOOL scale Week 48				
	Yes	36 (72)	28 (62)	64 (67)
	No	14 (28)	17 (38)	31 (33)
SCHOOL scale Week 72				
	Yes	32 (64)	20 (44)	52 (55)
	No	18 (36)	25 (56)	43 (45)
SCHOOL scale Week 96				
	Yes	18 (36)	14 (31)	32 (34)
	No	32 (64)	31 (69)	63 (66)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups041822.sas date: 18APR2022

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_EDSSBL_EQZERO

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Physical Functioning.

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	9 (43)	17 (89)	26 (65)
Mean (SD)	-6.6 (25.31)	0.2 (11.61)	-2.2 (17.38)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 3.1	-3.1, 3.1	-3.1, 3.1
Min, Max	-72, 16	-22, 19	-72, 19
Week 48			
n (%)	8 (38)	14 (74)	22 (55)
Mean (SD)	-12.5 (32.35)	1.8 (12.54)	-3.4 (22.26)
Median	0.0	3.1	1.6
Q1,Q3	-14.1, 3.1	-3.1, 9.4	-3.1, 6.3
Min, Max	-88, 9	-22, 25	-88, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	7 (33)	8 (42)	15 (38)
Mean (SD)	-9.4 (18.58)	2.0 (14.56)	-3.3 (16.97)
Median	0.0	-1.6	0.0
Q1,Q3	-18.8, 3.1	-6.3, 17.2	-9.4, 6.3
Min, Max	-47, 6	-22, 19	-47, 19
Week 96			
n (%)	6 (29)	7 (37)	13 (33)
Mean (SD)	-6.8 (13.17)	4.0 (16.11)	-1.0 (15.28)
Median	-3.1	3.1	0.0
Q1,Q3	-9.4, 0.0	-6.3, 18.8	-6.3, 6.3
Min, Max	-31, 6	-22, 25	-31, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Emotional Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	9 (43)	17 (89)	26 (65)
Mean (SD)	-1.7 (16.77)	-5.6 (20.22)	-4.2 (18.85)
Median	-5.0	-5.0	-5.0
Q1,Q3	-5.0, 10.0	-20.0, 10.0	-20.0, 10.0
Min, Max	-30, 20	-40, 30	-40, 30
Week 48			
n (%)	8 (38)	14 (74)	22 (55)
Mean (SD)	10.0 (18.90)	-4.3 (19.00)	0.9 (19.80)
Median	5.0	-2.5	2.5
Q1,Q3	0.0, 27.5	-20.0, 10.0	-15.0, 10.0
Min, Max	-20, 35	-40, 30	-40, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	7 (33)	8 (42)	15 (38)
Mean (SD)	7.1 (12.20)	-5.0 (20.35)	0.7 (17.61)
Median	0.0	-10.0	0.0
Q1,Q3	-5.0, 20.0	-20.0, 10.0	-15.0, 20.0
Min, Max	-5, 20	-30, 30	-30, 30
Week 96			
n (%)	6 (29)	7 (37)	13 (33)
Mean (SD)	0.0 (3.16)	-1.4 (33.51)	-0.8 (23.79)
Median	0.0	-20.0	0.0
Q1,Q3	0.0, 0.0	-30.0, 35.0	-20.0, 5.0
Min, Max	-5, 5	-40, 40	-40, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Social Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	9 (43)	17 (89)	26 (65)
Mean (SD)	-6.7 (11.99)	1.8 (15.61)	-1.2 (14.79)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 0.0	-5.0, 5.0	-5.0, 0.0
Min, Max	-35, 0	-30, 35	-35, 35
Week 48			
n (%)	8 (38)	14 (74)	22 (55)
Mean (SD)	-6.3 (16.64)	0.7 (18.80)	-1.8 (17.96)
Median	0.0	2.5	0.0
Q1,Q3	-12.5, 0.0	-5.0, 10.0	-5.0, 5.0
Min, Max	-40, 15	-40, 35	-40, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	7 (33)	8 (42)	15 (38)
Mean (SD)	1.4 (6.27)	2.5 (17.11)	2.0 (12.79)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 0.0	-7.5, 5.0	0.0, 5.0
Min, Max	-5, 15	-15, 40	-15, 40
Week 96			
n (%)	6 (29)	7 (37)	13 (33)
Mean (SD)	-2.5 (11.73)	7.9 (26.12)	3.1 (20.67)
Median	0.0	5.0	0.0
Q1,Q3	0.0, 0.0	-15.0, 35.0	0.0, 10.0
Min, Max	-25, 10	-30, 45	-30, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Work/Study/School Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	9 (43)	17 (89)	26 (65)
Mean (SD)	-1.7 (16.96)	-6.8 (18.28)	-5.0 (17.66)
Median	-5.0	-5.0	-5.0
Q1,Q3	-15.0, 5.0	-15.0, 0.0	-15.0, 5.0
Min, Max	-20, 30	-45, 25	-45, 30
Week 48			
n (%)	8 (38)	14 (74)	22 (55)
Mean (SD)	5.0 (11.65)	-0.4 (16.92)	1.6 (15.15)
Median	2.5	0.0	0.0
Q1,Q3	0.0, 7.5	-5.0, 10.0	0.0, 10.0
Min, Max	-10, 30	-35, 25	-35, 30

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	7 (33)	8 (42)	15 (38)
Mean (SD)	-2.9 (17.29)	-4.4 (20.26)	-3.7 (18.27)
Median	-10.0	0.0	-5.0
Q1,Q3	-15.0, 10.0	-15.0, 12.5	-15.0, 10.0
Min, Max	-20, 30	-45, 15	-45, 30
Week 96			
n (%)	6 (29)	7 (37)	13 (33)
Mean (SD)	-1.7 (8.16)	4.3 (31.94)	1.5 (23.40)
Median	-2.5	15.0	0.0
Q1,Q3	-10.0, 5.0	-35.0, 35.0	-10.0, 15.0
Min, Max	-10, 10	-35, 45	-35, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_EDSSBL_GTZERO

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Physical Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	27 (54)	32 (71)	59 (62)
Mean (SD)	2.0 (14.43)	-1.0 (14.71)	0.4 (14.53)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 9.4	-12.5, 6.3	-9.4, 6.3
Min, Max	-34, 38	-22, 41	-34, 41
Week 48			
n (%)	25 (50)	23 (51)	48 (51)
Mean (SD)	4.6 (14.24)	-8.6 (14.93)	-1.7 (15.88)
Median	3.1	-9.4	-1.6
Q1,Q3	-3.1, 12.5	-21.9, 3.1	-9.4, 7.8
Min, Max	-25, 38	-34, 19	-34, 38

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 72			
n (%)	22 (44)	18 (40)	40 (42)
Mean (SD)	-4.5 (12.64)	-5.7 (18.13)	-5.1 (15.16)
Median	-4.7	0.0	-1.6
Q1,Q3	-12.5, 3.1	-9.4, 6.3	-10.9, 4.7
Min, Max	-34, 22	-38, 22	-38, 22
Week 96			
n (%)	12 (24)	12 (27)	24 (25)
Mean (SD)	-0.5 (13.04)	-0.3 (14.50)	-0.4 (13.49)
Median	1.6	-3.1	0.0
Q1,Q3	-7.8, 3.1	-9.4, 0.0	-9.4, 3.1
Min, Max	-22, 28	-16, 34	-22, 34

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	27 (54)	32 (71)	59 (62)
Mean (SD)	2.0 (18.31)	-0.2 (18.86)	0.8 (18.48)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-12.5, 10.0	-10.0, 10.0
Min, Max	-25, 50	-45, 40	-45, 50
Week 48			
n (%)	25 (50)	23 (51)	48 (51)
Mean (SD)	7.8 (24.46)	-2.4 (14.76)	2.9 (20.83)
Median	0.0	5.0	2.5
Q1,Q3	-5.0, 25.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-45, 65	-30, 20	-45, 65

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	22 (44)	18 (40)	40 (42)
Mean (SD)	1.4 (21.11)	3.1 (13.41)	2.1 (17.86)
Median	0.0	5.0	2.5
Q1,Q3	-10.0, 20.0	-5.0, 10.0	-10.0, 12.5
Min, Max	-45, 40	-20, 35	-45, 40
Week 96			
n (%)	12 (24)	12 (27)	24 (25)
Mean (SD)	-4.6 (19.12)	2.9 (16.30)	-0.8 (17.80)
Median	-2.5	7.5	0.0
Q1,Q3	-15.0, 5.0	-7.5, 15.0	-10.0, 10.0
Min, Max	-45, 25	-30, 25	-45, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	27 (54)	32 (71)	59 (62)
Mean (SD)	2.6 (16.25)	-0.2 (14.28)	1.1 (15.14)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 15.0	-7.5, 2.5	-5.0, 5.0
Min, Max	-30, 40	-25, 40	-30, 40
Week 48			
n (%)	25 (50)	23 (51)	48 (51)
Mean (SD)	3.0 (10.51)	-1.1 (25.00)	1.0 (18.79)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-10.0, 0.0	-5.0, 5.0
Min, Max	-20, 25	-70, 75	-70, 75

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 72			
n (%)	22 (44)	18 (40)	40 (42)
Mean (SD)	3.0 (13.86)	-10.6 (22.09)	-3.1 (19.04)
Median	0.0	-5.0	0.0
Q1,Q3	-5.0, 10.0	-20.0, 0.0	-7.5, 10.0
Min, Max	-35, 35	-50, 40	-50, 40
Week 96			
n (%)	12 (24)	12 (27)	24 (25)
Mean (SD)	-1.3 (20.01)	0.8 (25.39)	-0.2 (22.38)
Median	0.0	0.0	0.0
Q1,Q3	-7.5, 12.5	-7.5, 0.0	-7.5, 2.5
Min, Max	-40, 35	-30, 75	-40, 75

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	27 (54)	32 (71)	59 (62)
Mean (SD)	2.8 (19.03)	-1.3 (15.66)	0.6 (17.25)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-15.0, 5.0	-10.0, 5.0
Min, Max	-40, 50	-25, 55	-40, 55
Week 48			
n (%)	25 (50)	23 (51)	48 (51)
Mean (SD)	8.2 (20.66)	-2.0 (21.36)	3.3 (21.40)
Median	5.0	0.0	5.0
Q1,Q3	-10.0, 20.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-35, 60	-40, 50	-40, 60

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	22 (44)	18 (40)	40 (42)
Mean (SD)	3.9 (24.39)	-3.6 (15.13)	0.5 (20.84)
Median	2.5	0.0	0.0
Q1,Q3	-10.0, 20.0	-5.0, 5.0	-10.0, 12.5
Min, Max	-40, 60	-35, 25	-40, 60
Week 96			
n (%)	12 (24)	11 (24)	23 (24)
Mean (SD)	9.6 (13.73)	-0.9 (18.14)	4.6 (16.51)
Median	7.5	5.0	5.0
Q1,Q3	0.0, 20.0	-5.0, 10.0	-5.0, 15.0
Min, Max	-10, 40	-40, 25	-40, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 13MAY2022

109MS306_table46_48_CHG_DESCRIBE_EDSSBL_EQZERO

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Physical Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	11 (52)	18 (95)	29 (73)
Mean (SD)	90.6 (9.68)	75.5 (16.23)	81.3 (15.78)
Median	93.8	71.9	84.4
Q1,Q3	84.4, 100.0	59.4, 87.5	71.9, 93.8
Min, Max	69, 100	47, 100	47, 100
Week 24			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	75.6 (28.14)	75.7 (18.43)	75.6 (23.13)
Median	82.8	78.1	79.7
Q1,Q3	60.9, 100.0	68.8, 90.6	65.6, 93.8
Min, Max	13, 100	25, 100	13, 100
Week 48			
n (%)	15 (71)	15 (79)	30 (75)
Mean (SD)	76.0 (26.03)	75.8 (16.89)	75.9 (21.56)
Median	87.5	78.1	79.7
Q1,Q3	65.6, 93.8	59.4, 93.8	62.5, 93.8
Min, Max	13, 100	50, 100	13, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_
SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	14 (67)	9 (47)	23 (58)
Mean (SD)	76.6 (19.18)	81.3 (15.07)	78.4 (17.47)
Median	76.6	75.0	75.0
Q1,Q3	65.6, 90.6	71.9, 96.9	65.6, 96.9
Min, Max	44, 100	59, 100	44, 100
Week 96			
n (%)	11 (52)	8 (42)	19 (48)
Mean (SD)	79.5 (16.50)	84.4 (15.40)	81.6 (15.79)
Median	78.1	87.5	81.3
Q1,Q3	65.6, 96.9	70.3, 98.4	65.6, 96.9
Min, Max	50, 100	63, 100	50, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Emotional Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	11 (52)	18 (95)	29 (73)
Mean (SD)	71.8 (22.28)	71.1 (18.11)	71.4 (19.41)
Median	80.0	70.0	70.0
Q1,Q3	50.0, 95.0	60.0, 90.0	60.0, 90.0
Min, Max	40, 100	25, 95	25, 100
Week 24			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	64.7 (25.46)	66.1 (17.37)	65.4 (21.23)
Median	60.0	70.0	67.5
Q1,Q3	50.0, 90.0	55.0, 80.0	50.0, 80.0
Min, Max	20, 100	25, 95	20, 100
Week 48			
n (%)	15 (71)	15 (79)	30 (75)
Mean (SD)	71.3 (23.26)	66.7 (14.60)	69.0 (19.23)
Median	65.0	65.0	65.0
Q1,Q3	45.0, 95.0	60.0, 75.0	55.0, 90.0
Min, Max	40, 100	40, 95	40, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	14 (67)	9 (47)	23 (58)
Mean (SD)	71.9 (20.77)	68.9 (9.28)	70.7 (16.99)
Median	72.5	70.0	70.0
Q1,Q3	60.0, 90.0	60.0, 75.0	60.0, 80.0
Min, Max	35, 100	55, 80	35, 100
Week 96			
n (%)	11 (52)	8 (42)	19 (48)
Mean (SD)	64.1 (21.89)	69.4 (23.37)	66.3 (22.04)
Median	60.0	60.0	60.0
Q1,Q3	45.0, 90.0	50.0, 95.0	50.0, 90.0
Min, Max	40, 100	45, 100	40, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Social Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	11 (52)	18 (95)	29 (73)
Mean (SD)	95.9 (9.17)	87.8 (15.07)	90.9 (13.57)
Median	100.0	95.0	100.0
Q1,Q3	100.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	75, 100	55, 100	55, 100
Week 24			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	88.8 (11.62)	90.3 (14.19)	89.6 (12.87)
Median	90.0	97.5	92.5
Q1,Q3	82.5, 100.0	90.0, 100.0	85.0, 100.0
Min, Max	65, 100	50, 100	50, 100
Week 48			
n (%)	15 (71)	15 (79)	30 (75)
Mean (SD)	86.3 (14.57)	86.0 (15.95)	86.2 (15.01)
Median	90.0	95.0	95.0
Q1,Q3	80.0, 100.0	70.0, 100.0	75.0, 100.0
Min, Max	55, 100	55, 100	55, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	14 (67)	9 (47)	23 (58)
Mean (SD)	95.4 (7.46)	90.0 (10.00)	93.3 (8.74)
Median	100.0	95.0	95.0
Q1,Q3	95.0, 100.0	80.0, 100.0	85.0, 100.0
Min, Max	75, 100	75, 100	75, 100
Week 96			
n (%)	11 (52)	8 (42)	19 (48)
Mean (SD)	94.1 (8.31)	91.9 (15.10)	93.2 (11.33)
Median	100.0	100.0	100.0
Q1,Q3	90.0, 100.0	85.0, 100.0	90.0, 100.0
Min, Max	75, 100	65, 100	65, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. Work/Study/School Functioning

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	11 (52)	18 (95)	29 (73)
Mean (SD)	77.7 (23.60)	75.3 (18.35)	76.2 (20.12)
Median	90.0	75.0	80.0
Q1,Q3	55.0, 100.0	60.0, 90.0	60.0, 95.0
Min, Max	45, 100	40, 100	40, 100
Week 24			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	68.8 (26.49)	69.4 (18.06)	69.1 (22.07)
Median	72.5	67.5	70.0
Q1,Q3	50.0, 90.0	55.0, 85.0	55.0, 85.0
Min, Max	0, 95	30, 100	0, 100
Week 48			
n (%)	15 (71)	15 (79)	30 (75)
Mean (SD)	71.3 (26.89)	74.3 (22.03)	72.8 (24.20)
Median	80.0	80.0	80.0
Q1,Q3	55.0, 90.0	55.0, 95.0	55.0, 90.0
Min, Max	15, 100	35, 100	15, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	14 (67)	9 (47)	23 (58)
Mean (SD)	74.6 (19.26)	73.3 (20.00)	74.1 (19.11)
Median	82.5	80.0	80.0
Q1,Q3	60.0, 90.0	55.0, 85.0	55.0, 90.0
Min, Max	35, 95	40, 100	35, 100
Week 96			
n (%)	11 (52)	8 (42)	19 (48)
Mean (SD)	73.6 (22.59)	75.0 (16.90)	74.2 (19.88)
Median	75.0	75.0	75.0
Q1,Q3	55.0, 95.0	62.5, 87.5	55.0, 95.0
Min, Max	40, 100	50, 100	40, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

109MS306_table46_48_CHG_DESCRIBE_EDSSBL_GTZERO

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Physical Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	36 (72)	35 (78)	71 (75)
Mean (SD)	71.4 (26.85)	75.2 (21.81)	73.3 (24.39)
Median	78.1	78.1	78.1
Q1,Q3	54.7, 93.8	65.6, 93.8	59.4, 93.8
Min, Max	0, 100	19, 100	0, 100
Week 24			
n (%)	40 (80)	40 (89)	80 (84)
Mean (SD)	77.7 (19.73)	75.2 (20.44)	76.5 (20.00)
Median	81.3	78.1	78.1
Q1,Q3	59.4, 96.9	65.6, 93.8	62.5, 93.8
Min, Max	38, 100	19, 100	19, 100
Week 48			
n (%)	37 (74)	29 (64)	66 (69)
Mean (SD)	75.2 (20.90)	73.2 (21.96)	74.3 (21.23)
Median	78.1	75.0	75.0
Q1,Q3	59.4, 93.8	62.5, 90.6	62.5, 93.8
Min, Max	31, 100	16, 100	16, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_
SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	32 (64)	20 (44)	52 (55)
Mean (SD)	71.7 (20.96)	76.1 (22.24)	73.4 (21.36)
Median	71.9	84.4	76.6
Q1,Q3	51.6, 87.5	57.8, 93.8	54.7, 90.6
Min, Max	28, 100	31, 100	28, 100
Week 96			
n (%)	18 (36)	14 (31)	32 (34)
Mean (SD)	78.6 (22.79)	81.3 (16.40)	79.8 (19.99)
Median	90.6	85.9	87.5
Q1,Q3	65.6, 96.9	68.8, 96.9	65.6, 96.9
Min, Max	38, 100	53, 100	38, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	36 (72)	35 (78)	71 (75)
Mean (SD)	61.5 (25.26)	68.7 (22.11)	65.1 (23.87)
Median	67.5	75.0	70.0
Q1,Q3	45.0, 77.5	55.0, 85.0	50.0, 85.0
Min, Max	0, 100	20, 100	0, 100
Week 24			
n (%)	39 (78)	40 (89)	79 (83)
Mean (SD)	67.4 (21.85)	67.5 (20.69)	67.5 (21.14)
Median	70.0	70.0	70.0
Q1,Q3	55.0, 85.0	50.0, 82.5	50.0, 85.0
Min, Max	0, 100	30, 100	0, 100
Week 48			
n (%)	37 (74)	29 (64)	66 (69)
Mean (SD)	69.6 (23.93)	69.5 (21.60)	69.5 (22.77)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 90.0	60.0, 85.0	50.0, 90.0
Min, Max	0, 100	15, 100	0, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	32 (64)	20 (44)	52 (55)
Mean (SD)	66.9 (23.92)	72.8 (20.03)	69.1 (22.49)
Median	70.0	72.5	70.0
Q1,Q3	47.5, 82.5	57.5, 87.5	52.5, 85.0
Min, Max	20, 100	30, 100	20, 100
Week 96			
n (%)	18 (36)	14 (31)	32 (34)
Mean (SD)	67.2 (27.61)	68.9 (25.58)	68.0 (26.33)
Median	75.0	72.5	75.0
Q1,Q3	50.0, 85.0	60.0, 90.0	52.5, 87.5
Min, Max	15, 100	10, 100	10, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	36 (72)	35 (78)	71 (75)
Mean (SD)	80.1 (24.39)	86.1 (20.04)	83.1 (22.40)
Median	90.0	95.0	95.0
Q1,Q3	65.0, 100.0	75.0, 100.0	70.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 24			
n (%)	40 (80)	40 (89)	80 (84)
Mean (SD)	85.5 (17.61)	85.1 (16.23)	85.3 (16.83)
Median	92.5	90.0	90.0
Q1,Q3	75.0, 100.0	75.0, 100.0	75.0, 100.0
Min, Max	45, 100	50, 100	45, 100
Week 48			
n (%)	37 (74)	29 (64)	66 (69)
Mean (SD)	80.9 (23.18)	89.3 (19.31)	84.6 (21.81)
Median	95.0	100.0	97.5
Q1,Q3	65.0, 100.0	90.0, 100.0	75.0, 100.0
Min, Max	25, 100	15, 100	15, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	32 (64)	20 (44)	52 (55)
Mean (SD)	83.9 (21.20)	81.3 (24.49)	82.9 (22.32)
Median	95.0	95.0	95.0
Q1,Q3	67.5, 100.0	70.0, 100.0	70.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 96			
n (%)	18 (36)	14 (31)	32 (34)
Mean (SD)	82.8 (23.21)	89.6 (16.81)	85.8 (20.64)
Median	92.5	100.0	97.5
Q1,Q3	70.0, 100.0	90.0, 100.0	75.0, 100.0
Min, Max	30, 100	50, 100	30, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	35 (70)	35 (78)	70 (74)
Mean (SD)	61.0 (29.33)	66.6 (19.62)	63.8 (24.93)
Median	60.0	70.0	67.5
Q1,Q3	35.0, 85.0	55.0, 80.0	45.0, 85.0
Min, Max	5, 100	25, 100	5, 100
Week 24			
n (%)	40 (80)	38 (84)	78 (82)
Mean (SD)	66.0 (23.80)	65.7 (19.80)	65.8 (21.80)
Median	70.0	65.0	65.0
Q1,Q3	47.5, 82.5	50.0, 80.0	50.0, 80.0
Min, Max	25, 100	20, 100	20, 100
Week 48			
n (%)	36 (72)	29 (64)	65 (68)
Mean (SD)	66.1 (22.62)	70.2 (19.48)	67.9 (21.21)
Median	70.0	75.0	70.0
Q1,Q3	50.0, 85.0	55.0, 90.0	50.0, 85.0
Min, Max	15, 100	20, 95	15, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	32 (64)	20 (44)	52 (55)
Mean (SD)	63.9 (22.13)	68.5 (20.84)	65.7 (21.56)
Median	57.5	72.5	70.0
Q1,Q3	50.0, 87.5	55.0, 82.5	50.0, 85.0
Min, Max	15, 100	20, 100	15, 100
Week 96			
n (%)	18 (36)	14 (31)	32 (34)
Mean (SD)	68.6 (26.83)	76.1 (19.63)	71.9 (23.89)
Median	67.5	80.0	75.0
Q1,Q3	50.0, 95.0	55.0, 90.0	55.0, 92.5
Min, Max	20, 100	45, 100	20, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 13MAY2022

109MS306_table46_48_CHG_HEDGESCI_EDSSBL_EQZERO

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.219	-0.600	1.038
	48	0.715	-0.233	1.663
	72	0.711	-0.340	1.761
	96	0.058	-1.033	1.148
PHYSICAL FUNCTIONING	24	-0.371	-1.195	0.453
	48	-0.688	-1.634	0.258
	72	-0.685	-1.733	0.363
	96	-0.727	-1.859	0.405
SCHOOL FUNCTIONING	24	0.253	-0.567	1.072
	48	0.38	-0.547	1.307
	72	0.08	-0.935	1.095
	96	-0.246	-1.341	0.850
SOCIAL FUNCTIONING	24	-0.577	-1.410	0.257
	48	-0.417	-1.346	0.512
	72	-0.081	-1.096	0.934
	96	-0.497	-1.607	0.613

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_HEDGESCI_SubGr.sas date: 13MAY2022

109MS306_table46_48_CHG_HEDGESCI_EDSSBL_GTZERO

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.276	-0.251	0.803
	48	0.497	-0.097	1.091
	72	-0.173	-0.804	0.458
	96	-0.474	-1.322	0.375
PHYSICAL FUNCTIONING	24	0.235	-0.291	0.762
	48	0.997	0.376	1.619
	72	0.043	-0.586	0.673
	96	-0.079	-0.916	0.757
SCHOOL FUNCTIONING	24	0.36	-0.168	0.889
	48	0.636	0.037	1.236
	72	0.321	-0.312	0.955
	96	0.638	-0.220	1.497
SOCIAL FUNCTIONING	24	0.272	-0.255	0.799
	48	0.353	-0.236	0.943
	72	0.723	0.073	1.374
	96	-0.134	-0.970	0.703

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_HEDGESCI_SubGr.sas date: 13MAY2022

109MS306_table46_48_CHG_LSMEANS_edsseq0

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Emotional Functioning

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	9 (43)	17 (89)
Lsmean (SE)	-0.70 (6.246)	-7.68 (5.280)
Lsmean_95 % CI	(-13.649, 12.257)	(-18.634, 3.266)
Diffrence (95% CI)	6.989 (-9.626, 23.603)	
SE_Difference	8.0113	
p-value	0.3925	
Week 48		
n (%)	8 (38)	14 (74)
Lsmean (SE)	11.49 (5.602)	-5.85 (4.744)
Lsmean_95 % CI	(-0.282, 23.257)	(-15.815, 4.119)
Diffrence (95% CI)	17.335 (1.935, 32.735)	
SE_Difference	7.3298	
p-value	0.0295	
Week 72		
n (%)	7 (33)	8 (42)
Lsmean (SE)	7.61 (5.155)	-5.53 (4.882)
Lsmean_95 % CI	(-3.737, 18.956)	(-16.278, 5.214)
Diffrence (95% CI)	13.142 (-2.628, 28.911)	
SE_Difference	7.1645	
p-value	0.0938	
Week 96		
n (%)	6 (29)	7 (37)

	DMF (N= 21)	**IFN B-1a (N= 19)**
Lsmean (SE)	2.50 (9.523)	-3.55 (8.659)
Lsmean_95 % CI	(-19.038, 24.046)	(-23.139, 16.038)
Diffrence (95% CI)	6.054 (-23.451, 35.559)	
SE_Difference	3.0427	
p-value	0.6535	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Physical Functioning

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	9 (43)	17 (89)
Lsmean (SE)	-5.00 (6.630)	1.88 (5.381)
Lsmean_95 % CI	(-18.746, 8.752)	(-9.278, 13.040)
Diffrence (95% CI)	-6.878 (-25.548, 11.793)	
SE_Difference	9.0025	
p-value	0.4530	
Week 48		
n (%)	8 (38)	14 (74)
Lsmean (SE)	-7.87 (8.273)	2.97 (6.704)
Lsmean_95 % CI	(-25.247, 9.515)	(-11.118, 17.053)
Diffrence (95% CI)	-10.833 (-34.949, 13.283)	
SE_Difference	1.4784	
p-value	0.3578	
Week 72		
n (%)	7 (33)	8 (42)
Lsmean (SE)	-8.23 (6.594)	1.66 (6.229)
Lsmean_95 % CI	(-22.747, 6.280)	(-12.052, 15.367)
Diffrence (95% CI)	-9.891 (-31.537, 11.755)	
SE_Difference	9.8346	
p-value	0.3362	
Week 96		

	DMF (N= 21)	**IFN B-1a (N= 19)**
n (%)	6 (29)	7 (37)
Lsmean (SE)	-4.55 (6.933)	1.75 (6.175)
Lsmean_95 % CI	(-20.231, 11.138)	(-12.222, 15.715)
Diffrence (95% CI)	-6.293 (-29.229, 16.643)	
SE_Difference	0.1388	
p-value	0.5502	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Work/Study/School Functioning

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	9 (43)	17 (89)
Lsmean (SE)	0.74 (5.413)	-5.91 (4.579)
Lsmean_95 % CI	(-10.482, 11.971)	(-15.405, 3.588)
Diffrence (95% CI)	6.653 (-7.848, 21.154)	
SE_Difference	6.9921	
p-value	0.3517	
Week 48		
n (%)	8 (38)	14 (74)
Lsmean (SE)	6.05 (5.313)	-1.29 (4.486)
Lsmean_95 % CI	(-5.109, 17.217)	(-10.714, 8.138)
Diffrence (95% CI)	7.342 (-7.306, 21.990)	
SE_Difference	6.9722	
p-value	0.3063	
Week 72		
n (%)	7 (33)	8 (42)
Lsmean (SE)	-1.63 (6.319)	-6.17 (5.982)
Lsmean_95 % CI	(-15.533, 12.281)	(-19.332, 6.999)
Diffrence (95% CI)	4.540 (-14.788, 23.869)	
SE_Difference	8.7816	
p-value	0.6154	
Week 96		
n (%)	6 (29)	7 (37)
Lsmean (SE)	3.14 (9.089)	0.57 (8.255)

	DMF (N= 21)	**IFN B-1a (N= 19)**
Lsmean_95 % CI	(-17.417, 23.704)	(-18.107, 19.242)
Diffrence (95% CI)	2.576 (-25.907, 31.060)	
SE_Difference	2.5910	
p-value	0.8424	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. Social Functioning

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	9 (43)	17 (89)
Lsmean (SE)	-3.41 (4.651)	-0.66 (3.980)
Lsmean_95 % CI	(-13.052, 6.240)	(-8.917, 7.591)
Diffrence (95% CI)	-2.743 (-15.705, 10.219)	
SE_Difference	6.2500	
p-value	0.6650	
Week 48		
n (%)	8 (38)	14 (74)
Lsmean (SE)	-1.14 (5.842)	-1.87 (4.933)
Lsmean_95 % CI	(-13.409, 11.137)	(-12.229, 8.499)
Diffrence (95% CI)	0.729 (-16.038, 17.496)	
SE_Difference	7.9806	
p-value	0.9282	
Week 72		
n (%)	7 (33)	8 (42)
Lsmean (SE)	6.25 (2.594)	-2.10 (2.466)
Lsmean_95 % CI	(0.545, 11.963)	(-7.531, 3.327)
Diffrence (95% CI)	8.356 (0.053, 16.659)	
SE_Difference	3.7723	
p-value	0.0488	
Week 96		
n (%)	6 (29)	7 (37)

	DMF (N= 21)	**IFN B-1a (N= 19)**
Lsmean (SE)	6.23 (6.741)	0.28 (6.029)
Lsmean_95 % CI	(-9.023, 21.474)	(-13.356, 13.921)
Diffrence (95% CI)	5.943 (-16.176, 28.062)	
SE_Difference	9.7776	
p-value	0.5583	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

109MS306_table46_48_CHG_LSMEANS_edssgt0

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	27 (54)	32 (71)
Lsmean (SE)	0.56 (3.513)	0.23 (3.081)
Lsmean_95 % CI	(-6.485, 7.597)	(-5.949, 6.401)
Diffrence (95% CI)	0.330 (-7.939, 8.599)	
SE_Difference	4.1263	
p-value	0.9365	
Week 48		
n (%)	25 (50)	23 (51)
Lsmean (SE)	5.95 (4.568)	-1.65 (4.052)
Lsmean_95 % CI	(-3.252, 15.161)	(-9.815, 6.517)
Diffrence (95% CI)	7.604 (-2.880, 18.087)	
SE_Difference	5.2017	
p-value	0.1509	
Week 72		
n (%)	22 (44)	18 (40)
Lsmean (SE)	1.91 (4.277)	3.70 (4.480)
Lsmean_95 % CI	(-6.760, 10.588)	(-5.391, 12.782)
Diffrence (95% CI)	-1.782 (-12.755, 9.191)	
SE_Difference	5.4104	
p-value	0.7438	
Week 96		
n (%)	12 (24)	12 (27)

	DMF (N= 50)	**IFN B-1a (N= 45)**
Lsmean (SE)	-1.24 (5.430)	4.21 (5.441)
Lsmean_95 % CI	(-12.565, 10.090)	(-7.138, 15.563)
Diffrence (95% CI)	-5.450 (-21.004, 10.104)	
SE_Difference	7.4562	
p-value	0.4733	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Physical Functioning

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	27 (54)	32 (71)
Lsmean (SE)	1.91 (2.945)	-1.61 (2.538)
Lsmean_95 % CI	(-3.992, 7.813)	(-6.701, 3.473)
Diffrence (95% CI)	3.525 (-3.371, 10.420)	
SE_Difference	3.4407	
p-value	0.3101	
Week 48		
n (%)	25 (50)	23 (51)
Lsmean (SE)	3.34 (3.482)	-8.12 (3.086)
Lsmean_95 % CI	(-3.682, 10.354)	(-14.345, -1.904)
Diffrence (95% CI)	11.460 (3.428, 19.493)	
SE_Difference	3.9854	
p-value	0.0062	
Week 72		
n (%)	22 (44)	18 (40)
Lsmean (SE)	-5.11 (3.646)	-5.14 (3.887)
Lsmean_95 % CI	(-12.500, 2.288)	(-13.025, 2.741)
Diffrence (95% CI)	0.036 (-9.478, 9.550)	
SE_Difference	4.6910	
p-value	0.9940	
Week 96		
n (%)	12 (24)	12 (27)
Lsmean (SE)	-0.027 (4.108)	-0.15 (4.250)
Lsmean_95 % CI	(-8.596, 8.542)	(-9.014, 8.715)

	DMF (N= 50)	**IFN B-1a (N= 45)**
Diffrence (95% CI)	0.123 (-11.558, 11.804)	
SE_Difference	5.5996	
p-value	0.9827	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	27 (54)	32 (71)
Lsmean (SE)	0.067 (3.359)	-1.70 (2.946)
Lsmean_95 % CI	(-6.663, 6.798)	(-7.600, 4.207)
Diffrence (95% CI)	1.764 (-6.175, 9.703)	
SE_Difference	3.9616	
p-value	0.6579	
Week 48		
n (%)	25 (50)	23 (51)
Lsmean (SE)	5.28 (4.596)	0.068 (4.103)
Lsmean_95 % CI	(-3.982, 14.544)	(-8.201, 8.337)
Diffrence (95% CI)	5.213 (-5.496, 15.921)	
SE_Difference	5.3135	
p-value	0.3319	
Week 72		
n (%)	22 (44)	18 (40)
Lsmean (SE)	4.38 (4.500)	1.02 (4.837)
Lsmean_95 % CI	(-4.749, 13.502)	(-8.788, 10.832)
Diffrence (95% CI)	3.355 (-8.601, 15.310)	
SE_Difference	5.8948	
p-value	0.5728	
Week 96		
n (%)	12 (24)	11 (24)
Lsmean (SE)	10.02 (4.328)	2.20 (4.671)
Lsmean_95 % CI	(0.963, 19.080)	(-7.573, 11.982)

	DMF (N= 50)	**IFN B-1a (N= 45)**
Diffrence (95% CI)	7.817 (-5.022, 20.655)	
SE_Difference	6.1340	
p-value	0.2179	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent Assessment- mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	27 (54)	32 (71)
Lsmean (SE)	2.11 (2.464)	0.54 (2.148)
Lsmean_95 % CI	(-2.825, 7.049)	(-3.760, 4.849)
Diffrence (95% CI)	1.567 (-4.241, 7.376)	
SE_Difference	2.8985	
p-value	0.5909	
Week 48		
n (%)	25 (50)	23 (51)
Lsmean (SE)	3.29 (4.409)	0.71 (3.903)
Lsmean_95 % CI	(-5.597, 12.173)	(-7.162, 8.572)
Diffrence (95% CI)	2.583 (-7.589, 12.755)	
SE_Difference	5.0470	
p-value	0.6114	
Week 72		
n (%)	22 (44)	18 (40)
Lsmean (SE)	3.70 (4.282)	-7.65 (4.605)
Lsmean_95 % CI	(-4.983, 12.385)	(-16.989, 1.689)
Diffrence (95% CI)	11.351 (0.008, 22.693)	
SE_Difference	5.5927	
p-value	0.0498	
Week 96		
n (%)	12 (24)	12 (27)
Lsmean (SE)	-2.53 (6.050)	1.89 (6.381)
Lsmean_95 % CI	(-15.145, 10.095)	(-11.418, 15.204)

	DMF (N= 50)	**IFN B-1a (N= 45)**
Diffrence (95% CI)	-4.418 (-21.915, 13.079)	
SE_Difference	8.3877	
p-value	0.6042	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Participant

MCID

109MS306_Table45_47_MCID_15PCT_EFFECTMEASURES_edsseq0

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having a MCID of 15% of the total score when comparing each timepoint to baseline score by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
Feelings scale Week 24 >=15% increase from baseline	Effect measure	0.500	0.563	-0.097
	95% CI	(0.078, 3.186)	(0.118, 2.672)	(-0.349, 0.154)
	p-value	0.4632	0.4692	0.4483
Feelings scale Week 48 >=15% increase from baseline	Effect measure	1.846	1.687	0.076
	95% CI	(0.267, 12.758)	(0.322, 8.854)	(-0.164, 0.317)
	p-value	0.5342	0.5361	0.5329
Feelings scale Week 72 >=15% increase from baseline	Effect measure	0.714	0.750	-0.042
	95% CI	(0.103, 4.930)	(0.143, 3.935)	(-0.278, 0.195)
	p-value	0.7328	0.7337	0.7298
Feelings scale Week 96 >=15% increase from baseline	Effect measure	0.808	0.844	-0.035
	95% CI	(0.151, 4.319)	(0.222, 3.212)	(-0.306, 0.236)
	p-value	0.8028	0.8033	0.8017

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Result	OR	RR	ARR
Health scale Week 24 >=15% increase from baseline	Effect measure	0.233	0.281	-0.160
	95% CI	(0.023, 2.349)	(0.035, 2.263)	(-0.385, 0.066)
	p-value	0.2167	0.2331	0.1655

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Result	OR	RR	ARR
School scale Week 72 >=15% increase from baseline	Effect measure	1.133	1.125	0.007
	95% CI	(0.065, 19.739)	(0.076, 16.553)	(-0.152, 0.166)
	p-value	0.9316	0.9316	0.9318
School scale Week 96 >=15% increase from baseline	Effect measure	0.533	0.562	-0.049
	95% CI	(0.044, 6.508)	(0.056, 5.633)	(-0.236, 0.139)
	p-value	0.6224	0.6245	0.6113

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table45_47_MCID_15PCT_EFFECTMEASURES_edssgt0

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having a MCID of 15% of the total score when comparing each timepoint to baseline score by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
Feelings scale Week 24 >=15% increase from baseline	Effect measure	1.250	1.188	0.039
	95% CI	(0.434, 3.603)	(0.525, 2.688)	(-0.147, 0.226)
	p-value	0.6795	0.6801	0.6784
Feelings scale Week 48 >=15% increase from baseline	Effect measure	1.806	1.544	0.114
	95% CI	(0.649, 5.021)	(0.722, 3.303)	(-0.080, 0.309)
	p-value	0.2575	0.2632	0.2489
Feelings scale Week 72 >=15% increase from baseline	Effect measure	3.960	2.850	0.243
	95% CI	(1.269, 12.354)	(1.148, 7.077)	(0.059, 0.428)
	p-value	0.0177	0.0240	0.0097
Feelings scale Week 96 >=15% increase from baseline	Effect measure	1.250	1.188	0.039
	95% CI	(0.434, 3.603)	(0.525, 2.688)	(-0.147, 0.226)
	p-value	0.6795	0.6801	0.6784

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Result	OR	RR	ARR
Health scale Week 24 >=15% increase from baseline	Effect measure	6.828	5.225	0.222
	95% CI	(1.401, 33.281)	(1.238, 22.047)	(0.067, 0.378)
	p-value	0.0175	0.0244	0.0051

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Result	OR	RR	ARR
School scale Week 72 >=15% increase from baseline	Effect measure	2.095	1.786	0.124
	95% CI	(0.686, 6.400)	(0.734, 4.344)	(-0.059, 0.307)
	p-value	0.1941	0.2007	0.1829
School scale Week 96 >=15% increase from baseline	Effect measure	2.667	2.111	0.175
	95% CI	(0.890, 7.988)	(0.895, 4.979)	(-0.013, 0.363)
	p-value	0.0797	0.0878	0.0673

NOTE1: To create YES/NO event variables, we calculated timepoint score minus baseline and assessed if that change was >=15% (coded as YES). Scales are 0 to 12, so 15% = 1.8)

NOTE2: If baseline score is missing, we do NOT include them in analyses. If timepoint score is missing, event variable = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table45_47_MCID_15pct_NPERCENT_EVENT_edsseq0

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS equal to 0

	Event (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Feelings scale Week 24 >=15% increase from baseline				
	Yes	2 (10)	4 (21)	6 (15)
	No	14 (67)	14 (74)	28 (70)
	Missing	5 (24)	1 (5)	6 (15)
Feelings scale Week 48 >=15% increase from baseline				
	Yes	3 (14)	2 (11)	5 (13)
	No	13 (62)	16 (84)	29 (73)
	Missing	5 (24)	1 (5)	6 (15)
Feelings scale Week 72 >=15% increase from baseline				
	Yes	2 (10)	3 (16)	5 (13)
	No	14 (67)	15 (79)	29 (73)
	Missing	5 (24)	1 (5)	6 (15)
Feelings scale Week 96 >=15% increase from baseline				
	Yes	3 (14)	4 (21)	7 (18)
	No	13 (62)	14 (74)	27 (68)
	Missing	5 (24)	1 (5)	6 (15)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Event (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Health scale Week 24 >=15% increase from baseline				
	Yes	1 (5)	4 (21)	5 (13)
	No	15 (71)	14 (74)	29 (73)
	Missing	5 (24)	1 (5)	6 (15)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Event (n (%))	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
School scale Week 72 >=15% increase from baseline				
	Yes	1 (5)	1 (5)	2 (5)
	No	15 (71)	17 (89)	32 (80)
	Missing	5 (24)	1 (5)	6 (15)
School scale Week 96 >=15% increase from baseline				
	Yes	1 (5)	2 (11)	3 (8)
	No	15 (71)	16 (84)	31 (78)
	Missing	5 (24)	1 (5)	6 (15)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table45_47_MCID_15pct_NPERCENT_EVENT_edssgt0

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) for events (>=15% MCID) at each timepoint by study arm. Subgroup analysis for EDSS greater than 0

	Event (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Feelings scale Week 24 >=15% increase from baseline				
	Yes	10 (20)	8 (18)	18 (19)
	No	30 (60)	30 (67)	60 (63)
	Missing	10 (20)	7 (16)	17 (18)
Feelings scale Week 48 >=15% increase from baseline				
	Yes	13 (26)	8 (18)	21 (22)
	No	27 (54)	30 (67)	57 (60)
	Missing	10 (20)	7 (16)	17 (18)
Feelings scale Week 72 >=15% increase from baseline				
	Yes	15 (30)	5 (11)	20 (21)
	No	25 (50)	33 (73)	58 (61)
	Missing	10 (20)	7 (16)	17 (18)
Feelings scale Week 96 >=15% increase from baseline				
	Yes	10 (20)	8 (18)	18 (19)
	No	30 (60)	30 (67)	60 (63)
	Missing	10 (20)	7 (16)	17 (18)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Event (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Health scale Week 24 >=15% increase from baseline				
	Yes	11 (22)	2 (4)	13 (14)
	No	29 (58)	36 (80)	65 (68)
	Missing	10 (20)	7 (16)	17 (18)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

	Event (n (%))	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
School scale Week 72 >=15% increase from baseline				
	Yes	11 (22)	6 (13)	17 (18)
	No	28 (56)	32 (71)	60 (63)
	Missing	11 (22)	7 (16)	18 (19)
School scale Week 96 >=15% increase from baseline				
	Yes	13 (26)	6 (13)	19 (20)
	No	26 (52)	32 (71)	58 (61)
	Missing	11 (22)	7 (16)	18 (19)

NOTE1: An event is yes when the MCID is >=15%. Each scale is 0 to 12, so 15% of 12 is 1.8.

NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0

NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm

NOTE4: Ns in this table refer to patients.

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban041822.sas date: 18APR2022

109MS306_Table45_47_MCID_15PCT_NPERCENT_RESPONSE_edsseq0

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment-ITT Population, Aged 13 years and older (n=135). N(%) for having non-missing responses at each timepoint by study arm. Subgroup analysis for EDSS equal to 0

	Response (n (%))	DMF (N=21)	IFN-B1a (N=19)	Total (N=40)
Feelings scale Week 0				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
Feelings scale Week 24				
	Yes	21 (100)	19 (100)	40 (100)
Feelings scale Week 48				
	Yes	19 (90)	19 (100)	38 (95)
	No	2 (10)	0 (0)	2 (5)
Feelings scale Week 72				
	Yes	17 (81)	14 (74)	31 (78)
	No	4 (19)	5 (26)	9 (23)
Feelings scale Week 96				
	Yes	15 (71)	13 (68)	28 (70)
	No	6 (29)	6 (32)	12 (30)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN-B1a (N=19)	Total (N=40)
Get along scale Week 0				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
Get along scale Week 24				
	Yes	21 (100)	19 (100)	40 (100)
Get along scale Week 48				
	Yes	19 (90)	19 (100)	38 (95)
	No	2 (10)	0 (0)	2 (5)
Get along scale Week 72				
	Yes	17 (81)	14 (74)	31 (78)
	No	4 (19)	5 (26)	9 (23)
Get along scale Week 96				
	Yes	15 (71)	13 (68)	28 (70)
	No	6 (29)	6 (32)	12 (30)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN-B1a (N=19)	Total (N=40)
Health scale Week 0				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
Health scale Week 24				
	Yes	21 (100)	19 (100)	40 (100)
Health scale Week 48				
	Yes	19 (90)	19 (100)	38 (95)
	No	2 (10)	0 (0)	2 (5)
Health scale Week 72				
	Yes	17 (81)	14 (74)	31 (78)
	No	4 (19)	5 (26)	9 (23)
Health scale Week 96				
	Yes	15 (71)	13 (68)	28 (70)
	No	6 (29)	6 (32)	12 (30)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=21)	IFN-B1a (N=19)	Total (N=40)
School scale Week 0				
	Yes	16 (76)	18 (95)	34 (85)
	No	5 (24)	1 (5)	6 (15)
School scale Week 24				
	Yes	21 (100)	19 (100)	40 (100)
School scale Week 48				
	Yes	19 (90)	19 (100)	38 (95)
	No	2 (10)	0 (0)	2 (5)
School scale Week 72				
	Yes	17 (81)	14 (74)	31 (78)
	No	4 (19)	5 (26)	9 (23)
School scale Week 96				
	Yes	15 (71)	13 (68)	28 (70)
	No	6 (29)	6 (32)	12 (30)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

109MS306_Table45_47_MCID_15PCT_NPERCENT_RESPONSE_edssgt0

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment-ITT Population, Aged 13 years and older (n=135). N(%) for having non-missing responses at each timepoint by study arm. Subgroup analysis for EDSS greater than 0

	Response (n (%))	DMF (N=50)	IFN-B1a (N=45)	Total (N=95)
Feelings scale Week 0				
	Yes	40 (80)	38 (84)	78 (82)
	No	10 (20)	7 (16)	17 (18)
Feelings scale Week 24				
	Yes	46 (92)	43 (96)	89 (94)
	No	4 (8)	2 (4)	6 (6)
Feelings scale Week 48				
	Yes	43 (86)	33 (73)	76 (80)
	No	7 (14)	12 (27)	19 (20)
Feelings scale Week 72				
	Yes	42 (84)	27 (60)	69 (73)
	No	8 (16)	18 (40)	26 (27)
Feelings scale Week 96				
	Yes	39 (78)	25 (56)	64 (67)
	No	11 (22)	20 (44)	31 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN-B1a (N=45)	Total (N=95)
Get along scale Week 0				
	Yes	40 (80)	38 (84)	78 (82)
	No	10 (20)	7 (16)	17 (18)
Get along scale Week 24				
	Yes	46 (92)	43 (96)	89 (94)
	No	4 (8)	2 (4)	6 (6)
Get along scale Week 48				
	Yes	43 (86)	33 (73)	76 (80)
	No	7 (14)	12 (27)	19 (20)
Get along scale Week 72				
	Yes	42 (84)	27 (60)	69 (73)
	No	8 (16)	18 (40)	26 (27)
Get along scale Week 96				
	Yes	39 (78)	25 (56)	64 (67)
	No	11 (22)	20 (44)	31 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN-B1a (N=45)	Total (N=95)
Health scale Week 0				
	Yes	40 (80)	38 (84)	78 (82)
	No	10 (20)	7 (16)	17 (18)
Health scale Week 24				
	Yes	46 (92)	43 (96)	89 (94)
	No	4 (8)	2 (4)	6 (6)
Health scale Week 48				
	Yes	43 (86)	33 (73)	76 (80)
	No	7 (14)	12 (27)	19 (20)
Health scale Week 72				
	Yes	42 (84)	27 (60)	69 (73)
	No	8 (16)	18 (40)	26 (27)
Health scale Week 96				
	Yes	39 (78)	25 (56)	64 (67)
	No	11 (22)	20 (44)	31 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

	Response (n (%))	DMF (N=50)	IFN-B1a (N=45)	Total (N=95)
School scale Week 0				
	Yes	39 (78)	38 (84)	77 (81)
	No	11 (22)	7 (16)	18 (19)
School scale Week 24				
	Yes	45 (90)	42 (93)	87 (92)
	No	5 (10)	3 (7)	8 (8)
School scale Week 48				
	Yes	42 (84)	33 (73)	75 (79)
	No	8 (16)	12 (27)	20 (21)
School scale Week 72				
	Yes	42 (84)	27 (60)	69 (73)
	No	8 (16)	18 (40)	26 (27)
School scale Week 96				
	Yes	39 (78)	25 (56)	64 (67)
	No	11 (22)	20 (44)	31 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint

NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_subgroups_ban0418222.sas date: 18APR2022

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_EQZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About My Health and Activities

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-4.0 (14.82)	1.0 (13.73)	-1.2 (14.23)
Median	-3.1	0.0	0.0
Q1,Q3	-15.6, 3.1	-9.4, 9.4	-9.4, 6.3
Min, Max	-34, 28	-31, 28	-34, 28
Week 48			
n (%)	12 (57)	16 (84)	28 (70)
Mean (SD)	-7.3 (13.55)	6.8 (12.87)	0.8 (14.75)
Median	-3.1	9.4	3.1
Q1,Q3	-10.9, 1.6	1.6, 15.6	-4.7, 14.1
Min, Max	-38, 9	-31, 19	-38, 19

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	11 (52)	10 (53)	21 (53)
Mean (SD)	-10.2 (14.86)	5.0 (17.13)	-3.0 (17.41)
Median	-9.4	9.4	-3.1
Q1,Q3	-21.9, 3.1	-3.1, 18.8	-15.6, 9.4
Min, Max	-41, 9	-22, 22	-41, 22
Week 96			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-11.5 (18.02)	12.1 (16.82)	-0.4 (20.81)
Median	-9.4	10.9	3.1
Q1,Q3	-18.8, 3.1	1.6, 20.3	-12.5, 9.4
Min, Max	-50, 9	-13, 44	-50, 44

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About My Feelings

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-4.7 (15.41)	-4.0 (17.97)	-4.3 (16.60)
Median	-5.0	-5.0	-5.0
Q1,Q3	-10.0, 5.0	-20.0, 10.0	-15.0, 5.0
Min, Max	-45, 15	-30, 30	-45, 30
Week 48			
n (%)	12 (57)	16 (84)	28 (70)
Mean (SD)	0.0 (13.82)	-6.1 (18.86)	-3.5 (16.88)
Median	2.5	-10.0	-5.0
Q1,Q3	-10.0, 7.5	-15.0, 5.0	-15.0, 7.5
Min, Max	-25, 25	-45, 35	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	11 (52)	10 (53)	21 (53)
Mean (SD)	-2.7 (15.06)	6.3 (16.64)	1.5 (16.09)
Median	0.0	3.8	0.0
Q1,Q3	-15.0, 10.0	0.0, 15.0	-10.0, 10.0
Min, Max	-35, 15	-20, 40	-35, 40
Week 96			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-9.4 (19.76)	10.3 (18.34)	-0.1 (21.11)
Median	-5.0	7.5	0.0
Q1,Q3	-20.0, 0.0	-2.5, 23.8	-5.0, 15.0
Min, Max	-50, 15	-15, 40	-50, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. How I get Along With Others

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	-3.3 (12.05)	0.8 (13.01)	-1.1 (12.56)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 0.0	-5.0, 10.0	-5.0, 5.0
Min, Max	-35, 20	-35, 25	-35, 25
Week 48			
n (%)	12 (57)	16 (84)	28 (70)
Mean (SD)	-2.1 (7.22)	4.4 (12.76)	1.6 (11.06)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 0.0	0.0, 10.0	-2.5, 5.0
Min, Max	-15, 10	-20, 35	-20, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	11 (52)	10 (53)	21 (53)
Mean (SD)	-3.2 (7.51)	5.0 (8.50)	0.7 (8.84)
Median	0.0	7.5	0.0
Q1,Q3	-5.0, 0.0	0.0, 10.0	-5.0, 10.0
Min, Max	-20, 10	-10, 15	-20, 15
Week 96			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-7.2 (11.49)	12.5 (11.02)	2.1 (14.90)
Median	0.0	12.5	0.0
Q1,Q3	-15.0, 0.0	2.5, 20.0	0.0, 10.0
Min, Max	-30, 0	0, 30	-30, 30

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About Work or School

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Week 24			
n (%)	15 (71)	18 (95)	33 (83)
Mean (SD)	1.0 (14.29)	-7.2 (15.65)	-3.5 (15.38)
Median	0.0	-5.0	-5.0
Q1,Q3	-10.0, 5.0	-15.0, 5.0	-15.0, 5.0
Min, Max	-20, 30	-40, 15	-40, 30
Week 48			
n (%)	12 (57)	16 (84)	28 (70)
Mean (SD)	0.0 (9.05)	-6.6 (19.81)	-3.8 (16.19)
Median	5.0	-2.5	0.0
Q1,Q3	-5.0, 5.0	-20.0, 7.5	-10.0, 5.0
Min, Max	-20, 10	-45, 25	-45, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	11 (52)	10 (53)	21 (53)
Mean (SD)	-10.0 (9.75)	-2.5 (14.58)	-6.4 (12.56)
Median	-5.0	0.0	-5.0
Q1,Q3	-20.0, -5.0	-20.0, 5.0	-20.0, 0.0
Min, Max	-25, 5	-25, 20	-25, 20
Week 96			
n (%)	9 (43)	8 (42)	17 (43)
Mean (SD)	-11.7 (17.32)	1.3 (22.00)	-5.6 (20.15)
Median	-10.0	2.5	-5.0
Q1,Q3	-20.0, 5.0	-15.0, 15.0	-20.0, 5.0
Min, Max	-45, 5	-30, 35	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_EDSSBL_GTZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About My Health and Activities

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	32 (64)	35 (78)	67 (71)
Mean (SD)	5.5 (13.11)	-1.1 (10.47)	2.1 (12.17)
Median	4.7	0.0	0.0
Q1,Q3	0.0, 17.2	-6.3, 3.1	-3.1, 9.4
Min, Max	-19, 34	-31, 25	-31, 34
Week 48			
n (%)	28 (56)	25 (56)	53 (56)
Mean (SD)	3.8 (12.31)	-4.1 (10.47)	0.1 (12.05)
Median	3.1	0.0	0.0
Q1,Q3	0.0, 12.5	-3.1, 3.1	-3.1, 6.3
Min, Max	-22, 28	-31, 6	-31, 28

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	25 (50)	20 (44)	45 (47)
Mean (SD)	2.6 (14.84)	-4.7 (11.58)	-0.6 (13.84)
Median	0.0	-1.6	0.0
Q1,Q3	-6.3, 12.5	-10.9, 3.1	-9.4, 6.3
Min, Max	-25, 38	-28, 19	-28, 38
Week 96			
n (%)	15 (30)	14 (31)	29 (31)
Mean (SD)	-4.6 (17.07)	-1.3 (13.52)	-3.0 (15.27)
Median	0.0	1.6	0.0
Q1,Q3	-21.9, 6.3	-6.3, 6.3	-15.6, 6.3
Min, Max	-34, 25	-31, 19	-34, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About My Feelings

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	32 (64)	35 (78)	67 (71)
Mean (SD)	7.7 (17.73)	-0.7 (18.95)	3.3 (18.72)
Median	2.5	0.0	0.0
Q1,Q3	-5.0, 12.5	-5.0, 10.0	-5.0, 10.0
Min, Max	-20, 55	-60, 35	-60, 55
Week 48			
n (%)	28 (56)	25 (56)	53 (56)
Mean (SD)	9.3 (25.04)	1.8 (15.47)	5.8 (21.22)
Median	2.5	0.0	0.0
Q1,Q3	-5.0, 30.0	-10.0, 15.0	-5.0, 15.0
Min, Max	-40, 65	-25, 25	-40, 65

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	25 (50)	20 (44)	45 (47)
Mean (SD)	4.8 (20.13)	2.0 (16.50)	3.6 (18.45)
Median	5.0	2.5	5.0
Q1,Q3	-5.0, 20.0	-12.5, 12.5	-5.0, 15.0
Min, Max	-30, 45	-25, 35	-30, 45
Week 96			
n (%)	15 (30)	14 (31)	29 (31)
Mean (SD)	-2.0 (22.10)	6.4 (15.74)	2.1 (19.43)
Median	-5.0	7.5	5.0
Q1,Q3	-20.0, 15.0	-5.0, 20.0	-10.0, 20.0
Min, Max	-45, 35	-20, 25	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. How I get Along With Others

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	32 (64)	35 (78)	67 (71)
Mean (SD)	1.7 (11.19)	0.1 (7.90)	0.9 (9.57)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 5.0	-5.0, 5.0	0.0, 5.0
Min, Max	-30, 25	-20, 15	-30, 25
Week 48			
n (%)	28 (56)	25 (56)	53 (56)
Mean (SD)	0.4 (11.22)	-2.2 (8.79)	-0.8 (10.13)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 5.0	-5.0, 5.0	0.0, 5.0
Min, Max	-30, 25	-25, 10	-30, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	25 (50)	20 (44)	45 (47)
Mean (SD)	2.8 (12.42)	-0.3 (8.19)	1.4 (10.75)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-2.5, 5.0	0.0, 5.0
Min, Max	-30, 30	-20, 15	-30, 30
Week 96			
n (%)	15 (30)	14 (31)	29 (31)
Mean (SD)	-3.3 (18.19)	2.1 (13.97)	-0.7 (16.24)
Median	0.0	2.5	0.0
Q1,Q3	-5.0, 5.0	0.0, 5.0	-5.0, 5.0
Min, Max	-45, 35	-25, 35	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About Work or School

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Week 24			
n (%)	32 (64)	35 (78)	67 (71)
Mean (SD)	4.7 (18.00)	0.9 (11.85)	2.7 (15.11)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-5.0, 5.0	-10.0, 10.0
Min, Max	-20, 50	-35, 30	-35, 50
Week 48			
n (%)	28 (56)	25 (56)	53 (56)
Mean (SD)	7.9 (20.75)	3.8 (12.10)	5.9 (17.18)
Median	5.0	5.0	5.0
Q1,Q3	-5.0, 20.0	0.0, 10.0	-5.0, 10.0
Min, Max	-30, 55	-20, 30	-30, 55

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	25 (50)	20 (44)	45 (47)
Mean (SD)	4.8 (17.47)	3.0 (14.36)	4.0 (16.01)
Median	5.0	0.0	0.0
Q1,Q3	-10.0, 20.0	-5.0, 12.5	-10.0, 15.0
Min, Max	-25, 40	-35, 30	-35, 40
Week 96			
n (%)	15 (30)	14 (31)	29 (31)
Mean (SD)	4.3 (32.67)	-1.4 (15.74)	1.6 (25.64)
Median	5.0	0.0	5.0
Q1,Q3	-20.0, 25.0	-15.0, 10.0	-15.0, 20.0
Min, Max	-75, 55	-35, 25	-75, 55

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 07APR2022

109MS306_table45_47_CHG_DESCRIBE_EDSSBL_EQZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About My Health and Activities

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	84.4 (19.90)	78.3 (16.13)	81.2 (17.98)
Median	90.6	76.6	87.5
Q1,Q3	79.7, 96.9	62.5, 93.8	71.9, 96.9
Min, Max	19, 100	53, 100	19, 100
Week 24			
n (%)	21 (100)	19 (100)	40 (100)
Mean (SD)	77.2 (19.47)	79.4 (19.02)	78.3 (19.04)
Median	81.3	81.3	81.3
Q1,Q3	65.6, 96.9	75.0, 93.8	67.2, 95.3
Min, Max	41, 100	22, 100	22, 100
Week 48			
n (%)	19 (90)	19 (100)	38 (95)
Mean (SD)	78.3 (18.97)	83.4 (13.18)	80.8 (16.31)
Median	81.3	87.5	85.9
Q1,Q3	59.4, 96.9	78.1, 93.8	68.8, 93.8
Min, Max	44, 100	59, 100	44, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	17 (81)	14 (74)	31 (78)
Mean (SD)	75.2 (20.45)	85.5 (9.14)	79.8 (16.92)
Median	75.0	89.1	87.5
Q1,Q3	59.4, 93.8	78.1, 90.6	68.8, 93.8
Min, Max	41, 100	69, 97	41, 100
Week 96			
n (%)	15 (71)	13 (68)	28 (70)
Mean (SD)	78.1 (17.95)	80.3 (18.50)	79.1 (17.90)
Median	84.4	81.3	82.8
Q1,Q3	68.8, 93.8	71.9, 90.6	71.9, 92.2
Min, Max	38, 100	28, 100	28, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About My Feelings

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	70.0 (24.43)	74.6 (18.15)	72.4 (21.13)
Median	70.0	77.5	75.0
Q1,Q3	52.5, 92.5	60.0, 90.0	60.0, 90.0
Min, Max	20, 100	38, 100	20, 100
Week 24			
n (%)	21 (100)	19 (100)	40 (100)
Mean (SD)	64.8 (23.32)	69.7 (20.85)	67.1 (22.04)
Median	60.0	75.0	65.0
Q1,Q3	50.0, 80.0	55.0, 90.0	55.0, 87.5
Min, Max	15, 100	30, 100	15, 100
Week 48			
n (%)	19 (90)	19 (100)	38 (95)
Mean (SD)	68.7 (28.86)	68.7 (20.54)	68.7 (24.71)
Median	75.0	70.0	72.5
Q1,Q3	45.0, 95.0	55.0, 90.0	55.0, 90.0
Min, Max	10, 100	25, 100	10, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	17 (81)	14 (74)	31 (78)
Mean (SD)	63.2 (27.15)	75.4 (18.96)	68.7 (24.22)
Median	65.0	77.5	75.0
Q1,Q3	40.0, 90.0	60.0, 95.0	50.0, 90.0
Min, Max	20, 100	45, 100	20, 100
Week 96			
n (%)	15 (71)	13 (68)	28 (70)
Mean (SD)	64.3 (26.45)	67.7 (21.76)	65.9 (24.00)
Median	60.0	65.0	62.5
Q1,Q3	45.0, 90.0	60.0, 85.0	45.0, 87.5
Min, Max	25, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. How I get Along With Others

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	92.8 (12.91)	86.7 (14.65)	89.6 (14.00)
Median	100.0	87.5	95.0
Q1,Q3	90.0, 100.0	75.0, 100.0	85.0, 100.0
Min, Max	60, 100	45, 100	45, 100
Week 24			
n (%)	21 (100)	19 (100)	40 (100)
Mean (SD)	88.1 (12.60)	88.1 (13.56)	88.1 (12.89)
Median	90.0	90.0	90.0
Q1,Q3	80.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	60, 100	50, 100	50, 100
Week 48			
n (%)	19 (90)	19 (100)	38 (95)
Mean (SD)	88.4 (17.48)	90.0 (9.72)	89.2 (13.98)
Median	95.0	95.0	95.0
Q1,Q3	85.0, 100.0	85.0, 95.0	85.0, 100.0
Min, Max	30, 100	65, 100	30, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	17 (81)	14 (74)	31 (78)
Mean (SD)	85.9 (17.07)	94.3 (6.75)	89.7 (13.90)
Median	90.0	97.5	95.0
Q1,Q3	80.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	35, 100	85, 100	35, 100
Week 96			
n (%)	15 (71)	13 (68)	28 (70)
Mean (SD)	88.0 (13.86)	92.7 (11.83)	90.2 (12.94)
Median	95.0	100.0	95.0
Q1,Q3	75.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	65, 100	60, 100	60, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant>s Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero. About Work or School

	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Baseline			
n (%)	16 (76)	18 (95)	34 (85)
Mean (SD)	72.2 (24.22)	73.6 (17.39)	72.9 (20.56)
Median	80.0	77.5	80.0
Q1,Q3	57.5, 90.0	60.0, 90.0	60.0, 90.0
Min, Max	5, 100	45, 100	5, 100
Week 24			
n (%)	21 (100)	19 (100)	40 (100)
Mean (SD)	71.0 (21.72)	66.1 (22.33)	68.6 (21.87)
Median	70.0	60.0	65.0
Q1,Q3	55.0, 90.0	50.0, 85.0	55.0, 90.0
Min, Max	30, 100	15, 100	15, 100
Week 48			
n (%)	19 (90)	19 (100)	38 (95)
Mean (SD)	71.1 (26.07)	67.1 (20.30)	69.1 (23.13)
Median	80.0	70.0	70.0
Q1,Q3	60.0, 90.0	45.0, 80.0	50.0, 85.0
Min, Max	0, 100	40, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**	**Total (N= 40)**
Week 72			
n (%)	17 (81)	14 (74)	31 (78)
Mean (SD)	63.2 (25.31)	71.1 (14.57)	66.8 (21.20)
Median	65.0	67.5	65.0
Q1,Q3	45.0, 80.0	65.0, 80.0	50.0, 80.0
Min, Max	5, 100	45, 95	5, 100
Week 96			
n (%)	15 (71)	13 (68)	28 (70)
Mean (SD)	67.7 (23.74)	63.8 (22.74)	65.9 (22.94)
Median	65.0	65.0	65.0
Q1,Q3	55.0, 90.0	55.0, 75.0	55.0, 87.5
Min, Max	25, 100	15, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 13MAY2022

109MS306_table45_47_CHG_DESCRIBE_EDSSBL_GTZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About My Health and Activities

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	40 (80)	38 (84)	78 (82)
Mean (SD)	73.9 (23.21)	80.2 (19.73)	77.0 (21.67)
Median	78.1	87.5	82.8
Q1,Q3	62.5, 92.2	71.9, 93.8	65.6, 93.8
Min, Max	0, 100	28, 100	0, 100
Week 24			
n (%)	46 (92)	43 (96)	89 (94)
Mean (SD)	79.6 (16.37)	78.1 (20.20)	78.9 (18.23)
Median	82.8	84.4	84.4
Q1,Q3	71.9, 93.8	65.6, 93.8	71.9, 93.8
Min, Max	34, 100	25, 100	25, 100
Week 48			
n (%)	43 (86)	33 (73)	76 (80)
Mean (SD)	76.5 (20.04)	80.4 (20.04)	78.2 (20.00)
Median	81.3	87.5	81.3
Q1,Q3	65.6, 90.6	71.9, 93.8	70.3, 93.8
Min, Max	0, 100	13, 100	0, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	28 (62)	70 (74)
Mean (SD)	77.8 (21.17)	78.5 (18.81)	78.0 (20.13)
Median	84.4	87.5	85.9
Q1,Q3	68.8, 93.8	64.1, 93.8	65.6, 93.8
Min, Max	22, 100	44, 100	22, 100
Week 96			
n (%)	39 (78)	26 (58)	65 (68)
Mean (SD)	78.8 (19.99)	84.3 (16.50)	81.0 (18.73)
Median	84.4	89.1	84.4
Q1,Q3	68.8, 93.8	75.0, 100.0	71.9, 96.9
Min, Max	9, 100	50, 100	9, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About My Feelings

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	40 (80)	38 (84)	78 (82)
Mean (SD)	62.4 (25.77)	74.1 (18.59)	68.1 (23.18)
Median	65.0	75.0	72.5
Q1,Q3	47.5, 80.0	55.0, 85.0	55.0, 85.0
Min, Max	0, 100	30, 100	0, 100
Week 24			
n (%)	46 (92)	43 (96)	89 (94)
Mean (SD)	71.4 (22.00)	71.7 (20.78)	71.6 (21.30)
Median	75.0	75.0	75.0
Q1,Q3	60.0, 90.0	60.0, 90.0	60.0, 90.0
Min, Max	20, 100	25, 100	20, 100
Week 48			
n (%)	43 (86)	33 (73)	76 (80)
Mean (SD)	71.0 (23.52)	73.3 (22.73)	72.0 (23.05)
Median	70.0	75.0	75.0
Q1,Q3	60.0, 95.0	60.0, 95.0	60.0, 95.0
Min, Max	15, 100	15, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	28 (62)	70 (74)
Mean (SD)	71.3 (23.63)	71.3 (21.63)	71.3 (22.69)
Median	77.5	67.5	75.0
Q1,Q3	60.0, 90.0	57.5, 90.0	60.0, 90.0
Min, Max	15, 100	25, 100	15, 100
Week 96			
n (%)	39 (78)	26 (58)	65 (68)
Mean (SD)	67.3 (24.70)	76.0 (21.82)	70.8 (23.80)
Median	70.0	80.0	75.0
Q1,Q3	50.0, 90.0	60.0, 95.0	55.0, 90.0
Min, Max	15, 100	20, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. How I get Along With Others

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	40 (80)	38 (84)	78 (82)
Mean (SD)	83.1 (21.65)	90.3 (14.88)	86.6 (18.89)
Median	95.0	95.0	95.0
Q1,Q3	70.0, 100.0	85.0, 100.0	75.0, 100.0
Min, Max	20, 100	45, 100	20, 100
Week 24			
n (%)	46 (92)	43 (96)	89 (94)
Mean (SD)	86.6 (18.32)	90.5 (13.88)	88.5 (16.35)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	25, 100	50, 100	25, 100
Week 48			
n (%)	43 (86)	33 (73)	76 (80)
Mean (SD)	83.4 (21.76)	90.0 (19.08)	86.3 (20.77)
Median	95.0	100.0	95.0
Q1,Q3	70.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	30, 100	20, 100	20, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	28 (62)	70 (74)
Mean (SD)	87.0 (17.15)	91.4 (13.67)	88.8 (15.89)
Median	95.0	100.0	95.0
Q1,Q3	75.0, 100.0	87.5, 100.0	80.0, 100.0
Min, Max	30, 100	50, 100	30, 100
Week 96			
n (%)	39 (78)	26 (58)	65 (68)
Mean (SD)	86.2 (19.24)	94.0 (10.39)	89.3 (16.65)
Median	95.0	100.0	100.0
Q1,Q3	75.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	30, 100	65, 100	30, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero. About Work or School

	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Baseline			
n (%)	39 (78)	38 (84)	77 (81)
Mean (SD)	60.0 (25.37)	69.2 (17.99)	64.5 (22.38)
Median	60.0	75.0	70.0
Q1,Q3	40.0, 80.0	55.0, 85.0	50.0, 80.0
Min, Max	0, 100	25, 95	0, 100
Week 24			
n (%)	45 (90)	42 (93)	87 (92)
Mean (SD)	66.2 (22.24)	68.7 (21.89)	67.4 (21.98)
Median	65.0	75.0	70.0
Q1,Q3	50.0, 80.0	50.0, 85.0	50.0, 85.0
Min, Max	25, 100	10, 100	10, 100
Week 48			
n (%)	42 (84)	33 (73)	75 (79)
Mean (SD)	67.1 (20.84)	72.3 (20.31)	69.4 (20.63)
Median	65.0	75.0	70.0
Q1,Q3	55.0, 85.0	55.0, 85.0	55.0, 85.0
Min, Max	15, 100	30, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

	DMF (N= 50)	**IFN B-1a (N= 45)**	**Total (N= 95)**
Week 72			
n (%)	42 (84)	28 (62)	70 (74)
Mean (SD)	65.8 (23.29)	73.0 (21.01)	68.7 (22.53)
Median	70.0	80.0	75.0
Q1,Q3	50.0, 80.0	57.5, 90.0	55.0, 85.0
Min, Max	15, 100	25, 100	15, 100
Week 96			
n (%)	39 (78)	26 (58)	65 (68)
Mean (SD)	68.2 (21.47)	76.0 (21.40)	71.3 (21.62)
Median	70.0	82.5	75.0
Q1,Q3	55.0, 85.0	55.0, 95.0	55.0, 90.0
Min, Max	15, 100	30, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 07APR2022

109MS306_table45_47_CHG_HEDGESCI_EDSSBL_EQZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score EQ Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	-0.038	-0.723	0.647
	48	0.36	-0.395	1.115
	72	-0.567	-1.442	0.308
	96	-1.034	-2.056	-0.012
GET ALONG WITH OTHERS	24	-0.325	-1.015	0.364
	48	-0.6	-1.366	0.166
	72	-1.024	-1.940	-0.108
	96	-1.75	-2.890	-0.610
HEALTH AND ACTIVITIES	24	-0.351	-1.042	0.339
	48	-1.074	-1.877	-0.270
	72	-0.953	-1.862	-0.045
	96	-1.349	-2.417	-0.281
SCHOOL	24	0.546	-0.152	1.245
	48	0.406	-0.350	1.163
	72	-0.611	-1.489	0.267
	96	-0.658	-1.639	0.323

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table45_47_CHG_HEDGESCI_EDSSBL_GTZERO

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSSBL Score GT Zero

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	0.455	-0.030	0.941
	48	0.355	-0.189	0.899
	72	0.15	-0.438	0.739
	96	-0.437	-1.174	0.301
GET ALONG WITH OTHERS	24	0.164	-0.316	0.644
	48	0.252	-0.289	0.794
	72	0.283	-0.308	0.875
	96	-0.336	-1.070	0.398
HEALTH AND ACTIVITIES	24	0.554	0.065	1.043
	48	0.69	0.134	1.246
	72	0.542	-0.057	1.141
	96	-0.21	-0.940	0.521
SCHOOL	24	0.254	-0.228	0.735
	48	0.236	-0.306	0.777
	72	0.111	-0.477	0.700
	96	0.222	-0.509	0.953

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.

Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 07APR2022

109MS306_table45_47_CHG_LSMEANS_edsseq0

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. About My Health and Activities

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	-1.26 (3.466)	4.56 (3.651)
Lsmean_95 % CI	(-8.352, 5.825)	(-2.905, 12.031)
Diffrence (95% CI)	-5.827 (-15.564, 3.910)	
SE_Difference	4.7607	
p-value	0.2308	
Week 48		
n (%)	12 (57)	16 (84)
Lsmean (SE)	-2.98 (3.806)	7.87 (3.644)
Lsmean_95 % CI	(-10.833, 4.877)	(0.349, 15.389)
Diffrence (95% CI)	-10.847 (-21.837, 0.143)	
SE_Difference	5.3248	
p-value	0.0528	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	11 (52)	10 (53)
Lsmean (SE)	-5.31 (4.185)	4.29 (4.607)
Lsmean_95 % CI	(-14.140, 3.520)	(-5.435, 14.006)
Diffrence (95% CI)	-9.596 (-23.109, 3.917)	
SE_Difference	6.4046	
p-value	0.1524	
Week 96		
n (%)	9 (43)	8 (42)
Lsmean (SE)	-6.83 (6.335)	7.87 (6.919)
Lsmean_95 % CI	(-20.512, 6.860)	(-7.080, 22.815)
Diffrence (95% CI)	-14.694 (-36.873, 7.486)	
SE_Difference	0.2663	
p-value	0.1760	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. About My Feelings

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	-3.42 (4.412)	-0.78 (4.496)
Lsmean_95 % CI	(-12.442, 5.606)	(-9.974, 8.416)
Diffrence (95% CI)	-2.639 (-14.649, 9.372)	
SE_Difference	5.8724	
p-value	0.6565	
Week 48		
n (%)	12 (57)	16 (84)
Lsmean (SE)	1.59 (5.103)	-3.30 (4.881)
Lsmean_95 % CI	(-8.941, 12.121)	(-13.375, 6.775)
Diffrence (95% CI)	4.890 (-8.790, 18.570)	
SE_Difference	6.6280	
p-value	0.4678	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	11 (52)	10 (53)
Lsmean (SE)	-0.51 (4.446)	9.33 (4.752)
Lsmean_95 % CI	(-9.892, 8.868)	(-0.701, 19.352)
Diffrence (95% CI)	-9.838 (-23.161, 3.486)	
SE_Difference	6.3149	
p-value	0.1377	
Week 96		
n (%)	9 (43)	8 (42)
Lsmean (SE)	-7.90 (6.025)	11.75 (6.435)
Lsmean_95 % CI	(-20.912, 5.121)	(-2.147, 25.656)
Diffrence (95% CI)	-19.650 (-38.585, -0.715)	
SE_Difference	8.7644	
p-value	0.0430	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. How I get Along With Others

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	-1.33 (2.961)	0.17 (3.187)
Lsmean_95 % CI	(-7.384, 4.728)	(-6.344, 6.693)
Diffrence (95% CI)	-1.502 (-9.972, 6.967)	
SE_Difference	4.1411	
p-value	0.7194	
Week 48		
n (%)	12 (57)	16 (84)
Lsmean (SE)	0.48 (2.790)	1.86 (2.756)
Lsmean_95 % CI	(-5.277, 6.240)	(-3.826, 7.550)
Diffrence (95% CI)	-1.381 (-9.333, 6.571)	
SE_Difference	3.8528	
p-value	0.7232	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	11 (52)	10 (53)
Lsmean (SE)	-1.06 (1.767)	4.84 (1.984)
Lsmean_95 % CI	(-4.791, 2.667)	(0.654, 9.027)
Diffrence (95% CI)	-5.903 (-11.519, -0.286)	
SE_Difference	2.6620	
p-value	0.0405	
Week 96		
n (%)	9 (43)	8 (42)
Lsmean (SE)	-5.42 (3.729)	11.53 (4.119)
Lsmean_95 % CI	(-13.481, 2.632)	(2.633, 20.430)
Diffrence (95% CI)	-16.956 (-29.508, -4.405)	
SE_Difference	5.8097	
p-value	0.0120	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS equal to 0. *About Work or School*

	DMF (N= 21)	IFN B-1a (N= 19)
Week 24		
n (%)	15 (71)	18 (95)
Lsmean (SE)	1.93 (3.995)	-5.22 (4.083)
Lsmean_95 % CI	(-6.243, 10.100)	(-13.572, 3.128)
Diffrence (95% CI)	7.151 (-3.741, 18.043)	
SE_Difference	5.3255	
p-value	0.1898	
Week 48		
n (%)	12 (57)	16 (84)
Lsmean (SE)	1.42 (4.938)	-5.62 (4.667)
Lsmean_95 % CI	(-8.767, 11.616)	(-15.253, 4.011)
Diffrence (95% CI)	7.045 (-6.115, 20.205)	
SE_Difference	6.3762	
p-value	0.2801	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 21)	**IFN B-1a (N= 19)**
Week 72		
n (%)	11 (52)	10 (53)
Lsmean (SE)	-8.94 (3.837)	-1.52 (4.081)
Lsmean_95 % CI	(-17.031, -0.842)	(-10.130, 7.089)
Diffrence (95% CI)	-7.416 (-18.887, 4.056)	
SE_Difference	5.4372	
p-value	0.1904	
Week 96		
n (%)	9 (43)	8 (42)
Lsmean (SE)	-11.92 (7.079)	0.55 (7.524)
Lsmean_95 % CI	(-27.210, 3.377)	(-15.707, 16.802)
Diffrence (95% CI)	-12.464 (-34.791, 9.863)	
SE_Difference	0.3345	
p-value	0.2493	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

109MS306_table45_47_CHG_LSMEANS_edssgt0

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. About My Health and Activities

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	32 (64)	35 (78)
Lsmean (SE)	4.74 (2.061)	-0.95 (1.993)
Lsmean_95 % CI	(0.623, 8.861)	(-4.934, 3.033)
Diffrence (95% CI)	5.693 (0.517, 10.868)	
SE_Difference	2.5899	
p-value	0.0316	
Week 48		
n (%)	28 (56)	25 (56)
Lsmean (SE)	0.94 (2.373)	-5.36 (2.438)
Lsmean_95 % CI	(-3.831, 5.705)	(-10.260, -0.460)
Diffrence (95% CI)	6.297 (0.131, 12.463)	
SE_Difference	3.0683	
p-value	0.0455	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	25 (50)	20 (44)
Lsmean (SE)	2.64 (2.801)	-1.88 (3.310)
Lsmean_95 % CI	(-3.020, 8.294)	(-8.566, 4.803)
Diffrence (95% CI)	4.519 (-3.445, 12.484)	
SE_Difference	3.9436	
p-value	0.2584	
Week 96		
n (%)	15 (30)	14 (31)
Lsmean (SE)	-4.78 (3.936)	-0.091 (4.429)
Lsmean_95 % CI	(-12.886, 3.329)	(-9.212, 9.031)
Diffrence (95% CI)	-4.688 (-16.536, 7.161)	
SE_Difference	5.7528	
p-value	0.4228	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. About My Feelings

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	32 (64)	35 (78)
Lsmean (SE)	6.77 (3.209)	2.97 (3.153)
Lsmean_95 % CI	(0.356, 13.183)	(-3.335, 9.266)
Diffrence (95% CI)	3.804 (-4.478, 12.086)	
SE_Difference	4.1444	
p-value	0.3622	
Week 48		
n (%)	28 (56)	25 (56)
Lsmean (SE)	4.85 (4.020)	2.85 (4.136)
Lsmean_95 % CI	(-3.228, 12.929)	(-5.464, 11.159)
Diffrence (95% CI)	2.003 (-8.489, 12.495)	
SE_Difference	5.2212	
p-value	0.7029	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	25 (50)	20 (44)
Lsmean (SE)	2.73 (3.743)	3.67 (4.370)
Lsmean_95 % CI	(-4.828, 10.288)	(-5.158, 12.491)
Diffrence (95% CI)	-0.937 (-11.543, 9.669)	
SE_Difference	5.2516	
p-value	0.8593	
Week 96		
n (%)	15 (30)	14 (31)
Lsmean (SE)	-3.31 (4.708)	9.52 (5.303)
Lsmean_95 % CI	(-13.007, 6.386)	(-1.398, 20.443)
Diffrence (95% CI)	-12.833 (-27.161, 1.495)	
SE_Difference	6.9567	
p-value	0.0770	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. How I get Along With Others

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	32 (64)	35 (78)
Lsmean (SE)	2.55 (1.694)	1.78 (1.635)
Lsmean_95 % CI	(-0.833, 5.938)	(-1.490, 5.044)
Diffrence (95% CI)	0.776 (-3.491, 5.043)	
SE_Difference	2.1352	
p-value	0.7176	
Week 48		
n (%)	28 (56)	25 (56)
Lsmean (SE)	-0.89 (2.225)	-3.04 (2.252)
Lsmean_95 % CI	(-5.360, 3.582)	(-7.565, 1.486)
Diffrence (95% CI)	2.151 (-3.540, 7.841)	
SE_Difference	2.8315	
p-value	0.4512	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	25 (50)	20 (44)
Lsmean (SE)	2.35 (2.114)	0.92 (2.453)
Lsmean_95 % CI	(-1.923, 6.617)	(-4.030, 5.876)
Diffrence (95% CI)	1.424 (-4.465, 7.313)	
SE_Difference	2.9160	
p-value	0.6280	
Week 96		
n (%)	15 (30)	14 (31)
Lsmean (SE)	-3.30 (3.693)	1.58 (4.139)
Lsmean_95 % CI	(-10.908, 4.303)	(-6.941, 10.108)
Diffrence (95% CI)	-4.886 (-15.909, 6.137)	
SE_Difference	5.3521	
p-value	0.3700	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for EDSS greater than 0. About Work or School

	DMF (N= 50)	IFN B-1a (N= 45)
Week 24		
n (%)	32 (64)	35 (78)
Lsmean (SE)	3.36 (2.751)	1.91 (2.711)
Lsmean_95 % CI	(-2.139, 8.857)	(-3.506, 7.330)
Diffrence (95% CI)	1.447 (-5.593, 8.487)	
SE_Difference	3.5230	
p-value	0.6826	
Week 48		
n (%)	28 (56)	25 (56)
Lsmean (SE)	3.50 (3.278)	3.89 (3.435)
Lsmean_95 % CI	(-3.085, 10.089)	(-3.009, 10.795)
Diffrence (95% CI)	-0.391 (-8.990, 8.208)	
SE_Difference	4.2788	
p-value	0.9276	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

	DMF (N= 50)	**IFN B-1a (N= 45)**
Week 72		
n (%)	25 (50)	20 (44)
Lsmean (SE)	5.26 (3.344)	7.48 (4.034)
Lsmean_95 % CI	(-1.495, 12.012)	(-0.672, 15.623)
Diffrence (95% CI)	-2.217 (-11.836, 7.403)	
SE_Difference	4.7631	
p-value	0.6441	
Week 96		
n (%)	15 (30)	14 (31)
Lsmean (SE)	1.46 (6.142)	3.35 (7.108)
Lsmean_95 % CI	(-11.193, 14.106)	(-11.291, 17.986)
Diffrence (95% CI)	-1.891 (-21.055, 17.274)	
SE_Difference	9.3051	
p-value	0.8406	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented

Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.

NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)

NOTE4: Treatment group, age group and baseline score were covariates.

NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.

Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 13MAY2022

Sicherheit

AESI

109MS306_table75_any_edsseq0_AESI_EFFECTMEASURES

Overall rate and effect measures of EDSS = 0 patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	6.143	1.114	0.105
-	95% CI	(0.276 , 136.528)	(0.959 , 1.295)	(-0.083 , 0.293)
-	p-value	0.251	0.158	0.434
Gastrointestinal disorders	Effect measure	15.938	3.845	0.599
-	95% CI	(3.382 , 75.096)	(1.571 , 9.412)	(0.35 , 0.848)
-	p-value	0	0.003	0
Abdominal pain	Effect measure	13.5	8.143	0.376
-	95% CI	(1.509 , 120.783)	(1.135 , 58.424)	(0.142 , 0.61)
-	p-value	0.02	0.037	0.002
Vomiting	Effect measure	5.625	4.524	0.185
-	95% CI	(0.593 , 53.377)	(0.579 , 35.331)	(-0.023 , 0.393)
-	p-value	0.132	0.15	0.081
Diarrhoea	Effect measure	10.029	8.163	0.19
-	95% CI	(0.503 , 199.858)	(0.469 , 142.069)	(-0.028 , 0.409)
-	p-value	0.131	0.15	0.101
Infections and infestations	Effect measure	0.778	0.905	-0.06
-	95% CI	(0.218 , 2.773)	(0.546 , 1.499)	(-0.363 , 0.243)
-	p-value	0.698	0.698	0.697
Nasopharyngitis	Effect measure	0.467	0.543	-0.12
-	95% CI	(0.095 , 2.295)	(0.149 , 1.972)	(-0.369 , 0.128)
-	p-value	0.348	0.353	0.342
Vascular disorders	Effect measure	19.8	9.952	0.471
-	95% CI	(2.22 , 176.6)	(1.415 , 70.007)	(0.235 , 0.707)
-	p-value	0.007	0.021	0
Flushing	Effect measure	42.714	20.86	0.524
-	95% CI	(2.283 , 799.243)	(1.315 , 331.008)	(0.26 , 0.788)
-	p-value	0.012	0.031	0

AESI	Result	OR	RR	ARR
General disorders and administration site conditions	Effect measure	0.061	0.151	-0.536
-	95% CI	(0.011 , 0.346)	(0.039 , 0.589)	(-0.787 , -0.286)
-	p-value	0.002	0.006	0
Respiratory, thoracic and mediastinal disorders	Effect measure	3.4	2.714	0.18
-	95% CI	(0.594 , 19.457)	(0.621 , 11.865)	(-0.057 , 0.418)
-	p-value	0.169	0.185	0.136
Skin and subcutaneous tissue disorders	Effect measure	16.355	11.791	0.286
-	95% CI	(0.854 , 313.336)	(0.71 , 195.917)	(0.042 , 0.529)
-	p-value	0.064	0.085	0.017

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_any_edsseq0_AESI_NPERCENT

Overall rate and effect measures of EDSS = 0 patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Number of subjects with any AESI	21 (100)	17 (89)	38 (95)
Gastrointestinal disorders	17 (81)	4 (21)	21 (53)
Abdominal pain	9 (43)	1 (5)	10 (25)
Vomiting	5 (24)	1 (5)	6 (15)
Diarrhoea	4 (19)	0	4 (10)
Infections and infestations	12 (57)	12 (63)	24 (60)
Nasopharyngitis	3 (14)	5 (26)	8 (20)
Vascular disorders	11 (52)	1 (5)	12 (30)
Flushing	11 (52)	0	11 (28)
General disorders and administration site conditions	2 (10)	12 (63)	14 (35)
Respiratory, thoracic and mediastinal disorders	6 (29)	2 (11)	8 (20)
Skin and subcutaneous tissue disorders	6 (29)	0	6 (15)

109MS306_table75_any_edssgt0_AESI_EFFECTMEASURES

Overall rate and effect measures of EDSS ≥0 patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	5.75	1.38	0.253
-	95% CI	(1.741 , 18.995)	(1.105 , 1.723)	(0.096 , 0.41)
-	p-value	0.004	0.004	0.002
Gastrointestinal disorders	Effect measure	4.661	2.025	0.364
-	95% CI	(1.956 , 11.104)	(1.318 , 3.112)	(0.177 , 0.552)
-	p-value	0.001	0.001	0
Abdominal pain	Effect measure	6.282	4.275	0.291
-	95% CI	(1.94 , 20.339)	(1.572 , 11.623)	(0.133 , 0.449)
-	p-value	0.002	0.004	0
Vomiting	Effect measure	2.891	2.475	0.131
-	95% CI	(0.849 , 9.846)	(0.848 , 7.224)	(-0.011 , 0.273)
-	p-value	0.09	0.097	0.07
Diarrhoea	Effect measure	2.562	2.25	0.111
-	95% CI	(0.743 , 8.843)	(0.758 , 6.674)	(-0.027 , 0.25)
-	p-value	0.136	0.144	0.116
Infections and infestations	Effect measure	2.348	1.62	0.207
-	95% CI	(1.021 , 5.399)	(0.996 , 2.634)	(0.012 , 0.402)
-	p-value	0.045	0.052	0.038
Nasopharyngitis	Effect measure	3.601	2.925	0.171
-	95% CI	(1.079 , 12.024)	(1.028 , 8.323)	(0.024 , 0.318)
-	p-value	0.037	0.044	0.023
Vascular disorders	Effect measure	8.731	5.175	0.371
-	95% CI	(2.716 , 28.066)	(1.938 , 13.822)	(0.21 , 0.532)
-	p-value	0	0.001	0
Flushing	Effect measure	22.667	15.3	0.318
-	95% CI	(2.87 , 179.033)	(2.121 , 110.39)	(0.18 , 0.456)
-	p-value	0.003	0.007	0
General disorders and administration site conditions	Effect measure	0.439	0.54	-0.153
-	95% CI	(0.17 , 1.136)	(0.262 , 1.111)	(-0.327 , 0.021)
-	p-value	0.09	0.094	0.084

AESI	Result	OR	RR	ARR
Respiratory, thoracic and mediastinal disorders	Effect measure	5.444	4.2	0.213
-	95% CI	(1.449 , 20.463)	(1.29 , 13.67)	(0.069 , 0.358)
-	p-value	0.012	0.017	0.004
Skin and subcutaneous tissue disorders	Effect measure	15.459	11.7	0.238
-	95% CI	(1.931 , 123.795)	(1.593 , 85.907)	(0.109 , 0.367)
-	p-value	0.01	0.016	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_any_edssgt0_AESI_NPERCENT

Overall rate and effect measures of EDSS ≥0 patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Number of subjects with any AESI	46 (92)	30 (67)	76 (80)
Gastrointestinal disorders	36 (72)	16 (36)	52 (55)
Abdominal pain	19 (38)	4 (9)	23 (24)
Vomiting	11 (22)	4 (9)	15 (16)
Diarrhoea	10 (20)	4 (9)	14 (15)
Infections and infestations	27 (54)	15 (33)	42 (44)
Nasopharyngitis	13 (26)	4 (9)	17 (18)
Vascular disorders	23 (46)	4 (9)	27 (28)
Flushing	17 (34)	1 (2)	18 (19)
General disorders and administration site conditions	9 (18)	15 (33)	24 (25)
Respiratory, thoracic and mediastinal disorders	14 (28)	3 (7)	17 (18)
Skin and subcutaneous tissue disorders	13 (26)	1 (2)	14 (15)

109MS306_table75_Nonsevere_edsseq0_AESI_EFFECTMEASURES

Overall rate and effect measures of EDSS = 0 patients with ≥1 non-Severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	6.143	1.114	0.105
-	95% CI	(0.276 , 136.528)	(0.959 , 1.295)	(-0.083 , 0.293)
-	p-value	0.251	0.158	0.434
Gastrointestinal disorders	Effect measure	15.938	3.845	0.599
-	95% CI	(3.382 , 75.096)	(1.571 , 9.412)	(0.35 , 0.848)
-	p-value	0	0.003	0
Abdominal pain	Effect measure	13.5	8.143	0.376
-	95% CI	(1.509 , 120.783)	(1.135 , 58.424)	(0.142 , 0.61)
-	p-value	0.02	0.037	0.002
Vomiting	Effect measure	5.625	4.524	0.185
-	95% CI	(0.593 , 53.377)	(0.579 , 35.331)	(-0.023 , 0.393)
-	p-value	0.132	0.15	0.081
Diarrhoea	Effect measure	10.029	8.163	0.19
-	95% CI	(0.503 , 199.858)	(0.469 , 142.069)	(-0.028 , 0.409)
-	p-value	0.131	0.15	0.101
Vascular disorders	Effect measure	19.8	9.952	0.471
-	95% CI	(2.22 , 176.6)	(1.415 , 70.007)	(0.235 , 0.707)
-	p-value	0.007	0.021	0
Flushing	Effect measure	42.714	20.86	0.524
-	95% CI	(2.283 , 799.243)	(1.315 , 331.008)	(0.26 , 0.788)
-	p-value	0.012	0.031	0
General disorders and administration site conditions	Effect measure	0.061	0.151	-0.536
-	95% CI	(0.011 , 0.346)	(0.039 , 0.589)	(-0.787 , -0.286)
-	p-value	0.002	0.006	0
Respiratory, thoracic and mediastinal disorders	Effect measure	3.4	2.714	0.18
-	95% CI	(0.594 , 19.457)	(0.621 , 11.865)	(-0.057 , 0.418)
-	p-value	0.169	0.185	0.136
Skin and subcutaneous tissue disorders	Effect measure	16.355	11.791	0.286
-	95% CI	(0.854 , 313.336)	(0.71 , 195.917)	(0.042 , 0.529)
-	p-value	0.064	0.085	0.017

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_edsseq0_AESI_NPERCENT

Overall rate and effect measures of EDSS = 0 patients with ≥1 non-Severe AESI, related to CSR Table 75

AESI	DMF (N=21)	IFN B-1a (N=19)	Total (N=40)
Number of subjects with any AESI	21 (100)	17 (89)	38 (95)
Gastrointestinal disorders	17 (81)	4 (21)	21 (53)
Abdominal pain	9 (43)	1 (5)	10 (25)
Vomiting	5 (24)	1 (5)	6 (15)
Diarrhoea	4 (19)	0	4 (10)
Vascular disorders	11 (52)	1 (5)	12 (30)
Flushing	11 (52)	0	11 (28)
General disorders and administration site conditions	2 (10)	12 (63)	14 (35)
Respiratory, thoracic and mediastinal disorders	6 (29)	2 (11)	8 (20)
Skin and subcutaneous tissue disorders	6 (29)	0	6 (15)

NOTE1: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_edssgt0_AESI_EFFECTMEASURES

Overall rate and effect measures of EDSS ≥0 patients with ≥1 non-Severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	5.75	1.38	0.253
-	95% CI	(1.741 , 18.995)	(1.105 , 1.723)	(0.096 , 0.41)
-	p-value	0.004	0.004	0.002
Gastrointestinal disorders	Effect measure	4.661	2.025	0.364
-	95% CI	(1.956 , 11.104)	(1.318 , 3.112)	(0.177 , 0.552)
-	p-value	0.001	0.001	0
Abdominal pain	Effect measure	6.282	4.275	0.291
-	95% CI	(1.94 , 20.339)	(1.572 , 11.623)	(0.133 , 0.449)
-	p-value	0.002	0.004	0
Vomiting	Effect measure	2.891	2.475	0.131
-	95% CI	(0.849 , 9.846)	(0.848 , 7.224)	(-0.011 , 0.273)
-	p-value	0.09	0.097	0.07
Diarrhoea	Effect measure	2.562	2.25	0.111
-	95% CI	(0.743 , 8.843)	(0.758 , 6.674)	(-0.027 , 0.25)
-	p-value	0.136	0.144	0.116
Vascular disorders	Effect measure	8.731	5.175	0.371
-	95% CI	(2.716 , 28.066)	(1.938 , 13.822)	(0.21 , 0.532)
-	p-value	0	0.001	0
Flushing	Effect measure	22.667	15.3	0.318
-	95% CI	(2.87 , 179.033)	(2.121 , 110.39)	(0.18 , 0.456)
-	p-value	0.003	0.007	0
General disorders and administration site conditions	Effect measure	0.439	0.54	-0.153
-	95% CI	(0.17 , 1.136)	(0.262 , 1.111)	(-0.327 , 0.021)
-	p-value	0.09	0.094	0.084
Respiratory, thoracic and mediastinal disorders	Effect measure	5.444	4.2	0.213
-	95% CI	(1.449 , 20.463)	(1.29 , 13.67)	(0.069 , 0.358)
-	p-value	0.012	0.017	0.004
Skin and subcutaneous tissue disorders	Effect measure	15.459	11.7	0.238
-	95% CI	(1.931 , 123.795)	(1.593 , 85.907)	(0.109 , 0.367)
-	p-value	0.01	0.016	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_edssgt0_AESI_NPERCENT

Overall rate and effect measures of EDSS ≥0 patients with ≥1 non-Severe AESI, related to CSR Table 75

AESI	DMF (N=50)	IFN B-1a (N=45)	Total (N=95)
Number of subjects with any AESI	46 (92)	30 (67)	76 (80)
Gastrointestinal disorders	36 (72)	16 (36)	52 (55)
Abdominal pain	19 (38)	4 (9)	23 (24)
Vomiting	11 (22)	4 (9)	15 (16)
Diarrhoea	10 (20)	4 (9)	14 (15)
Vascular disorders	23 (46)	4 (9)	27 (28)
Flushing	17 (34)	1 (2)	18 (19)
General disorders and administration site conditions	9 (18)	15 (33)	24 (25)
Respiratory, thoracic and mediastinal disorders	14 (28)	3 (7)	17 (18)
Skin and subcutaneous tissue disorders	13 (26)	1 (2)	14 (15)

NOTE1: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

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109MS306_Table12_AE_EFFECTMEASURES_edsseq0

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
>=1 any AE	Effect measure	NA	NA	NA
	95% CI	NA	NA	NA
	p-value	NA	NA	NA
>=1 mild AE	Effect measure	0.867	0.905	-0.030
	95% CI	(0.224, 3.355)	(0.351, 2.331)	(-0.315, 0.255)
	p-value	0.8358	0.8358	0.8359
>=1 moderate AE	Effect measure	1.458	1.131	0.083
	95% CI	(0.386, 5.506)	(0.730, 1.751)	(-0.208, 0.373)
	p-value	0.5778	0.5811	0.5768
>=1 serious AE	Effect measure	0.510	0.603	-0.125
	95% CI	(0.119, 2.188)	(0.200, 1.817)	(-0.393, 0.143)
	p-value	0.3647	0.3688	0.3597

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm

NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a

NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban042122.sas date: 21APR2022

109MS306_Table12_AE_EFFECTMEASURES_edssgt0

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
>=1 any AE	Effect measure	1.119	1.007	0.007
	95% CI	(0.214, 5.847)	(0.907, 1.119)	(-0.092, 0.105)
	p-value	0.8939	0.8942	0.8942
>=1 mild AE	Effect measure	0.991	0.995	-0.002
	95% CI	(0.438, 2.240)	(0.620, 1.595)	(-0.201, 0.197)
	p-value	0.9825	0.9825	0.9825
>=1 moderate AE	Effect measure	2.214	1.607	0.189
	95% CI	(0.956, 5.129)	(0.960, 2.691)	(-0.005, 0.383)
	p-value	0.0636	0.0713	0.0559
>=1 serious AE	Effect measure	0.554	0.643	-0.111
	95% CI	(0.217, 1.413)	(0.318, 1.300)	(-0.286, 0.064)
	p-value	0.2162	0.2190	0.2131

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm

NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a

NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban042122.sas date: 21APR2022

109MS306_Table12_AE_NPERCENT_event_edsseq0

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135).N(%) for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS equal to 0

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
>=1 any AE				
	Yes	21 (100)	19 (100)	40 (100)
	No	0 (0)	0 (0)	0 (0)
>=1 mild AE				
	Yes	6 (29)	6 (32)	12 (30)
	No	15 (71)	13 (68)	28 (70)
>=1 moderate AE				
	Yes	15 (71)	12 (63)	27 (68)
	No	6 (29)	7 (37)	13 (33)
>=1 serious AE				
	Yes	4 (19)	6 (32)	10 (25)
	No	17 (81)	13 (68)	30 (75)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban042122.sas

109MS306_Table12_AE_NPERCENT_event_edssgt0

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS greater than 0

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
>=1 any AE				
	Yes	47 (94)	42 (93)	89 (94)
	No	3 (6)	3 (7)	6 (6)
>=1 mild AE				
	Yes	21 (42)	19 (42)	40 (42)
	No	29 (58)	26 (58)	55 (58)
>=1 moderate AE				
	Yes	25 (50)	14 (31)	39 (41)
	No	25 (50)	31 (69)	56 (59)
>=1 serious AE				
	Yes	10 (20)	14 (31)	24 (25)
	No	40 (80)	31 (69)	71 (75)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban042122.sas

UE nach Schweregrad

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_edsseq0

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
Gastrointestinal Disorders	Effect measure	15.938	3.845	0.599
	95% CI	(3.382, 75.096)	(1.571, 9.412)	(0.350, 0.848)
	p-value	0.0005	0.0032	<0.0001
Gastrointestinal Disorders , MILD	Effect measure	21.250	6.786	0.609
	95% CI	(3.713, 121.61)	(1.779, 25.877)	(0.372, 0.846)
	p-value	0.0006	0.0051	<0.0001
___Abdominal Pain	Effect measure	13.500	8.143	0.376
	95% CI	(1.509, 120.78)	(1.135, 58.424)	(0.142, 0.610)
	p-value	0.0199	0.0370	0.0017
___Abdominal Pain , MILD	Effect measure	9.000	6.333	0.281
	95% CI	(0.989, 81.929)	(0.856, 46.857)	(0.055, 0.506)
	p-value	0.0512	0.0707	0.0146
___Vomiting	Effect measure	5.625	4.524	0.185
	95% CI	(0.593, 53.377)	(0.579, 35.331)	(-0.023, 0.393)
	p-value	0.1325	0.1501	0.0805

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

	Result	OR	RR	ARR
___Vomiting , MILD	Effect measure	5.000	4.535	0.095
	95% CI	(0.225, 111.05)	(0.232, 88.735)	(-0.080, 0.271)
	p-value	0.3090	0.3191	0.4813
___Diarrhoea	Effect measure	10.029	8.163	0.190
	95% CI	(0.503, 199.86)	(0.469, 142.07)	(-0.028, 0.409)
	p-value	0.1310	0.1497	0.1014
Vascular Disorders	Effect measure	9.350	4.976	0.419
	95% CI	(1.713, 51.032)	(1.261, 19.640)	(0.164, 0.673)
	p-value	0.0098	0.0220	0.0013
Vascular Disorders , MILD	Effect measure	4.250	3.167	0.228
	95% CI	(0.759, 23.813)	(0.747, 13.416)	(-0.016, 0.472)
	p-value	0.0998	0.1176	0.0673
___Flushing	Effect measure	42.714	20.860	0.524
	95% CI	(2.283, 799.24)	(1.315, 331.01)	(0.260, 0.788)
	p-value	0.0120	0.0312	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

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NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

	Result	OR	RR	ARR
___Flushing , MILD	Effect measure	20.172	13.605	0.333
	95% CI	(1.064, 382.45)	(0.830, 222.90)	(0.082, 0.585)
	p-value	0.0454	0.0673	0.0059
Respiratory Thoracic And Mediastinal Disorders	Effect measure	1.875	1.583	0.123
	95% CI	(0.450, 7.821)	(0.548, 4.571)	(-0.150, 0.395)
	p-value	0.3883	0.3956	0.3771
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	1.172	1.131	0.028
	95% CI	(0.264, 5.208)	(0.355, 3.604)	(-0.231, 0.286)
	p-value	0.8349	0.8352	0.8344
Skin And Subcutaneous Tissue Disorders	Effect measure	20.172	13.605	0.333
	95% CI	(1.064, 382.45)	(0.830, 222.90)	(0.082, 0.585)
	p-value	0.0454	0.0673	0.0059
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	16.355	11.791	0.286
	95% CI	(0.854, 313.34)	(0.710, 195.92)	(0.042, 0.529)
	p-value	0.0636	0.0853	0.0169

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

	Result	OR	RR	ARR
General Disorders And Administration Site Conditions	Effect measure	0.022	0.302	-0.662
	95% CI	(0.002, 0.206)	(0.152, 0.598)	(-0.879, -0.444)
	p-value	0.0008	0.0006	<0.0001
General Disorders And Administration Site Conditions , MILD	Effect measure	0.144	0.348	-0.446
	95% CI	(0.036, 0.582)	(0.153, 0.793)	(-0.723, -0.169)
	p-value	0.0065	0.0120	0.0016
___Influenza Like Illness	Effect measure	0.077	0.165	-0.484
	95% CI	(0.014, 0.427)	(0.042, 0.649)	(-0.739, -0.229)
	p-value	0.0034	0.0100	0.0002
___Influenza Like Illness , MILD	Effect measure	0.180	0.259	-0.273
	95% CI	(0.032, 1.018)	(0.061, 1.095)	(-0.524, -0.023)
	p-value	0.0523	0.0663	0.0326
Injury Poisoning And Procedural Complications	Effect measure	2.000	1.810	0.085
	95% CI	(0.322, 12.414)	(0.373, 8.784)	(-0.132, 0.303)
	p-value	0.4568	0.4619	0.4423

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.444	0.603	-0.188
	95% CI	(0.120, 1.642)	(0.264, 1.377)	(-0.484, 0.108)
	p-value	0.2238	0.2302	0.2136

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

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NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

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109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_edssgt0

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of adverse event by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
Gastrointestinal Disorders	Effect measure	4.661	2.025	0.364
	95% CI	(1.956, 11.104)	(1.318, 3.112)	(0.177, 0.552)
	p-value	0.0005	0.0013	0.0001
Gastrointestinal Disorders , MILD	Effect measure	3.058	1.864	0.269
	95% CI	(1.314, 7.117)	(1.137, 3.057)	(0.077, 0.461)
	p-value	0.0095	0.0136	0.0062
___Abdominal Pain	Effect measure	6.282	4.275	0.291
	95% CI	(1.940, 20.339)	(1.572, 11.623)	(0.133, 0.449)
	p-value	0.0022	0.0044	0.0003
___Abdominal Pain , MILD	Effect measure	7.212	5.100	0.273
	95% CI	(1.947, 26.711)	(1.600, 16.259)	(0.123, 0.424)
	p-value	0.0031	0.0059	0.0004
___Vomiting	Effect measure	2.891	2.475	0.131
	95% CI	(0.849, 9.846)	(0.848, 7.224)	(-0.011, 0.273)
	p-value	0.0895	0.0973	0.0699

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

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NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

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	Result	OR	RR	ARR
___Vomiting , MILD	Effect measure	5.375	4.500	0.156
	95% CI	(1.109, 26.045)	(1.041, 19.450)	(0.029, 0.282)
	p-value	0.0367	0.0440	0.0157
___Diarrhoea	Effect measure	2.563	2.250	0.111
	95% CI	(0.743, 8.843)	(0.758, 6.674)	(-0.027, 0.250)
	p-value	0.1365	0.1438	0.1161
Vascular Disorders	Effect measure	8.731	5.175	0.371
	95% CI	(2.716, 28.066)	(1.938, 13.822)	(0.210, 0.532)
	p-value	0.0003	0.0010	<0.0001
Vascular Disorders , MILD	Effect measure	8.581	5.700	0.313
	95% CI	(2.331, 31.582)	(1.806, 17.986)	(0.160, 0.466)
	p-value	0.0012	0.0030	0.0001
___Flushing	Effect measure	22.667	15.300	0.318
	95% CI	(2.870, 179.03)	(2.121, 110.39)	(0.180, 0.456)
	p-value	0.0031	0.0068	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

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NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

	Result	OR	RR	ARR
___Flushing , MILD	Effect measure	32.760	24.327	0.260
	95% CI	(1.884, 569.52)	(1.488, 397.69)	(0.117, 0.403)
	p-value	0.0166	0.0252	0.0001
Respiratory Thoracic And Mediastinal Disorders	Effect measure	4.824	3.600	0.231
	95% CI	(1.473, 15.796)	(1.300, 9.973)	(0.077, 0.385)
	p-value	0.0093	0.0137	0.0032
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	4.393	3.375	0.211
	95% CI	(1.334, 14.463)	(1.209, 9.423)	(0.059, 0.363)
	p-value	0.0149	0.0202	0.0064
Skin And Subcutaneous Tissue Disorders	Effect measure	6.000	4.500	0.233
	95% CI	(1.606, 22.421)	(1.393, 14.533)	(0.087, 0.380)
	p-value	0.0077	0.0119	0.0018
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	5.444	4.200	0.213
	95% CI	(1.449, 20.463)	(1.290, 13.670)	(0.069, 0.358)
	p-value	0.0121	0.0172	0.0037

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

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	Result	OR	RR	ARR
Injury Poisoning And Procedural Complications	Effect measure	6.789	5.400	0.196
	95% CI	(1.428, 32.286)	(1.277, 22.832)	(0.063, 0.328)
	p-value	0.0161	0.0219	0.0039
General Disorders And Administration Site Conditions	Effect measure	0.127	0.319	-0.469
	95% CI	(0.051, 0.320)	(0.183, 0.558)	(-0.646, -0.291)
	p-value	<0.0001	0.0001	<0.0001
General Disorders And Administration Site Conditions , MILD	Effect measure	0.133	0.289	-0.442
	95% CI	(0.052, 0.341)	(0.153, 0.545)	(-0.619, -0.265)
	p-value	<0.0001	0.0001	<0.0001
___Influenza Like Illness	Effect measure	0.010	0.020	-0.489
	95% CI	(0.001, 0.178)	(0.001, 0.321)	(-0.656, -0.322)
	p-value	0.0016	0.0057	<0.0001
___Influenza Like Illness , MILD	Effect measure	0.018	0.027	-0.356
	95% CI	(0.001, 0.306)	(0.002, 0.442)	(-0.517, -0.195)
	p-value	0.0055	0.0113	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

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	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.450	0.626	-0.191
	95% CI	(0.196, 1.036)	(0.382, 1.027)	(-0.386, 0.004)
	p-value	0.0605	0.0637	0.0548

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

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NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban042522.sasdate: 25APR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_edsseq0

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type (of maximum severity when applicable) of adverse event by study arm. Subgroup analysis for EDSS equal to 0

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Gastrointestinal Disorders				
	Yes	17 (81)	4 (21)	21 (53)
	No	4 (19)	15 (79)	19 (48)
Gastrointestinal Disorders , MILD				
	Yes	15 (71)	2 (11)	17 (43)
	No	6 (29)	17 (89)	23 (58)
___Abdominal Pain				
	Yes	9 (43)	1 (5)	10 (25)
	No	12 (57)	18 (95)	30 (75)
___Abdominal Pain , MILD				
	Yes	7 (33)	1 (5)	8 (20)
	No	14 (67)	18 (95)	32 (80)
___Vomiting				
	Yes	5 (24)	1 (5)	6 (15)
	No	16 (76)	18 (95)	34 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
___Vomiting , MILD				
	Yes	2 (10)	0 (0)	2 (5)
	No	19 (90)	19 (100)	38 (95)
___Diarrhoea				
	Yes	4 (19)	0 (0)	4 (10)
	No	17 (81)	19 (100)	36 (90)
Vascular Disorders				
	Yes	11 (52)	2 (11)	13 (33)
	No	10 (48)	17 (89)	27 (68)
Vascular Disorders , MILD				
	Yes	7 (33)	2 (11)	9 (23)
	No	14 (67)	17 (89)	31 (78)
___Flushing				
	Yes	11 (52)	0 (0)	11 (28)
	No	10 (48)	19 (100)	29 (73)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
___Flushing , MILD				
	Yes	7 (33)	0 (0)	7 (18)
	No	14 (67)	19 (100)	33 (83)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	7 (33)	4 (21)	11 (28)
	No	14 (67)	15 (79)	29 (73)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	5 (24)	4 (21)	9 (23)
	No	16 (76)	15 (79)	31 (78)
Skin And Subcutaneous Tissue Disorders				
	Yes	7 (33)	0 (0)	7 (18)
	No	14 (67)	19 (100)	33 (83)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	6 (29)	0 (0)	6 (15)
	No	15 (71)	19 (100)	34 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
General Disorders And Administration Site Conditions				
	Yes	6 (29)	18 (95)	24 (60)
	No	15 (71)	1 (5)	16 (40)
General Disorders And Administration Site Conditions , MILD				
	Yes	5 (24)	13 (68)	18 (45)
	No	16 (76)	6 (32)	22 (55)
___Influenza Like Illness				
	Yes	2 (10)	11 (58)	13 (33)
	No	19 (90)	8 (42)	27 (68)
___Influenza Like Illness , MILD				
	Yes	2 (10)	7 (37)	9 (23)
	No	19 (90)	12 (63)	31 (78)
Injury Poisoning And Procedural Complications				
	Yes	4 (19)	2 (11)	6 (15)
	No	17 (81)	17 (89)	34 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
___Multiple Sclerosis Relapse				
	Yes	6 (29)	9 (47)	15 (38)
	No	15 (71)	10 (53)	25 (63)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_edssgt0

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type (of maximum severity when applicable) of adverse event by study arm. Subgroup analysis for EDSS greater than 0

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Gastrointestinal Disorders				
	Yes	36 (72)	16 (36)	52 (55)
	No	14 (28)	29 (64)	43 (45)
Gastrointestinal Disorders , MILD				
	Yes	29 (58)	14 (31)	43 (45)
	No	21 (42)	31 (69)	52 (55)
___Abdominal Pain				
	Yes	19 (38)	4 (9)	23 (24)
	No	31 (62)	41 (91)	72 (76)
___Abdominal Pain , MILD				
	Yes	17 (34)	3 (7)	20 (21)
	No	33 (66)	42 (93)	75 (79)
___Vomiting				
	Yes	11 (22)	4 (9)	15 (16)
	No	39 (78)	41 (91)	80 (84)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
___Vomiting , MILD				
	Yes	10 (20)	2 (4)	12 (13)
	No	40 (80)	43 (96)	83 (87)
___Diarrhoea				
	Yes	10 (20)	4 (9)	14 (15)
	No	40 (80)	41 (91)	81 (85)
Vascular Disorders				
	Yes	23 (46)	4 (9)	27 (28)
	No	27 (54)	41 (91)	68 (72)
Vascular Disorders , MILD				
	Yes	19 (38)	3 (7)	22 (23)
	No	31 (62)	42 (93)	73 (77)
___Flushing				
	Yes	17 (34)	1 (2)	18 (19)
	No	33 (66)	44 (98)	77 (81)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
___Flushing , MILD				
	Yes	13 (26)	0 (0)	13 (14)
	No	37 (74)	45 (100)	82 (86)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	16 (32)	4 (9)	20 (21)
	No	34 (68)	41 (91)	75 (79)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	15 (30)	4 (9)	19 (20)
	No	35 (70)	41 (91)	76 (80)
Skin And Subcutaneous Tissue Disorders				
	Yes	15 (30)	3 (7)	18 (19)
	No	35 (70)	42 (93)	77 (81)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	14 (28)	3 (7)	17 (18)
	No	36 (72)	42 (93)	78 (82)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Injury Poisoning And Procedural Complications				
	Yes	12 (24)	2 (4)	14 (15)
	No	38 (76)	43 (96)	81 (85)
General Disorders And Administration Site Conditions				
	Yes	11 (22)	31 (69)	42 (44)
	No	39 (78)	14 (31)	53 (56)
General Disorders And Administration Site Conditions , MILD				
	Yes	9 (18)	28 (62)	37 (39)
	No	41 (82)	17 (38)	58 (61)
___Influenza Like Illness				
	Yes	0 (0)	22 (49)	22 (23)
	No	50 (100)	23 (51)	73 (77)
___Influenza Like Illness , MILD				
	Yes	0 (0)	16 (36)	16 (17)
	No	50 (100)	29 (64)	79 (83)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
___Multiple Sclerosis Relapse				
	Yes	16 (32)	23 (51)	39 (41)
	No	34 (68)	22 (49)	56 (59)

NOTE1: Events are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs

in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,

the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN042522.sas date: 25APR2022

UE nach SOC und PT

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_edsseq0

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for EDSS equal to 0

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.444	0.603	-0.188
	95% CI	(0.120, 1.642)	(0.264, 1.377)	(-0.484, 0.108)
	p-value	0.2238	0.2302	0.2136
Gastrointestinal Disorders	Effect measure	15.938	3.845	0.599
	95% CI	(3.382, 75.096)	(1.571, 9.412)	(0.350, 0.848)
	p-value	0.0005	0.0032	<0.0001
___Abdominal Pain	Effect measure	13.500	8.143	0.376
	95% CI	(1.509, 120.78)	(1.135, 58.424)	(0.142, 0.610)
	p-value	0.0199	0.0370	0.0017
___Vomiting	Effect measure	5.625	4.524	0.185
	95% CI	(0.593, 53.377)	(0.579, 35.331)	(-0.023, 0.393)
	p-value	0.1325	0.1501	0.0805
___Diarrhoea	Effect measure	10.029	8.163	0.190
	95% CI	(0.503, 199.86)	(0.469, 142.07)	(-0.028, 0.409)
	p-value	0.1310	0.1497	0.1014

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Result	OR	RR	ARR
Vascular Disorders	Effect measure	9.350	4.976	0.419
	95% CI	(1.713, 51.032)	(1.261, 19.640)	(0.164, 0.673)
	p-value	0.0098	0.0220	0.0013
___Flushing	Effect measure	42.714	20.860	0.524
	95% CI	(2.283, 799.24)	(1.315, 331.01)	(0.260, 0.788)
	p-value	0.0120	0.0312	<0.0001
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	1.875	1.583	0.123
	95% CI	(0.450, 7.821)	(0.548, 4.571)	(-0.150, 0.395)
	p-value	0.3883	0.3956	0.3771
Skin And Subcutaneous Tissue Disorders	Effect measure	20.172	13.605	0.333
	95% CI	(1.064, 382.45)	(0.830, 222.90)	(0.082, 0.585)
	p-value	0.0454	0.0673	0.0059
General Disorders And Administration Site Conditions	Effect measure	0.022	0.302	-0.662
	95% CI	(0.002, 0.206)	(0.152, 0.598)	(-0.879, -0.444)
	p-value	0.0008	0.0006	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Result	OR	RR	ARR
___Influenza Like Illness	Effect measure	0.077	0.165	-0.484
	95% CI	(0.014, 0.427)	(0.042, 0.649)	(-0.739, -0.229)
	p-value	0.0034	0.0100	0.0002
Injury, Poisoning And Procedural Complications	Effect measure	2.000	1.810	0.085
	95% CI	(0.322, 12.414)	(0.373, 8.784)	(-0.132, 0.303)
	p-value	0.4568	0.4619	0.4423

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_edssgt0

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for EDSS greater than 0

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.450	0.626	-0.191
	95% CI	(0.196, 1.036)	(0.382, 1.027)	(-0.386, 0.004)
	p-value	0.0605	0.0637	0.0548
Gastrointestinal Disorders	Effect measure	4.661	2.025	0.364
	95% CI	(1.956, 11.104)	(1.318, 3.112)	(0.177, 0.552)
	p-value	0.0005	0.0013	0.0001
___Abdominal Pain	Effect measure	6.282	4.275	0.291
	95% CI	(1.940, 20.339)	(1.572, 11.623)	(0.133, 0.449)
	p-value	0.0022	0.0044	0.0003
___Vomiting	Effect measure	2.891	2.475	0.131
	95% CI	(0.849, 9.846)	(0.848, 7.224)	(-0.011, 0.273)
	p-value	0.0895	0.0973	0.0699
___Diarrhoea	Effect measure	2.563	2.250	0.111
	95% CI	(0.743, 8.843)	(0.758, 6.674)	(-0.027, 0.250)
	p-value	0.1365	0.1438	0.1161

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Result	OR	RR	ARR
Vascular Disorders	Effect measure	8.731	5.175	0.371
	95% CI	(2.716, 28.066)	(1.938, 13.822)	(0.210, 0.532)
	p-value	0.0003	0.0010	<0.0001
___Flushing	Effect measure	22.667	15.300	0.318
	95% CI	(2.870, 179.03)	(2.121, 110.39)	(0.180, 0.456)
	p-value	0.0031	0.0068	<0.0001
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	4.824	3.600	0.231
	95% CI	(1.473, 15.796)	(1.300, 9.973)	(0.077, 0.385)
	p-value	0.0093	0.0137	0.0032
Skin And Subcutaneous Tissue Disorders	Effect measure	6.000	4.500	0.233
	95% CI	(1.606, 22.421)	(1.393, 14.533)	(0.087, 0.380)
	p-value	0.0077	0.0119	0.0018
Injury, Poisoning And Procedural Complications	Effect measure	6.789	5.400	0.196
	95% CI	(1.428, 32.286)	(1.277, 22.832)	(0.063, 0.328)
	p-value	0.0161	0.0219	0.0039

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Result	OR	RR	ARR
General Disorders And Administration Site Conditions	Effect measure	0.127	0.319	-0.469
	95% CI	(0.051, 0.320)	(0.183, 0.558)	(-0.646, -0.291)
	p-value	<0.0001	0.0001	<0.0001
___Influenza Like Illness	Effect measure	0.010	0.020	-0.489
	95% CI	(0.001, 0.178)	(0.001, 0.321)	(-0.656, -0.322)
	p-value	0.0016	0.0057	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_edsseq0

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for EDSS equal to 0

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
___Multiple Sclerosis Relapse				
	Yes	6 (29)	9 (47)	15 (38)
	No	15 (71)	10 (53)	25 (63)
Gastrointestinal Disorders				
	Yes	17 (81)	4 (21)	21 (53)
	No	4 (19)	15 (79)	19 (48)
___Abdominal Pain				
	Yes	9 (43)	1 (5)	10 (25)
	No	12 (57)	18 (95)	30 (75)
___Vomiting				
	Yes	5 (24)	1 (5)	6 (15)
	No	16 (76)	18 (95)	34 (85)
___Diarrhoea				
	Yes	4 (19)	0 (0)	4 (10)
	No	17 (81)	19 (100)	36 (90)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
Vascular Disorders				
	Yes	11 (52)	2 (11)	13 (33)
	No	10 (48)	17 (89)	27 (68)
___Flushing				
	Yes	11 (52)	0 (0)	11 (28)
	No	10 (48)	19 (100)	29 (73)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	7 (33)	4 (21)	11 (28)
	No	14 (67)	15 (79)	29 (73)
Skin And Subcutaneous Tissue Disorders				
	Yes	7 (33)	0 (0)	7 (18)
	No	14 (67)	19 (100)	33 (83)
General Disorders And Administration Site Conditions				
	Yes	6 (29)	18 (95)	24 (60)
	No	15 (71)	1 (5)	16 (40)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Event	DMF (N= 21)	IFN B-1a (N= 19)	Total (N= 40)
___Influenza Like Illness				
	Yes	2 (10)	11 (58)	13 (33)
	No	19 (90)	8 (42)	27 (68)
Injury, Poisoning And Procedural Complications				
	Yes	4 (19)	2 (11)	6 (15)
	No	17 (81)	17 (89)	34 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_edssgt0

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for EDSS greater than 0

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
___Multiple Sclerosis Relapse				
	Yes	16 (32)	23 (51)	39 (41)
	No	34 (68)	22 (49)	56 (59)
Gastrointestinal Disorders				
	Yes	36 (72)	16 (36)	52 (55)
	No	14 (28)	29 (64)	43 (45)
___Abdominal Pain				
	Yes	19 (38)	4 (9)	23 (24)
	No	31 (62)	41 (91)	72 (76)
___Vomiting				
	Yes	11 (22)	4 (9)	15 (16)
	No	39 (78)	41 (91)	80 (84)
___Diarrhoea				
	Yes	10 (20)	4 (9)	14 (15)
	No	40 (80)	41 (91)	81 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
Vascular Disorders				
	Yes	23 (46)	4 (9)	27 (28)
	No	27 (54)	41 (91)	68 (72)
___Flushing				
	Yes	17 (34)	1 (2)	18 (19)
	No	33 (66)	44 (98)	77 (81)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	16 (32)	4 (9)	20 (21)
	No	34 (68)	41 (91)	75 (79)
Skin And Subcutaneous Tissue Disorders				
	Yes	15 (30)	3 (7)	18 (19)
	No	35 (70)	42 (93)	77 (81)
Injury, Poisoning And Procedural Complications				
	Yes	12 (24)	2 (4)	14 (15)
	No	38 (76)	43 (96)	81 (85)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

	Event	DMF (N= 50)	IFN B-1a (N= 45)	Total (N= 95)
General Disorders And Administration Site Conditions				
	Yes	11 (22)	31 (69)	42 (44)
	No	39 (78)	14 (31)	53 (56)
___Influenza Like Illness				
	Yes	0 (0)	22 (49)	22 (23)
	No	50 (100)	23 (51)	73 (77)

NOTE1: Events are yes when a patient has at least 1 of the adverse events (AE) of interest

NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban042522.sas date: 25APR2022

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_age13to14

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

	DMF(N=18)	IFN B-1a (N=14)	Total (N=32)
Week 12 change from baseline			
n (%)	17 (94)	14(100)	31 (97)
Mean (SD)	0.12 (0.516)	0.07 (0.829)	0.10 (0.664)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.50	0.00, 0.50
Min, Max	-1.0, 1.0	-2.0, 1.5	-2.0, 1.5
Week 24 change from baseline			
n (%)	16 (89)	12(86)	28 (88)
Mean (SD)	0.00 (0.606)	0.38 (1.509)	0.16 (1.081)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.25	0.00, 0.00
Min, Max	-1.0, 1.5	-2.0, 4.5	-2.0, 4.5
Week 36 change from baseline			
n (%)	16 (89)	10(71)	26 (81)
Mean (SD)	0.00 (0.548)	0.10 (1.197)	0.04 (0.836)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.0, 1.0	-2.0, 2.0	-2.0, 2.0
Week 48 change from baseline			
n (%)	14 (78)	10(71)	24 (75)
Mean (SD)	0.11 (0.626)	0.00 (0.816)	0.06 (0.696)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.00	0.00, 0.00
Min, Max	-1.0, 1.0	-1.0, 2.0	-1.0, 2.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG). Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

	DMF(N=18)	IFN B-1a (N=14)	Total (N=32)
Week 60 change from baseline			
n (%)	16 (89)	9(64)	25 (78)
Mean (SD)	-0.19 (0.655)	0.78 (1.417)	0.16 (1.077)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 1.00	0.00, 0.00
Min, Max	-1.0, 1.0	-0.5, 4.0	-1.0, 4.0
Week 72 change from baseline			
n (%)	15 (83)	8(57)	23 (72)
Mean (SD)	-0.07 (0.417)	0.13 (1.217)	0.00 (0.769)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.25	0.00, 0.00
Min, Max	-1.0, 0.5	-2.0, 2.5	-2.0, 2.5
Week 84 change from baseline			
n (%)	16 (89)	7(50)	23 (72)
Mean (SD)	-0.06 (0.544)	0.00 (1.000)	-0.04 (0.689)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 1.00	0.00, 0.00
Min, Max	-1.0, 1.5	-2.0, 1.0	-2.0, 1.5
Week 96 change from baseline			
n (%)	16 (89)	7(50)	23 (72)
Mean (SD)	0.06 (0.479)	0.14 (0.690)	0.09 (0.536)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 1.00	0.00, 0.00
Min, Max	-1.0, 1.0	-1.0, 1.0	-1.0, 1.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_age15to17

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF(N=53)	IFN B-1a (N=50)	Total (N=103)
Week 12 change from baseline			
n (%)	52 (98)	47(94)	99 (96)
Mean (SD)	0.13 (0.773)	0.14 (0.712)	0.13 (0.741)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.25	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.0	-1.0, 2.5	-1.5, 3.0
Week 24 change from baseline			
n (%)	50 (94)	46(92)	96 (93)
Mean (SD)	0.27 (1.036)	0.15 (1.069)	0.21 (1.048)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.50
Min, Max	-2.0, 3.0	-1.5, 5.5	-2.0, 5.5
Week 36 change from baseline			
n (%)	50 (94)	46(92)	96 (93)
Mean (SD)	0.03 (0.823)	0.17 (0.858)	0.10 (0.839)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.5	-2.0, 2.5	-2.0, 2.5
Week 48 change from baseline			
n (%)	49 (92)	39(78)	88 (85)
Mean (SD)	0.13 (1.055)	0.14 (0.743)	0.14 (0.925)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.50	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.0	-2.0, 3.0	-2.0, 3.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

	DMF(N=53)	IFN B-1a (N=50)	Total (N=103)
Week 60 change from baseline			
n (%)	46 (87)	38(76)	84 (82)
Mean (SD)	-0.10 (0.929)	0.11 (1.014)	-0.01 (0.968)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-2.0, 2.0	-1.5, 5.0	-2.0, 5.0
Week 72 change from baseline			
n (%)	45 (85)	33(66)	78 (76)
Mean (SD)	0.09 (0.949)	0.00 (0.791)	0.05 (0.881)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.5	-2.0, 2.0	-2.0, 2.5
Week 84 change from baseline			
n (%)	40 (75)	32(64)	72 (70)
Mean (SD)	-0.09 (0.973)	0.25 (1.350)	0.06 (1.160)
Median	0.00	0.00	0.00
Q1, Q3	-0.75, 0.00	0.00, 0.00	-0.25, 0.00
Min, Max	-2.5, 3.0	-2.0, 6.0	-2.5, 6.0
Week 96 change from baseline			
n (%)	38 (72)	32(64)	70 (68)
Mean (SD)	-0.05 (1.267)	0.14 (0.825)	0.04 (1.085)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-5.0, 3.5	-2.0, 2.5	-5.0, 3.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_female

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF(N=50)	IFN B-1a (N=46)	Total (N=96)
Week 12 change from baseline			
n (%)	48 (96)	44(96)	92 (96)
Mean (SD)	0.18 (0.740)	0.14 (0.802)	0.16 (0.767)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.25	0.00, 0.50
Min, Max	-1.0, 3.0	-2.0, 2.5	-2.0, 3.0
Week 24 change from baseline			
n (%)	45 (90)	41(89)	86 (90)
Mean (SD)	0.28 (0.927)	0.24 (1.124)	0.26 (1.020)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 1.00	0.00, 0.00	0.00, 0.50
Min, Max	-1.5, 3.0	-2.0, 5.5	-2.0, 5.5
Week 36 change from baseline			
n (%)	46 (92)	39(85)	85 (89)
Mean (SD)	0.00 (0.715)	0.14 (0.910)	0.06 (0.808)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 2.0	-2.0, 2.5	-2.0, 2.5
Week 48 change from baseline			
n (%)	43 (86)	34(74)	77 (80)
Mean (SD)	0.21 (1.065)	0.06 (0.715)	0.14 (0.924)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 1.00	0.00, 0.00	0.00, 0.50
Min, Max	-1.5, 3.0	-2.0, 2.0	-2.0, 3.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

	DMF(N=50)	IFN B-1a (N=46)	Total (N=96)
Week 60 change from baseline			
n (%)	42 (84)	34(74)	76 (79)
Mean (SD)	-0.11 (0.859)	0.38 (1.206)	0.11 (1.051)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-1.5, 2.0	-1.0, 5.0	-1.5, 5.0
Week 72 change from baseline			
n (%)	41 (82)	30(65)	71 (74)
Mean (SD)	0.11 (0.862)	-0.07 (0.907)	0.04 (0.880)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.00	0.00, 0.50
Min, Max	-1.5, 2.5	-2.0, 2.5	-2.0, 2.5
Week 84 change from baseline			
n (%)	37 (74)	28(61)	65 (68)
Mean (SD)	-0.09 (0.881)	0.23 (1.404)	0.05 (1.138)
Median	0.00	0.00	0.00
Q1, Q3	-0.50, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.5, 2.0	-2.0, 6.0	-2.5, 6.0
Week 96 change from baseline			
n (%)	36 (72)	29(63)	65 (68)
Mean (SD)	-0.01 (1.149)	0.09 (0.656)	0.03 (0.956)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.50	0.00, 0.00	0.00, 0.00
Min, Max	-5.0, 2.5	-2.0, 2.0	-5.0, 2.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_male

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF(N=21)	IFN B-1a (N=18)	Total (N=39)
Week 12 change from baseline			
n (%)	21 (100)	17(94)	38 (97)
Mean (SD)	0.00 (0.652)	0.09 (0.537)	0.04 (0.597)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 1.5	-0.5, 2.0	-1.5, 2.0
Week 24 change from baseline			
n (%)	21 (100)	17(94)	38 (97)
Mean (SD)	0.05 (1.011)	0.09 (1.278)	0.07 (1.122)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.5	-1.5, 4.5	-2.0, 4.5
Week 36 change from baseline			
n (%)	20 (95)	17(94)	37 (95)
Mean (SD)	0.08 (0.878)	0.21 (0.953)	0.14 (0.903)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.25	0.00, 0.50	0.00, 0.50
Min, Max	-2.0, 2.5	-1.5, 2.0	-2.0, 2.5
Week 48 change from baseline			
n (%)	20 (95)	15(83)	35 (90)
Mean (SD)	-0.05 (0.724)	0.23 (0.842)	0.07 (0.778)
Median	0.00	0.00	0.00
Q1, Q3	-0.25, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 2.0	-0.5, 3.0	-1.5, 3.0

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

	DMF(N=21)	IFN B-1a (N=18)	Total (N=39)
Week 60 change from baseline			
n (%)	20 (95)	13(72)	33 (85)
Mean (SD)	-0.15 (0.890)	-0.15 (0.747)	-0.15 (0.824)
Median	0.00	0.00	0.00
Q1, Q3	-1.00, 0.00	0.00, 0.00	-0.50, 0.00
Min, Max	-2.0, 1.5	-1.5, 1.5	-2.0, 1.5
Week 72 change from baseline			
n (%)	19 (90)	11(61)	30 (77)
Mean (SD)	-0.08 (0.821)	0.27 (0.754)	0.05 (0.802)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-2.0, 2.0	-0.5, 2.0	-2.0, 2.0
Week 84 change from baseline			
n (%)	19 (90)	11(61)	30 (77)
Mean (SD)	-0.05 (0.864)	0.14 (0.977)	0.02 (0.895)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.0	-1.5, 2.5	-1.5, 3.0
Week 96 change from baseline			
n (%)	18 (86)	10(56)	28 (72)
Mean (SD)	-0.03 (0.992)	0.30 (1.135)	0.09 (1.037)
Median	0.00	0.00	0.00
Q1, Q3	0.00, 0.00	0.00, 0.00	0.00, 0.00
Min, Max	-1.5, 3.5	-1.5, 2.5	-1.5, 3.5

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on Change variable (CHG)
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_DESCRIBE(CHG FROM BL)_banupdate012622_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE_age13to14
Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135)

Subgroup analysis for AGES 13 TO 14

	DMF(N=18)	IFN B-1a (N=14)	Total (N=32)
Baseline			
n (%)	18 (100)	14(100)	32 (100)
Mean (SD)	0.97 (0.882)	1.18 (0.799)	1.06 (0.840)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	1.00, 2.00	0.00, 1.75
Min, Max	0.0, 3.0	0.0, 2.5	0.0, 3.0
Week 12			
n (%)	17 (94)	14(100)	31 (97)
Mean (SD)	1.09 (0.956)	1.25 (1.088)	1.16 (1.003)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 1.50	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0
Week 24			
n (%)	16 (89)	12(86)	28 (88)
Mean (SD)	1.03 (1.024)	1.54 (1.725)	1.25 (1.364)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.25	0.00, 2.00	0.00, 1.75
Min, Max	0.0, 3.5	0.0, 5.5	0.0, 5.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=18)	IFN B-1a (N=14)	Total (N=32)
Week 36			
n (%)	16 (89)	10(71)	26 (81)
Mean (SD)	1.03 (0.957)	1.25 (1.586)	1.12 (1.211)
Median	1.00	0.50	1.00
Q1, Q3	0.00, 1.50	0.00, 2.00	0.00, 1.50
Min, Max	0.0, 3.0	0.0, 4.5	0.0, 4.5
Week 48			
n (%)	14 (78)	10(71)	24 (75)
Mean (SD)	1.21 (1.032)	1.15 (1.415)	1.19 (1.178)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 3.0	0.0, 4.5	0.0, 4.5
Week 60			
n (%)	16 (89)	9(64)	25 (78)
Mean (SD)	0.84 (0.851)	1.83 (1.920)	1.20 (1.384)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 1.00	1.00, 2.00	0.00, 1.50
Min, Max	0.0, 3.0	0.0, 6.5	0.0, 6.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=18)	IFN B-1a (N=14)	Total (N=32)
Week 72			
n (%)	15 (83)	8(57)	23 (72)
Mean (SD)	0.97 (0.972)	1.00 (0.964)	0.98 (0.947)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.75	0.00, 2.00
Min, Max	0.0, 3.0	0.0, 2.5	0.0, 3.0
Week 84			
n (%)	16 (89)	7(50)	23 (72)
Mean (SD)	0.97 (0.957)	0.86 (0.690)	0.93 (0.870)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	0.00, 1.00	0.00, 1.50
Min, Max	0.0, 3.0	0.0, 2.0	0.0, 3.0
Week 96			
n (%)	16 (89)	7(50)	23 (72)
Mean (SD)	1.09 (0.841)	1.00 (1.155)	1.07 (0.921)
Median	1.00	1.00	1.00
Q1, Q3	0.50, 1.50	0.00, 2.00	0.00, 1.50
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE_age15to17

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

	DMF(N=53)	IFN B-1a (N=50)	Total (N=103)
Baseline			
n (%)	53 (100)	50(100)	103 (100)
Mean (SD)	1.22 (1.116)	1.15 (1.016)	1.18 (1.064)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 2.00
Min, Max	0.0, 5.0	0.0, 4.0	0.0, 5.0
Week 12			
n (%)	52 (98)	47(94)	99 (96)
Mean (SD)	1.33 (1.279)	1.21 (1.036)	1.27 (1.166)
Median	1.00	1.00	1.00
Q1, Q3	0.50, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 24			
n (%)	50 (94)	46(92)	96 (93)
Mean (SD)	1.52 (1.428)	1.22 (1.377)	1.38 (1.405)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=53)	IFN B-1a (N=50)	Total (N=103)
Week 36			
n (%)	50 (94)	46(92)	96 (93)
Mean (SD)	1.26 (1.364)	1.24 (1.129)	1.25 (1.250)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 48			
n (%)	49 (92)	39(78)	88 (85)
Mean (SD)	1.34 (1.459)	1.22 (1.081)	1.28 (1.299)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 60			
n (%)	46 (87)	38(76)	84 (82)
Mean (SD)	1.14 (1.377)	1.21 (1.293)	1.17 (1.332)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.0	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=53)	IFN B-1a (N=50)	Total (N=103)
Week 72			
n (%)	45 (85)	33(66)	78 (76)
Mean (SD)	1.36 (1.472)	1.17 (1.028)	1.28 (1.298)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 84			
n (%)	40 (75)	32(64)	72 (70)
Mean (SD)	1.16 (1.465)	1.45 (1.297)	1.29 (1.391)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	1.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.0	0.0, 7.0
Week 96			
n (%)	38 (72)	32(64)	70 (68)
Mean (SD)	1.24 (1.324)	1.30 (1.142)	1.26 (1.236)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 5.5	0.0, 4.0	0.0, 5.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE_female

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

	DMF(N=50)	IFN B-1a (N=46)	Total (N=96)
Baseline			
n (%)	50 (100)	46(100)	96 (100)
Mean (SD)	1.22 (1.139)	1.28 (0.976)	1.25 (1.059)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 2.00	1.00, 2.00	0.00, 2.00
Min, Max	0.0, 5.0	0.0, 4.0	0.0, 5.0
Week 12			
n (%)	48 (96)	44(96)	92 (96)
Mean (SD)	1.39 (1.306)	1.35 (1.065)	1.37 (1.190)
Median	1.00	1.50	1.00
Q1, Q3	1.00, 2.00	0.50, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 24			
n (%)	45 (90)	41(89)	86 (90)
Mean (SD)	1.57 (1.464)	1.45 (1.396)	1.51 (1.425)
Median	1.00	1.50	1.00
Q1, Q3	1.00, 2.00	0.00, 2.00	1.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=50)	IFN B-1a (N=46)	Total (N=96)
Week 36			
n (%)	46 (92)	39(85)	85 (89)
Mean (SD)	1.26 (1.377)	1.35 (1.204)	1.30 (1.294)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 48			
n (%)	43 (86)	34(74)	77 (80)
Mean (SD)	1.48 (1.539)	1.35 (1.209)	1.42 (1.396)
Median	1.00	1.25	1.00
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.5	0.0, 7.0
Week 60			
n (%)	42 (84)	34(74)	76 (79)
Mean (SD)	1.17 (1.404)	1.68 (1.512)	1.39 (1.466)
Median	1.00	1.50	1.25
Q1, Q3	0.00, 2.00	1.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.5	0.0, 7.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=50)	IFN B-1a (N=46)	Total (N=96)
Week 72			
n (%)	41 (82)	30(65)	71 (74)
Mean (SD)	1.39 (1.498)	1.25 (1.006)	1.33 (1.306)
Median	1.00	1.50	1.50
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 4.0	0.0, 7.0
Week 84			
n (%)	37 (74)	28(61)	65 (68)
Mean (SD)	1.22 (1.493)	1.61 (1.279)	1.38 (1.408)
Median	1.00	1.50	1.00
Q1, Q3	0.00, 2.00	1.00, 2.00	0.00, 2.00
Min, Max	0.0, 7.0	0.0, 6.0	0.0, 7.0
Week 96			
n (%)	36 (72)	29(63)	65 (68)
Mean (SD)	1.31 (1.272)	1.41 (1.165)	1.35 (1.217)
Median	1.00	1.50	1.50
Q1, Q3	0.00, 2.00	0.00, 2.00	0.00, 2.00
Min, Max	0.0, 5.5	0.0, 4.0	0.0, 5.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

109MS306_table40_CHG_DESCRIBE_male

Table 40: Summary of EDSS Score by Visit - ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

	DMF(N=21)	IFN B-1a (N=18)	Total (N=39)
Baseline			
n (%)	21 (100)	18(100)	39 (100)
Mean (SD)	1.00 (0.851)	0.83 (0.891)	0.92 (0.863)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 1.50
Min, Max	0.0, 2.5	0.0, 3.0	0.0, 3.0
Week 12			
n (%)	21 (100)	17(94)	38 (97)
Mean (SD)	1.00 (0.908)	0.88 (0.911)	0.95 (0.899)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	0.00, 1.50	0.00, 1.50
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0
Week 24			
n (%)	21 (100)	17(94)	38 (97)
Mean (SD)	1.05 (1.011)	0.88 (1.526)	0.97 (1.252)
Median	1.00	0.00	0.50
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 2.00
Min, Max	0.0, 3.0	0.0, 5.5	0.0, 5.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=21)	IFN B-1a (N=18)	Total (N=39)
Week 36			
n (%)	20 (95)	17(94)	37 (95)
Mean (SD)	1.08 (1.017)	1.00 (1.212)	1.04 (1.095)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.50	0.00, 2.00
Min, Max	0.0, 3.5	0.0, 4.0	0.0, 4.0
Week 48			
n (%)	20 (95)	15(83)	35 (90)
Mean (SD)	0.95 (0.826)	0.87 (0.915)	0.91 (0.853)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	0.00, 1.00	0.00, 1.50
Min, Max	0.0, 2.5	0.0, 3.0	0.0, 3.0
Week 60			
n (%)	20 (95)	13(72)	33 (85)
Mean (SD)	0.85 (0.890)	0.42 (0.572)	0.68 (0.799)
Median	1.00	0.00	1.00
Q1, Q3	0.00, 1.00	0.00, 1.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 1.5	0.0, 3.0

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

	DMF(N=21)	IFN B-1a (N=18)	Total (N=39)
Week 72			
n (%)	19 (90)	11(61)	30 (77)
Mean (SD)	0.97 (1.007)	0.82 (0.982)	0.92 (0.983)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 2.00	0.00, 1.00	0.00, 2.00
Min, Max	0.0, 3.0	0.0, 3.0	0.0, 3.0
Week 84			
n (%)	19 (90)	11(61)	30 (77)
Mean (SD)	0.89 (0.951)	0.68 (0.783)	0.82 (0.886)
Median	1.00	1.00	1.00
Q1, Q3	0.00, 1.50	0.00, 1.00	0.00, 1.00
Min, Max	0.0, 3.0	0.0, 2.5	0.0, 3.0
Week 96			
n (%)	18 (86)	10(56)	28 (72)
Mean (SD)	0.97 (1.021)	0.75 (0.920)	0.89 (0.975)
Median	1.00	0.50	1.00
Q1, Q3	0.00, 1.50	0.00, 1.00	0.00, 1.25
Min, Max	0.0, 3.5	0.0, 2.5	0.0, 3.5

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table40_DESCRIBE_banupdate012622.sas date: 08MAR2022

109MS306_table40_CHG_HEDGESCI_age13to14

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	-0.107	-0.815	0.601
24	-0.257	-1.008	0.495
36	-0.376	-1.174	0.421
48	-0.353	-1.171	0.465
60	-0.608	-1.443	0.227
72	-0.263	-1.125	0.598
84	-0.045	-0.933	0.844
96	0	-0.888	0.888

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source:
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109MS306_table40_CHG_HEDGESCI_age15to17

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	-0.06	-0.454	0.335
24	0.009	-0.391	0.410
36	-0.125	-0.526	0.276
48	-0.051	-0.472	0.370
60	-0.17	-0.600	0.261
72	0.064	-0.385	0.514
84	-0.183	-0.649	0.283
96	-0.1	-0.570	0.371

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_HEDGESCI_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_HEDGESCI_female

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	-0.06	-0.469	0.349
24	-0.018	-0.441	0.405
36	-0.168	-0.596	0.259
48	-0.045	-0.495	0.405
60	-0.354	-0.810	0.101
72	0.09	-0.381	0.561
84	-0.197	-0.689	0.295
96	-0.026	-0.515	0.463

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
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109MS306_table40_CHG_HEDGESCI_male

Summary of EDSS Score by Visit – mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
12	-0.1	-0.740	0.540
24	-0.116	-0.756	0.524
36	-0.173	-0.821	0.475
48	-0.306	-0.979	0.368
60	-0.013	-0.712	0.685
72	-0.221	-0.965	0.524
84	-0.096	-0.839	0.647
96	-0.223	-0.998	0.553

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_HEDGESCI_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_LSMEANS_age13to14

Table 40: Summary of EDSS Score by Visit – ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

TIME POINTS		DMF(N=18)	IFN B-1a (N=14)
12	n (%)	17 (94)	14 (100)
	Lsmean (SE)	0.12 (0.164)	0.07 (0.180)
	Lsmean_95 % CI	(-0.217, 0.452)	(-0.297, 0.440)
	Diffrence (95% CI)	0.046 (-0.452, 0.544)	
	SE_Difference	0.2434	
	p-value	0.8507	
24	n (%)	16 (89)	12 (86)
	Lsmean (SE)	0.00 (0.271)	0.38 (0.313)
	Lsmean_95 % CI	(-0.557, 0.557)	(-0.268, 1.018)
	Diffrence (95% CI)	-0.38 (-1.226, 0.476)	
	SE_Difference	0.4140	
	p-value	0.3734	
36	n (%)	16 (89)	10 (71)
	Lsmean (SE)	0.00 (0.213)	0.10 (0.269)
	Lsmean_95 % CI	(-0.439, 0.439)	(-0.456, 0.656)
	Diffrence (95% CI)	-0.10 (-0.808, 0.608)	
	SE_Difference	0.3432	
	p-value	0.7733	
48	n (%)	14 (78)	10 (71)
	Lsmean (SE)	0.11 (0.190)	0.00 (0.225)
	Lsmean_95 % CI	(-0.286, 0.501)	(-0.466, 0.466)
	Diffrence (95% CI)	0.11 (-0.502, 0.717)	
	SE_Difference	0.2940	
	p-value	0.7190	
60	n (%)	16 (89)	9 (64)
	Lsmean (SE)	-0.19 (0.247)	0.78 (0.330)
	Lsmean_95 % CI	(-0.699, 0.324)	(0.096, 1.460)

TIME POINTS		DMF(N=18)	IFN B-1a (N=14)
	Diffrence (95% CI)	-0.97 (-1.818, -0.113)	
	SE_Difference	0.4120	
	p-value	0.0282	
72	n (%)	15 (83)	8 (57)
	Lsmean (SE)	-0.07 (0.202)	0.13 (0.276)
	Lsmean_95 % CI	(-0.486, 0.353)	(-0.449, 0.699)
	Diffrence (95% CI)	-0.19 (-0.903, 0.519)	
	SE_Difference	0.3419	
	p-value	0.5810	
84	n (%)	16 (89)	7 (50)
	Lsmean (SE)	-0.06 (0.176)	0.00 (0.266)
	Lsmean_95 % CI	(-0.429, 0.304)	(-0.554, 0.554)
	Diffrence (95% CI)	-0.063 (-0.727, 0.602)	
	SE_Difference	0.3195	
	p-value	0.8468	
96	n (%)	16 (89)	7 (50)
	Lsmean (SE)	0.06 (0.137)	0.14 (0.207)
	Lsmean_95 % CI	(-0.222, 0.347)	(-0.287, 0.573)
	Diffrence (95% CI)	-0.080 (-0.596, 0.436)	
	SE_Difference	0.2481	
	p-value	0.7492	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
Note3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable).
Note4: Treatment group, age group and baseline EDSS score were as covariates.
Note5: For age sugroup analyses, we did NOT include AGE as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table40_CHG_LSMEANS_age15to17

Table 40: Summary of EDSS Score by Visit – ITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

TIME POINTS		DMF(N=53)	IFN B-1a (N=50)
12	n (%)	52 (98)	47 (94)
	Lsmean (SE)	0.13 (0.103)	0.14 (0.109)
	Lsmean_95 % CI	(-0.080, 0.330)	(-0.077, 0.354)
	Diffrence (95% CI)	-0.013 (-0.311, 0.284)	
	SE_Difference	0.1499	
	p-value	0.9295	
24	n (%)	50 (94)	46 (92)
	Lsmean (SE)	0.27 (0.149)	0.15 (0.155)
	Lsmean_95 % CI	(-0.025, 0.565)	(-0.156, 0.460)
	Diffrence (95% CI)	0.12 (-0.309, 0.545)	
	SE_Difference	0.2149	
	p-value	0.5849	
36	n (%)	50 (94)	46 (92)
	Lsmean (SE)	0.03 (0.119)	0.17 (0.124)
	Lsmean_95 % CI	(-0.206, 0.266)	(-0.072, 0.420)
	Diffrence (95% CI)	-0.14 (-0.485, 0.197)	
	SE_Difference	0.1716	
	p-value	0.4038	
48	n (%)	49 (92)	39 (78)
	Lsmean (SE)	0.13 (0.133)	0.14 (0.149)
	Lsmean_95 % CI	(-0.131, 0.397)	(-0.155, 0.437)
	Diffrence (95% CI)	-0.008 (-0.405, 0.388)	
	SE_Difference	0.1995	
	p-value	0.9666	
60	n (%)	46 (87)	38 (76)
	Lsmean (SE)	-0.10 (0.143)	0.11 (0.157)
	Lsmean_95 % CI	(-0.382, 0.186)	(-0.207, 0.418)

TIME POINTS		DMF(N=53)	IFN B-1a (N=50)
	Diffrence (95% CI)	-0.20 (-0.625, 0.219)	
	SE_Difference	0.2123	
	p-value	0.3415	
72	n (%)	45 (85)	33 (66)
	Lsmean (SE)	0.09 (0.132)	0.00 (0.154)
	Lsmean_95 % CI	(-0.174, 0.352)	(-0.307, 0.307)
	Diffrence (95% CI)	0.089 (-0.315, 0.493)	
	SE_Difference	0.2030	
	p-value	0.6628	
84	n (%)	40 (75)	32 (64)
	Lsmean (SE)	-0.09 (0.183)	0.25 (0.204)
	Lsmean_95 % CI	(-0.452, 0.277)	(-0.157, 0.657)
	Diffrence (95% CI)	-0.34 (-0.884, 0.209)	
	SE_Difference	0.2740	
	p-value	0.2222	
96	n (%)	38 (72)	32 (64)
	Lsmean (SE)	-0.05 (0.177)	0.14 (0.192)
	Lsmean_95 % CI	(-0.405, 0.300)	(-0.243, 0.524)
	Diffrence (95% CI)	-0.19 (-0.714, 0.328)	
	SE_Difference	0.2611	
	p-value	0.4617	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model.
Note3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable).
Note4: Treatment group, age group and baseline EDSS score were as covariates.
Note5: For age sugroup analyses, we did NOT include AGE as a covariate. For EDSS=0 subgroup analyses, we did NOT include baseline EDSS as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table40_CHG_LSMEANS_female

Table 40: Summary of EDSS Score by Visit – ITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

TIME POINTS		DMF(N=50)	IFN B-1a (N=46)
12	n (%)	48 (96)	44 (96)
	Lsmean (SE)	0.17 (0.124)	0.13 (0.125)
	Lsmean_95 % CI	(-0.076, 0.418)	(-0.118, 0.381)
	Diffrence (95% CI)	0.039 (-0.281, 0.359)	
	SE_Difference	0.1608	
	p-value	0.8089	
24	n (%)	45 (90)	41 (89)
	Lsmean (SE)	0.20 (0.174)	0.17 (0.178)
	Lsmean_95 % CI	(-0.145, 0.548)	(-0.186, 0.524)
	Diffrence (95% CI)	0.033 (-0.410, 0.476)	
	SE_Difference	0.2228	
	p-value	0.8830	
36	n (%)	46 (92)	39 (85)
	Lsmean (SE)	-0.03 (0.139)	0.10 (0.150)
	Lsmean_95 % CI	(-0.310, 0.243)	(-0.195, 0.401)
	Diffrence (95% CI)	-0.14 (-0.491, 0.218)	
	SE_Difference	0.1780	
	p-value	0.4450	
48	n (%)	43 (86)	34 (74)
	Lsmean (SE)	0.18 (0.171)	0.04 (0.181)
	Lsmean_95 % CI	(-0.157, 0.525)	(-0.323, 0.397)
	Diffrence (95% CI)	0.15 (-0.284, 0.577)	
	SE_Difference	0.2159	
	p-value	0.4987	
60	n (%)	42 (84)	34 (74)
	Lsmean (SE)	-0.03 (0.180)	0.46 (0.197)
	Lsmean_95 % CI	(-0.393, 0.326)	(0.066, 0.852)

TIME POINTS		DMF(N=50)	IFN B-1a (N=46)
	Diffrence (95% CI)	-0.49 (-0.969, -0.0162)	
	SE_Difference	0.2390	
	p-value	0.0429	
72	n (%)	41 (82)	30 (65)
	Lsmean (SE)	0.09 (0.160)	-0.08 (0.180)
	Lsmean_95 % CI	(-0.230, 0.411)	(-0.442, 0.278)
	Diffrence (95% CI)	0.17 (-0.253, 0.598)	
	SE_Difference	0.2131	
	p-value	0.4215	
84	n (%)	37 (74)	28 (61)
	Lsmean (SE)	-0.13 (0.205)	0.20 (0.239)
	Lsmean_95 % CI	(-0.541, 0.279)	(-0.277, 0.681)
	Diffrence (95% CI)	-0.33 (-0.899, 0.233)	
	SE_Difference	0.2831	
	p-value	0.2437	
96	n (%)	36 (72)	29 (63)
	Lsmean (SE)	0.02 (0.170)	0.14 (0.195)
	Lsmean_95 % CI	(-0.316, 0.363)	(-0.253, 0.528)
	Diffrence (95% CI)	-0.11 (-0.579, 0.351)	
	SE_Difference	0.2324	
	p-value	0.6252	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 08MAR2022

109MS306_table40_CHG_LSMEANS_male

Table 40: Summary of EDSS Score by Visit – ITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

TIME POINTS		DMF(N=21)	IFN B-1a (N=18)
12	n (%)	21 (100)	17 (94)
	Lsmean (SE)	0.01 (0.135)	0.04 (0.162)
	Lsmean_95 % CI	(-0.269, 0.280)	(-0.289, 0.371)
	Diffrence (95% CI)	-0.035 (-0.439, 0.369)	
	SE_Difference	0.1988	
	p-value	0.8620	
24	n (%)	21 (100)	17 (94)
	Lsmean (SE)	0.13 (0.256)	0.17 (0.308)
	Lsmean_95 % CI	(-0.389, 0.653)	(-0.456, 0.797)
	Diffrence (95% CI)	-0.038 (-0.805, 0.729)	
	SE_Difference	0.3774	
	p-value	0.9198	
36	n (%)	20 (95)	17 (94)
	Lsmean (SE)	0.10 (0.211)	0.18 (0.250)
	Lsmean_95 % CI	(-0.330, 0.528)	(-0.329, 0.687)
	Diffrence (95% CI)	-0.081 (-0.711, 0.550)	
	SE_Difference	0.3099	
	p-value	0.7963	
48	n (%)	20 (95)	15 (83)
	Lsmean (SE)	0.01 (0.169)	0.14 (0.209)
	Lsmean_95 % CI	(-0.338, 0.353)	(-0.284, 0.569)
	Diffrence (95% CI)	-0.13 (-0.664, 0.394)	
	SE_Difference	0.2593	
	p-value	0.6070	
60	n (%)	20 (95)	13 (72)
	Lsmean (SE)	-0.07 (0.168)	-0.35 (0.233)
	Lsmean_95 % CI	(-0.419, 0.270)	(-0.830, 0.122)

TIME POINTS		DMF(N=21)	IFN B-1a (N=18)
	Diffrence (95% CI)	0.28 (-0.284, 0.844)	
	SE_Difference	0.2759	
	p-value	0.3189	
72	n (%)	19 (90)	11 (61)
	Lsmean (SE)	-0.05 (0.192)	0.17 (0.279)
	Lsmean_95 % CI	(-0.443, 0.346)	(-0.404, 0.745)
	Diffrence (95% CI)	-0.22 (-0.902, 0.465)	
	SE_Difference	0.3325	
	p-value	0.5161	
84	n (%)	19 (90)	11 (61)
	Lsmean (SE)	-0.00 (0.197)	-0.07 (0.282)
	Lsmean_95 % CI	(-0.408, 0.403)	(-0.649, 0.509)
	Diffrence (95% CI)	0.068 (-0.619, 0.755)	
	SE_Difference	0.3342	
	p-value	0.8404	
96	n (%)	18 (86)	10 (56)
	Lsmean (SE)	0.06 (0.233)	-0.03 (0.344)
	Lsmean_95 % CI	(-0.424, 0.539)	(-0.743, 0.676)
	Diffrence (95% CI)	0.091 (-0.763, 0.945)	
	SE_Difference	0.4137	
	p-value	0.8273	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T40/109MS306_table40_CHG_LSMEANS_SubGr.sas date: 08MAR2022

Quality of Life

PedsQL Parents

Change

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)

Physical Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	36 (51)	49 (77)	85 (63)
Mean (SD)	-0.2 (17.76)	-0.6 (13.60)	-0.4 (15.40)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 6.3	-9.4, 6.3	-9.4, 6.3
Min, Max	-72, 38	-22, 41	-72, 41
Week 48			
n (%)	33 (46)	37 (58)	70 (52)
Mean (SD)	0.5 (20.89)	-4.6 (14.80)	-2.2 (17.98)
Median	0.0	-3.1	0.0
Q1,Q3	-3.1, 9.4	-18.8, 3.1	-9.4, 6.3
Min, Max	-88, 38	-34, 25	-88, 38

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	29 (41)	26 (41)	55 (41)
Mean (SD)	-5.7 (14.08)	-3.4 (17.21)	-4.6 (15.53)
Median	-3.1	0.0	0.0
Q1,Q3	-12.5, 3.1	-9.4, 6.3	-9.4, 6.3
Min, Max	-47, 22	-38, 22	-47, 22
Week 96			
n (%)	18 (25)	19 (30)	37 (27)
Mean (SD)	-2.6 (13.05)	1.3 (14.82)	-0.6 (13.93)
Median	0.0	0.0	0.0
Q1,Q3	-9.4, 3.1	-9.4, 12.5	-9.4, 3.1
Min, Max	-31, 28	-22, 34	-31, 34

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Emotional Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	36 (51)	49 (77)	85 (63)
Mean (SD)	1.1 (17.77)	-2.0 (19.31)	-0.7 (18.63)
Median	0.0	0.0	0.0
Q1,Q3	-7.5, 10.0	-15.0, 10.0	-15.0, 10.0
Min, Max	-30, 50	-45, 40	-45, 50
Week 48			
n (%)	33 (46)	37 (58)	70 (52)
Mean (SD)	8.3 (22.97)	-3.1 (16.26)	2.3 (20.39)
Median	5.0	0.0	2.5
Q1,Q3	-5.0, 25.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-45, 65	-40, 30	-45, 65

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	29 (41)	26 (41)	55 (41)
Mean (SD)	2.8 (19.30)	0.6 (15.90)	1.7 (17.64)
Median	0.0	2.5	0.0
Q1,Q3	-10.0, 20.0	-10.0, 10.0	-10.0, 15.0
Min, Max	-45, 40	-30, 35	-45, 40
Week 96			
n (%)	18 (25)	19 (30)	37 (27)
Mean (SD)	-3.1 (15.64)	1.3 (23.26)	-0.8 (19.77)
Median	0.0	5.0	0.0
Q1,Q3	-5.0, 5.0	-20.0, 20.0	-10.0, 10.0
Min, Max	-45, 25	-40, 40	-45, 40

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Social Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	36 (51)	49 (77)	85 (63)
Mean (SD)	0.3 (15.67)	0.5 (14.62)	0.4 (14.98)
Median	0.0	0.0	0.0
Q1,Q3	-7.5, 10.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-35, 40	-30, 40	-35, 40
Week 48			
n (%)	33 (46)	37 (58)	70 (52)
Mean (SD)	0.8 (12.63)	-0.4 (22.59)	0.1 (18.45)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-10.0, 5.0	-5.0, 5.0
Min, Max	-40, 25	-70, 75	-70, 75

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	29 (41)	26 (41)	55 (41)
Mean (SD)	2.6 (12.37)	-6.5 (21.25)	-1.7 (17.59)
Median	0.0	-2.5	0.0
Q1,Q3	-5.0, 10.0	-15.0, 0.0	-5.0, 5.0
Min, Max	-35, 35	-50, 40	-50, 40
Week 96			
n (%)	18 (25)	19 (30)	37 (27)
Mean (SD)	-1.7 (17.32)	3.4 (25.17)	0.9 (21.57)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-10.0, 5.0	-5.0, 5.0
Min, Max	-40, 35	-30, 75	-40, 75

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Work/Study/School Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	36 (51)	49 (77)	85 (63)
Mean (SD)	1.7 (18.40)	-3.2 (16.64)	-1.1 (17.46)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-15.0, 5.0	-15.0, 5.0
Min, Max	-40, 50	-45, 55	-45, 55
Week 48			
n (%)	33 (46)	37 (58)	70 (52)
Mean (SD)	7.4 (18.76)	-1.4 (19.57)	2.8 (19.55)
Median	5.0	0.0	0.0
Q1,Q3	0.0, 15.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-35, 60	-40, 50	-40, 60

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	29 (41)	26 (41)	55 (41)
Mean (SD)	2.2 (22.78)	-3.8 (16.45)	-0.6 (20.09)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 15.0	-15.0, 10.0	-15.0, 10.0
Min, Max	-40, 60	-45, 25	-45, 60
Week 96			
n (%)	18 (25)	18 (28)	36 (27)
Mean (SD)	5.8 (13.09)	1.1 (23.67)	3.5 (19.00)
Median	5.0	5.0	5.0
Q1,Q3	-5.0, 10.0	-10.0, 15.0	-5.0, 15.0
Min, Max	-10, 40	-40, 45	-40, 45

Source: bg12ms/109ms306/csr/t-ef-bvmt-sum-byvst.sas Run Date: 25MAR2021

109MS306_table46_48_CHG_DESCRIBE

Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135)

Physical Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	75.9 (25.23)	75.3 (19.93)	75.6 (22.46)
Median	84.4	78.1	79.7
Q1,Q3	62.5, 93.8	65.6, 90.6	64.1, 93.8
Min, Max	0, 100	19, 100	0, 100
Week 24			
n (%)	56 (79)	58 (91)	114 (84)
Mean (SD)	77.1 (22.20)	75.4 (19.68)	76.2 (20.88)
Median	81.3	78.1	78.1
Q1,Q3	59.4, 96.9	65.6, 90.6	62.5, 93.8
Min, Max	13, 100	19, 100	13, 100
Week 48			
n (%)	52 (73)	44 (69)	96 (71)
Mean (SD)	75.5 (22.24)	74.1 (20.21)	74.8 (21.23)
Median	82.8	75.0	78.1
Q1,Q3	62.5, 93.8	62.5, 90.6	62.5, 93.8
Min, Max	13, 100	16, 100	13, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	46 (65)	29 (45)	75 (56)
Mean (SD)	73.1 (20.35)	77.7 (20.16)	74.9 (20.26)
Median	73.4	81.3	75.0
Q1,Q3	53.1, 90.6	65.6, 93.8	59.4, 90.6
Min, Max	28, 100	31, 100	28, 100
Week 96			
n (%)	29 (41)	22 (34)	51 (38)
Mean (SD)	79.0 (20.32)	82.4 (15.74)	80.5 (18.39)
Median	87.5	85.9	87.5
Q1,Q3	65.6, 96.9	68.8, 96.9	65.6, 96.9
Min, Max	38, 100	53, 100	38, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135)

Emotional Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	63.9 (24.76)	69.5 (20.69)	66.9 (22.75)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 90.0	60.0, 90.0	52.5, 90.0
Min, Max	0, 100	20, 100	0, 100
Week 24			
n (%)	55 (77)	58 (91)	113 (84)
Mean (SD)	66.6 (22.75)	67.1 (19.58)	66.9 (21.09)
Median	70.0	70.0	70.0
Q1,Q3	55.0, 85.0	50.0, 80.0	50.0, 80.0
Min, Max	0, 100	25, 100	0, 100
Week 48			
n (%)	52 (73)	44 (69)	96 (71)
Mean (SD)	70.1 (23.52)	68.5 (19.37)	69.4 (21.62)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 92.5	60.0, 80.0	55.0, 90.0
Min, Max	0, 100	15, 100	0, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	46 (65)	29 (45)	75 (56)
Mean (SD)	68.4 (22.90)	71.6 (17.33)	69.6 (20.85)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 85.0	60.0, 80.0	55.0, 80.0
Min, Max	20, 100	30, 100	20, 100
Week 96			
n (%)	29 (41)	22 (34)	51 (38)
Mean (SD)	66.0 (25.23)	69.1 (24.23)	67.4 (24.60)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 85.0	50.0, 90.0	50.0, 90.0
Min, Max	15, 100	10, 100	10, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135)
Social Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	83.8 (22.73)	86.7 (18.37)	85.4 (20.48)
Median	100.0	95.0	95.0
Q1,Q3	70.0, 100.0	80.0, 100.0	75.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 24			
n (%)	56 (79)	58 (91)	114 (84)
Mean (SD)	86.4 (16.09)	86.7 (15.69)	86.6 (15.82)
Median	90.0	90.0	90.0
Q1,Q3	75.0, 100.0	75.0, 100.0	75.0, 100.0
Min, Max	45, 100	50, 100	45, 100
Week 48			
n (%)	52 (73)	44 (69)	96 (71)
Mean (SD)	82.5 (21.06)	88.2 (18.11)	85.1 (19.87)
Median	92.5	95.0	95.0
Q1,Q3	67.5, 100.0	80.0, 100.0	75.0, 100.0
Min, Max	25, 100	15, 100	15, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	46 (65)	29 (45)	75 (56)
Mean (SD)	87.4 (18.82)	84.0 (21.27)	86.1 (19.73)
Median	95.0	95.0	95.0
Q1,Q3	80.0, 100.0	75.0, 100.0	75.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 96			
n (%)	29 (41)	22 (34)	51 (38)
Mean (SD)	87.1 (19.57)	90.5 (15.88)	88.5 (17.98)
Median	95.0	100.0	100.0
Q1,Q3	85.0, 100.0	90.0, 100.0	85.0, 100.0
Min, Max	30, 100	50, 100	30, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment - mITT Population, Aged 13 years and older (n=135)

Work/Study/School Functioning

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	46 (65)	53 (83)	99 (73)
Mean (SD)	65.0 (28.73)	69.5 (19.47)	67.4 (24.19)
Median	65.0	70.0	70.0
Q1,Q3	45.0, 90.0	55.0, 85.0	55.0, 90.0
Min, Max	5, 100	25, 100	5, 100
Week 24			
n (%)	56 (79)	56 (88)	112 (83)
Mean (SD)	66.8 (24.38)	66.9 (19.18)	66.8 (21.84)
Median	70.0	65.0	70.0
Q1,Q3	50.0, 85.0	55.0, 85.0	50.0, 85.0
Min, Max	0, 100	20, 100	0, 100
Week 48			
n (%)	51 (72)	44 (69)	95 (70)
Mean (SD)	67.6 (23.80)	71.6 (20.22)	69.5 (22.19)
Median	70.0	75.0	75.0
Q1,Q3	50.0, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	15, 100	20, 100	15, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	46 (65)	29 (45)	75 (56)
Mean (SD)	67.2 (21.67)	70.0 (20.35)	68.3 (21.08)
Median	67.5	75.0	70.0
Q1,Q3	50.0, 90.0	55.0, 85.0	55.0, 85.0
Min, Max	15, 100	20, 100	15, 100
Week 96			
n (%)	29 (41)	22 (34)	51 (38)
Mean (SD)	70.5 (25.01)	75.7 (18.28)	72.7 (22.30)
Median	70.0	77.5	75.0
Q1,Q3	55.0, 95.0	60.0, 90.0	55.0, 95.0
Min, Max	20, 100	45, 100	20, 100

Source: bg12ms/109ms306/csr/t-ef-sum-pedsfss-paren.sas Run Date: 25MAR2021

109MS306_table46_48_CHG_HEDGESCI

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Parent's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.169	-0.262	0.600
	48	0.581	0.101	1.060
	72	0.123	-0.407	0.653
	96	-0.219	-0.866	0.427
PHYSICAL FUNCTIONING	24	0.026	-0.404	0.456
	48	0.286	-0.186	0.757
	72	-0.15	-0.680	0.380
	96	-0.28	-0.928	0.368
SCHOOL FUNCTIONING	24	0.278	-0.155	0.710
	48	0.457	-0.018	0.933
	72	0.304	-0.229	0.836
	96	0.247	-0.409	0.903
SOCIAL FUNCTIONING	24	-0.015	-0.446	0.415
	48	0.063	-0.407	0.532
	72	0.532	-0.007	1.071
	96	-0.234	-0.881	0.413

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T46_48/109MS306_table46_48_CHG_HEDGESCI.sas date: 17FEB2022

109MS306_table46_48_CHG_LSMEANS_updated_02042022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Emotional Functioning

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	36 (51)	49 (77)
Lsmean (SE)	0.11 (2.955)	-2.27 (2.617)
Lsmean_95 % CI	(-5.775, 5.985)	(-7.481, 2.933)
Diffrence (95% CI)	2.379 (-4.716, 9.474)	
SE_Difference	3.5658	
p-value	0.5066	
Week 48		
n (%)	33 (46)	37 (58)
Lsmean (SE)	7.51 (3.292)	-2.62 (3.035)
Lsmean_95 % CI	(0.933, 14.079)	(-8.679, 3.441)
Diffrence (95% CI)	10.125 (2.141, 18.109)	
SE_Difference	3.9989	
p-value	0.0137	
Week 72		
n (%)	29 (41)	26 (41)
Lsmean (SE)	3.08 (3.197)	1.09 (3.372)
Lsmean_95 % CI	(-3.342, 9.495)	(-5.682, 7.855)
Diffrence (95% CI)	1.990 (-6.727, 10.707)	
SE_Difference	4.3418	
p-value	0.6487	
Week 96		
n (%)	18 (25)	19 (30)

	DMF (N= 71)	**IFN B-1a (N= 64)**
Lsmean (SE)	-0.61 (4.582)	0.46 (4.519)
Lsmean_95 % CI	(-9.929, 8.717)	(-8.735, 9.653)
Diffrence (95% CI)	-1.065 (-14.153, 12.024)	
SE_Difference	6.4331	
p-value	0.8695	

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Physical Functioning

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	36 (51)	49 (77)
Lsmean (SE)	1.05 (2.656)	-1.15 (2.303)
Lsmean_95 % CI	(-4.231, 6.337)	(-5.728, 3.437)
Diffrence (95% CI)	2.198 (-4.163, 8.559)	
SE_Difference	3.1970	
p-value	0.4937	
Week 48		
n (%)	33 (46)	37 (58)
Lsmean (SE)	1.42 (3.252)	-4.33 (2.968)
Lsmean_95 % CI	(-5.074, 7.914)	(-10.260, 1.593)
Diffrence (95% CI)	5.754 (-2.122, 13.629)	
SE_Difference	3.9446	
p-value	0.1494	
Week 72		
n (%)	29 (41)	26 (41)
Lsmean (SE)	-4.73 (2.923)	-2.28 (3.079)
Lsmean_95 % CI	(-10.601, 1.134)	(-8.462, 3.902)
Diffrence (95% CI)	-2.453 (-10.450, 5.544)	
SE_Difference	3.9833	
p-value	0.5407	
Week 96		
n (%)	18 (25)	19 (30)
Lsmean (SE)	-1.50 (3.201)	1.04 (3.191)

	DMF (N= 71)	**IFN B-1a (N= 64)**
Lsmean_95 % CI	(-8.009, 5.015)	(-5.450, 7.533)
Diffrence (95% CI)	-2.539 (-11.675, 6.598)	
SE_Difference	4.4908	
p-value	0.5757	

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Work/Study/School Functioning

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	36 (51)	49 (77)
Lsmean (SE)	0.90 (2.752)	-2.86 (2.435)
Lsmean_95 % CI	(-4.575, 6.376)	(-7.702, 1.989)
Diffrence (95% CI)	3.757 (-2.869, 10.384)	
SE_Difference	3.3304	
p-value	0.2626	
Week 48		
n (%)	33 (46)	37 (58)
Lsmean (SE)	5.86 (3.276)	-0.19 (3.037)
Lsmean_95 % CI	(-0.686, 12.397)	(-6.253, 5.873)
Diffrence (95% CI)	6.046 (-1.976, 14.067)	
SE_Difference	4.0177	
p-value	0.1372	
Week 72		
n (%)	29 (41)	26 (41)
Lsmean (SE)	1.00 (3.483)	-1.88 (3.729)
Lsmean_95 % CI	(-5.987, 7.996)	(-9.369, 5.603)
Diffrence (95% CI)	2.888 (-6.787, 12.562)	
SE_Difference	4.8190	
p-value	0.5516	
Week 96		
n (%)	18 (25)	18 (28)
Lsmean (SE)	5.82 (4.010)	1.74 (4.122)
Lsmean_95 % CI	(-2.348, 13.987)	(-6.657, 10.134)

	DMF (N= 71)	**IFN B-1a (N= 64)**
Diffrence (95% CI)	4.081 (-7.518, 15.680)	
SE_Difference	5.6943	
p-value	0.4788	

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135)
Social Functioning

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	36 (51)	49 (77)
Lsmean (SE)	0.23 (2.091)	0.21 (1.839)
Lsmean_95 % CI	(-3.931, 4.390)	(-3.448, 3.870)
Diffrence (95% CI)	0.019 (-5.005, 5.042)	
SE_Difference	2.5247	
p-value	0.9941	
Week 48		
n (%)	33 (46)	37 (58)
Lsmean (SE)	1.30 (3.199)	0.32 (2.932)
Lsmean_95 % CI	(-5.085, 7.690)	(-5.536, 6.170)
Diffrence (95% CI)	0.986 (-6.782, 8.753)	
SE_Difference	3.8903	
p-value	0.8008	
Week 72		
n (%)	29 (41)	26 (41)
Lsmean (SE)	3.14 (3.154)	-4.54 (3.346)
Lsmean_95 % CI	(-3.197, 9.469)	(-11.256, 2.177)
Diffrence (95% CI)	7.675 (-1.023, 16.374)	
SE_Difference	4.3328	
p-value	0.0825	
Week 96		
n (%)	18 (25)	19 (30)
Lsmean (SE)	-0.81 (4.332)	3.32 (4.352)
Lsmean_95 % CI	(-9.625, 8.001)	(-5.530, 12.178)

	DMF (N= 71)	**IFN B-1a (N= 64)**
Diffrence (95% CI)	-4.136 (-16.490, 8.217)	
SE_Difference	6.0720	
p-value	0.5005	

Sub groups

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_age13to14

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Physical Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	0.8 (17.26)	-3.7 (10.53)	-1.8 (13.51)
Median	1.6	-3.1	0.0
Q1,Q3	-4.7, 12.5	-9.4, 0.0	-9.4, 6.3
Min, Max	-34, 22	-22, 16	-34, 22
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	4.2 (4.70)	-8.0 (13.45)	-3.1 (12.22)
Median	3.1	-3.1	0.0
Q1,Q3	0.0, 9.4	-9.4, 3.1	-9.4, 3.1
Min, Max	0, 9	-34, 3	-34, 9

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	-3.1 (8.68)	-3.6 (16.58)	-3.3 (12.47)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 1.6	-6.3, 6.3	-6.3, 3.1
Min, Max	-22, 6	-38, 16	-38, 16
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	-1.2 (8.99)	0.5 (9.36)	-0.4 (8.83)
Median	0.0	-1.6	0.0
Q1,Q3	-4.7, 4.7	-6.3, 0.0	-6.3, 3.1
Min, Max	-19, 9	-6, 19	-19, 19

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Emotional Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	-1.3 (11.26)	-10.0 (15.17)	-6.3 (14.03)
Median	0.0	-5.0	-5.0
Q1,Q3	-5.0, 7.5	-15.0, -5.0	-15.0, 0.0
Min, Max	-25, 10	-40, 20	-40, 20
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	3.3 (16.93)	-8.3 (22.36)	-3.7 (20.57)
Median	0.0	-15.0	0.0
Q1,Q3	-5.0, 5.0	-25.0, 15.0	-20.0, 15.0
Min, Max	-15, 35	-40, 20	-40, 35

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	-1.9 (15.34)	-0.7 (22.44)	-1.3 (18.27)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 7.5	-25.0, 20.0	-20.0, 15.0
Min, Max	-25, 20	-30, 30	-30, 30
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	-1.9 (2.59)	0.8 (29.40)	-0.7 (18.38)
Median	0.0	10.0	0.0
Q1,Q3	-5.0, 0.0	-30.0, 20.0	-5.0, 10.0
Min, Max	-5, 0	-40, 35	-40, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Social Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	-3.1 (19.07)	-0.5 (12.74)	-1.6 (15.28)
Median	0.0	0.0	0.0
Q1,Q3	-17.5, 5.0	-5.0, 5.0	-10.0, 5.0
Min, Max	-30, 30	-25, 25	-30, 30
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	3.3 (7.53)	-2.2 (17.16)	0.0 (14.02)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-5, 15	-40, 25	-40, 25

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	3.8 (6.94)	-2.9 (20.18)	0.7 (14.50)
Median	0.0	-5.0	0.0
Q1,Q3	0.0, 10.0	-15.0, 0.0	-5.0, 10.0
Min, Max	-5, 15	-20, 40	-20, 40
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	-3.1 (11.63)	2.5 (24.24)	-0.7 (17.53)
Median	0.0	0.0	0.0
Q1,Q3	-2.5, 0.0	-5.0, 5.0	-5.0, 0.0
Min, Max	-30, 10	-30, 45	-30, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Work/Study/School Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	8 (44)	11 (79)	19 (59)
Mean (SD)	-9.4 (19.17)	-0.5 (14.74)	-4.2 (16.85)
Median	-7.5	0.0	-5.0
Q1,Q3	-22.5, 2.5	-15.0, 10.0	-15.0, 10.0
Min, Max	-40, 20	-25, 25	-40, 25
Week 48			
n (%)	6 (33)	9 (64)	15 (47)
Mean (SD)	6.7 (14.02)	-6.7 (24.37)	-1.3 (21.34)
Median	2.5	0.0	0.0
Q1,Q3	0.0, 15.0	-35.0, 15.0	-10.0, 15.0
Min, Max	-10, 30	-40, 25	-40, 30

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	8 (44)	7 (50)	15 (47)
Mean (SD)	-5.0 (16.48)	-1.4 (23.22)	-3.3 (19.24)
Median	-7.5	5.0	-5.0
Q1,Q3	-17.5, 5.0	-15.0, 15.0	-15.0, 10.0
Min, Max	-25, 25	-45, 25	-45, 25
Week 96			
n (%)	8 (44)	6 (43)	14 (44)
Mean (SD)	5.6 (7.76)	-0.8 (28.36)	2.9 (18.78)
Median	5.0	7.5	5.0
Q1,Q3	0.0, 10.0	-35.0, 15.0	0.0, 10.0
Min, Max	-5, 20	-35, 35	-35, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_age15to17

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Physical Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	28 (53)	38 (76)	66 (64)
Mean (SD)	-0.4 (18.20)	0.3 (14.36)	0.0 (15.97)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 6.3	-12.5, 9.4	-9.4, 6.3
Min, Max	-72, 38	-22, 41	-72, 41
Week 48			
n (%)	27 (51)	28 (56)	55 (53)
Mean (SD)	-0.3 (23.00)	-3.6 (15.28)	-2.0 (19.34)
Median	0.0	-3.1	0.0
Q1,Q3	-6.3, 12.5	-18.8, 7.8	-9.4, 9.4
Min, Max	-88, 38	-28, 25	-88, 38

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	21 (40)	19 (38)	40 (39)
Mean (SD)	-6.7 (15.73)	-3.3 (17.88)	-5.1 (16.65)
Median	-6.3	0.0	-4.7
Q1,Q3	-15.6, 3.1	-9.4, 12.5	-14.1, 6.3
Min, Max	-47, 22	-38, 22	-47, 22
Week 96			
n (%)	10 (19)	13 (26)	23 (22)
Mean (SD)	-3.8 (15.99)	1.7 (17.10)	-0.7 (16.48)
Median	-3.1	0.0	0.0
Q1,Q3	-9.4, 3.1	-9.4, 12.5	-9.4, 3.1
Min, Max	-31, 28	-22, 34	-31, 34

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Emotional Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	28 (53)	38 (76)	66 (64)
Mean (SD)	1.8 (19.35)	0.3 (19.93)	0.9 (19.55)
Median	0.0	0.0	0.0
Q1,Q3	-12.5, 15.0	-15.0, 15.0	-15.0, 15.0
Min, Max	-30, 50	-45, 40	-45, 50
Week 48			
n (%)	27 (51)	28 (56)	55 (53)
Mean (SD)	9.4 (24.23)	-1.4 (13.87)	3.9 (20.22)
Median	5.0	2.5	5.0
Q1,Q3	-5.0, 25.0	-10.0, 10.0	-5.0, 15.0
Min, Max	-45, 65	-30, 30	-45, 65

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	21 (40)	19 (38)	40 (39)
Mean (SD)	4.5 (20.67)	1.1 (13.50)	2.9 (17.50)
Median	5.0	5.0	5.0
Q1,Q3	-10.0, 20.0	-5.0, 10.0	-7.5, 12.5
Min, Max	-45, 40	-20, 35	-45, 40
Week 96			
n (%)	10 (19)	13 (26)	23 (22)
Mean (SD)	-4.0 (21.32)	1.5 (21.25)	-0.9 (20.98)
Median	2.5	-5.0	0.0
Q1,Q3	-20.0, 5.0	-15.0, 20.0	-20.0, 20.0
Min, Max	-45, 25	-30, 40	-45, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Social Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	28 (53)	38 (76)	66 (64)
Mean (SD)	1.3 (14.82)	0.8 (15.27)	1.0 (14.97)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-35, 40	-30, 40	-35, 40
Week 48			
n (%)	27 (51)	28 (56)	55 (53)
Mean (SD)	0.2 (13.55)	0.2 (24.32)	0.2 (19.60)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-10.0, 5.0	-5.0, 5.0
Min, Max	-40, 25	-70, 75	-70, 75

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	21 (40)	19 (38)	40 (39)
Mean (SD)	2.1 (14.02)	-7.9 (22.00)	-2.6 (18.71)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-20.0, 5.0	-5.0, 5.0
Min, Max	-35, 35	-50, 40	-50, 40
Week 96			
n (%)	10 (19)	13 (26)	23 (22)
Mean (SD)	-0.5 (21.40)	3.8 (26.55)	2.0 (24.01)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 15.0	-10.0, 5.0	-10.0, 10.0
Min, Max	-40, 35	-30, 75	-40, 75

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Work/Study/School Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	28 (53)	38 (76)	66 (64)
Mean (SD)	4.8 (17.24)	-3.9 (17.25)	-0.2 (17.66)
Median	0.0	-5.0	0.0
Q1,Q3	-5.0, 10.0	-15.0, 5.0	-15.0, 5.0
Min, Max	-20, 50	-45, 55	-45, 55
Week 48			
n (%)	27 (51)	28 (56)	55 (53)
Mean (SD)	7.6 (19.87)	0.4 (17.95)	3.9 (19.09)
Median	5.0	0.0	5.0
Q1,Q3	-10.0, 20.0	-12.5, 10.0	-10.0, 10.0
Min, Max	-35, 60	-40, 50	-40, 60

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	21 (40)	19 (38)	40 (39)
Mean (SD)	5.0 (24.55)	-4.7 (13.89)	0.4 (20.55)
Median	5.0	0.0	0.0
Q1,Q3	-10.0, 20.0	-15.0, 0.0	-10.0, 12.5
Min, Max	-40, 60	-35, 15	-40, 60
Week 96			
n (%)	10 (19)	12 (24)	22 (21)
Mean (SD)	6.0 (16.63)	2.1 (22.31)	3.9 (19.57)
Median	2.5	2.5	2.5
Q1,Q3	-10.0, 20.0	-7.5, 15.0	-10.0, 15.0
Min, Max	-10, 40	-40, 45	-40, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_female

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Physical Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	24 (48)	34 (74)	58 (60)
Mean (SD)	-4.2 (18.97)	1.2 (13.91)	-1.0 (16.26)
Median	-1.6	0.0	0.0
Q1,Q3	-9.4, 6.3	-9.4, 9.4	-9.4, 6.3
Min, Max	-72, 25	-22, 41	-72, 41
Week 48			
n (%)	22 (44)	26 (57)	48 (50)
Mean (SD)	2.3 (14.47)	-2.5 (13.69)	-0.3 (14.11)
Median	3.1	-3.1	0.0
Q1,Q3	-3.1, 9.4	-9.4, 3.1	-9.4, 9.4
Min, Max	-28, 34	-25, 25	-28, 34

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	18 (36)	20 (43)	38 (40)
Mean (SD)	-9.0 (15.12)	-2.5 (17.46)	-5.6 (16.51)
Median	-6.3	0.0	-4.7
Q1,Q3	-15.6, 0.0	-7.8, 9.4	-15.6, 6.3
Min, Max	-47, 16	-38, 22	-47, 22
Week 96			
n (%)	11 (22)	15 (33)	26 (27)
Mean (SD)	-4.5 (16.14)	-0.4 (15.75)	-2.2 (15.73)
Median	-6.3	-6.3	-6.3
Q1,Q3	-18.8, 3.1	-9.4, 3.1	-9.4, 3.1
Min, Max	-31, 28	-22, 34	-31, 34

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	24 (48)	34 (74)	58 (60)
Mean (SD)	-3.1 (15.73)	-2.9 (21.04)	-3.0 (18.87)
Median	-5.0	-5.0	-5.0
Q1,Q3	-17.5, 10.0	-15.0, 10.0	-15.0, 10.0
Min, Max	-30, 30	-45, 40	-45, 40
Week 48			
n (%)	22 (44)	26 (57)	48 (50)
Mean (SD)	5.5 (20.58)	-5.8 (15.08)	-0.6 (18.50)
Median	0.0	-5.0	0.0
Q1,Q3	-5.0, 25.0	-15.0, 5.0	-15.0, 10.0
Min, Max	-45, 40	-40, 15	-45, 40

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	18 (36)	20 (43)	38 (40)
Mean (SD)	2.5 (17.26)	0.5 (15.12)	1.4 (15.98)
Median	0.0	5.0	2.5
Q1,Q3	-10.0, 15.0	-7.5, 10.0	-10.0, 10.0
Min, Max	-25, 40	-30, 35	-30, 40
Week 96			
n (%)	11 (22)	15 (33)	26 (27)
Mean (SD)	-5.0 (18.71)	-5.3 (20.74)	-5.2 (19.52)
Median	0.0	-5.0	-2.5
Q1,Q3	-20.0, 5.0	-20.0, 10.0	-20.0, 5.0
Min, Max	-45, 25	-40, 25	-45, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	24 (48)	34 (74)	58 (60)
Mean (SD)	-0.8 (17.24)	-1.3 (14.48)	-1.1 (15.53)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-5.0, 5.0	-10.0, 5.0
Min, Max	-35, 40	-30, 40	-35, 40
Week 48			
n (%)	22 (44)	26 (57)	48 (50)
Mean (SD)	1.8 (10.86)	-1.5 (24.49)	0.0 (19.35)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-10.0, 5.0	-5.0, 5.0
Min, Max	-20, 25	-70, 75	-70, 75

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	18 (36)	20 (43)	38 (40)
Mean (SD)	1.9 (14.67)	-8.8 (19.39)	-3.7 (17.92)
Median	0.0	-5.0	-2.5
Q1,Q3	-5.0, 10.0	-17.5, 0.0	-10.0, 5.0
Min, Max	-35, 35	-50, 40	-50, 40
Week 96			
n (%)	11 (22)	15 (33)	26 (27)
Mean (SD)	-0.9 (19.85)	1.0 (23.08)	0.2 (21.38)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 15.0	-10.0, 5.0	-5.0, 5.0
Min, Max	-40, 35	-30, 75	-40, 75

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	24 (48)	34 (74)	58 (60)
Mean (SD)	-1.3 (17.02)	-3.1 (18.01)	-2.3 (17.48)
Median	-2.5	0.0	0.0
Q1,Q3	-12.5, 10.0	-15.0, 5.0	-15.0, 5.0
Min, Max	-40, 45	-45, 55	-45, 55
Week 48			
n (%)	22 (44)	26 (57)	48 (50)
Mean (SD)	5.5 (17.11)	0.4 (20.44)	2.7 (18.96)
Median	5.0	0.0	5.0
Q1,Q3	-10.0, 15.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-35, 35	-40, 50	-40, 50

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	18 (36)	20 (43)	38 (40)
Mean (SD)	2.5 (20.45)	-5.0 (16.22)	-1.4 (18.49)
Median	2.5	-2.5	0.0
Q1,Q3	-10.0, 15.0	-15.0, 2.5	-15.0, 10.0
Min, Max	-40, 35	-45, 25	-45, 35
Week 96			
n (%)	11 (22)	14 (30)	25 (26)
Mean (SD)	5.5 (15.72)	-3.2 (20.44)	0.6 (18.67)
Median	5.0	2.5	5.0
Q1,Q3	-10.0, 20.0	-10.0, 15.0	-10.0, 15.0
Min, Max	-10, 40	-40, 25	-40, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE(CHG FROM BL)_male

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Physical Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	12 (57)	15 (83)	27 (69)
Mean (SD)	7.8 (12.10)	-4.6 (12.38)	0.9 (13.56)
Median	3.1	-3.1	0.0
Q1,Q3	0.0, 12.5	-15.6, 3.1	-6.3, 6.3
Min, Max	-3, 38	-22, 19	-22, 38
Week 48			
n (%)	11 (52)	11 (61)	22 (56)
Mean (SD)	-3.1 (30.59)	-9.7 (16.74)	-6.4 (24.29)
Median	0.0	-3.1	0.0
Q1,Q3	-6.3, 6.3	-28.1, 6.3	-18.8, 6.3
Min, Max	-88, 38	-34, 9	-88, 38

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	11 (52)	6 (33)	17 (44)
Mean (SD)	-0.3 (10.68)	-6.3 (17.57)	-2.4 (13.28)
Median	0.0	-3.1	0.0
Q1,Q3	-6.3, 3.1	-9.4, 0.0	-6.3, 3.1
Min, Max	-22, 22	-38, 16	-38, 22
Week 96			
n (%)	7 (33)	4 (22)	11 (28)
Mean (SD)	0.4 (5.54)	7.8 (9.38)	3.1 (7.65)
Median	0.0	6.3	0.0
Q1,Q3	0.0, 3.1	0.0, 15.6	0.0, 9.4
Min, Max	-9, 9	0, 19	-9, 19

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Emotional Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	12 (57)	15 (83)	27 (69)
Mean (SD)	9.6 (19.24)	0.0 (15.12)	4.3 (17.41)
Median	5.0	0.0	0.0
Q1,Q3	0.0, 20.0	-15.0, 10.0	-5.0, 20.0
Min, Max	-25, 50	-20, 30	-25, 50
Week 48			
n (%)	11 (52)	11 (61)	22 (56)
Mean (SD)	14.1 (27.28)	3.2 (17.93)	8.6 (23.21)
Median	20.0	5.0	7.5
Q1,Q3	-10.0, 35.0	-5.0, 15.0	-5.0, 20.0
Min, Max	-25, 65	-30, 30	-30, 65

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	11 (52)	6 (33)	17 (44)
Mean (SD)	3.2 (23.16)	0.8 (19.85)	2.4 (21.44)
Median	0.0	-5.0	0.0
Q1,Q3	-10.0, 20.0	-15.0, 20.0	-10.0, 20.0
Min, Max	-45, 30	-20, 30	-45, 30
Week 96			
n (%)	7 (33)	4 (22)	11 (28)
Mean (SD)	0.0 (9.57)	26.3 (13.77)	9.5 (16.95)
Median	0.0	27.5	0.0
Q1,Q3	-5.0, 0.0	15.0, 37.5	-5.0, 20.0
Min, Max	-10, 20	10, 40	-10, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Social Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	12 (57)	15 (83)	27 (69)
Mean (SD)	2.5 (12.34)	4.7 (14.57)	3.7 (13.42)
Median	0.0	0.0	0.0
Q1,Q3	-2.5, 5.0	0.0, 5.0	0.0, 5.0
Min, Max	-15, 30	-20, 35	-20, 35
Week 48			
n (%)	11 (52)	11 (61)	22 (56)
Mean (SD)	-1.4 (15.98)	2.3 (18.08)	0.5 (16.76)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-15.0, 20.0	0.0, 10.0
Min, Max	-40, 15	-25, 35	-40, 35

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	11 (52)	6 (33)	17 (44)
Mean (SD)	3.6 (7.78)	0.8 (27.28)	2.6 (16.50)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	0.0, 10.0	0.0, 10.0
Min, Max	-10, 15	-45, 40	-45, 40
Week 96			
n (%)	7 (33)	4 (22)	11 (28)
Mean (SD)	-2.9 (13.80)	12.5 (34.28)	2.7 (22.95)
Median	0.0	17.5	0.0
Q1,Q3	-10.0, 10.0	-15.0, 40.0	-10.0, 10.0
Min, Max	-30, 10	-30, 45	-30, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Work/Study/School Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	12 (57)	15 (83)	27 (69)
Mean (SD)	7.5 (20.39)	-3.3 (13.58)	1.5 (17.48)
Median	2.5	-5.0	0.0
Q1,Q3	-5.0, 22.5	-15.0, 5.0	-10.0, 5.0
Min, Max	-25, 50	-25, 25	-25, 50
Week 48			
n (%)	11 (52)	11 (61)	22 (56)
Mean (SD)	11.4 (22.03)	-5.5 (17.53)	3.0 (21.25)
Median	5.0	-5.0	0.0
Q1,Q3	0.0, 30.0	-20.0, 0.0	-10.0, 10.0
Min, Max	-15, 60	-40, 25	-40, 60

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	11 (52)	6 (33)	17 (44)
Mean (SD)	1.8 (27.23)	0.0 (18.17)	1.2 (23.82)
Median	-5.0	5.0	0.0
Q1,Q3	-15.0, 20.0	0.0, 10.0	-10.0, 10.0
Min, Max	-40, 60	-35, 15	-40, 60
Week 96			
n (%)	7 (33)	4 (22)	11 (28)
Mean (SD)	6.4 (8.52)	16.3 (31.19)	10.0 (18.97)
Median	10.0	22.5	10.0
Q1,Q3	0.0, 10.0	-7.5, 40.0	0.0, 20.0
Min, Max	-5, 20	-25, 45	-25, 45

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE (CHG FROM BL)_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE_age13to14

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Physical Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	10 (56)	11 (79)	21 (66)
Mean (SD)	89.4 (8.62)	79.8 (20.79)	84.4 (16.54)
Median	87.5	87.5	87.5
Q1,Q3	81.3, 100.0	59.4, 100.0	81.3, 100.0
Min, Max	78, 100	41, 100	41, 100
Week 24			
n (%)	16 (89)	13 (93)	29 (91)
Mean (SD)	75.8 (26.68)	76.7 (22.48)	76.2 (24.46)
Median	81.3	75.0	78.1
Q1,Q3	60.9, 100.0	62.5, 96.9	62.5, 100.0
Min, Max	13, 100	31, 100	13, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	77.1 (23.51)	75.0 (25.13)	76.2 (23.68)
Median	87.5	79.7	84.4
Q1,Q3	65.6, 93.8	65.6, 93.8	65.6, 93.8
Min, Max	38, 100	16, 100	16, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	78.5 (20.05)	82.0 (17.18)	79.7 (18.78)
Median	84.4	89.1	84.4
Q1,Q3	71.9, 100.0	65.6, 95.3	71.9, 96.9
Min, Max	41, 100	56, 100	41, 100
Week 96			
n (%)	14 (78)	7 (50)	21 (66)
Mean (SD)	83.3 (19.01)	84.8 (13.55)	83.8 (17.05)
Median	90.6	87.5	90.6
Q1,Q3	65.6, 100.0	75.0, 96.9	71.9, 96.9
Min, Max	38, 100	63, 100	38, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Emotional Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	10 (56)	11 (79)	21 (66)
Mean (SD)	76.0 (25.03)	76.8 (20.40)	76.4 (22.14)
Median	82.5	80.0	80.0
Q1,Q3	60.0, 95.0	70.0, 90.0	70.0, 90.0
Min, Max	25, 100	25, 100	25, 100
Week 24			
n (%)	15 (83)	13 (93)	28 (88)
Mean (SD)	66.3 (28.19)	66.5 (22.12)	66.4 (25.09)
Median	70.0	75.0	70.0
Q1,Q3	45.0, 90.0	50.0, 75.0	47.5, 87.5
Min, Max	0, 100	25, 100	0, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	68.8 (31.10)	70.0 (20.82)	69.3 (26.56)
Median	70.0	72.5	70.0
Q1,Q3	55.0, 95.0	50.0, 85.0	50.0, 95.0
Min, Max	0, 100	40, 100	0, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	73.7 (25.18)	78.1 (17.92)	75.2 (22.59)
Median	80.0	77.5	80.0
Q1,Q3	50.0, 95.0	62.5, 95.0	60.0, 95.0
Min, Max	20, 100	55, 100	20, 100
Week 96			
n (%)	14 (78)	7 (50)	21 (66)
Mean (SD)	74.6 (25.53)	75.7 (19.24)	75.0 (23.13)
Median	80.0	80.0	80.0
Q1,Q3	60.0, 95.0	60.0, 95.0	60.0, 95.0
Min, Max	25, 100	50, 100	25, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Social Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	10 (56)	11 (79)	21 (66)
Mean (SD)	94.0 (10.75)	87.7 (18.89)	90.7 (15.51)
Median	100.0	95.0	100.0
Q1,Q3	90.0, 100.0	75.0, 100.0	90.0, 100.0
Min, Max	70, 100	50, 100	50, 100
Week 24			
n (%)	16 (89)	13 (93)	29 (91)
Mean (SD)	82.8 (20.33)	85.4 (18.42)	84.0 (19.20)
Median	92.5	90.0	90.0
Q1,Q3	70.0, 100.0	80.0, 100.0	70.0, 100.0
Min, Max	45, 100	50, 100	45, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	81.2 (23.47)	87.0 (20.71)	83.7 (22.01)
Median	95.0	100.0	95.0
Q1,Q3	70.0, 100.0	80.0, 100.0	70.0, 100.0
Min, Max	30, 100	45, 100	30, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	87.0 (20.34)	90.0 (10.00)	88.0 (17.24)
Median	100.0	95.0	95.0
Q1,Q3	80.0, 100.0	80.0, 97.5	80.0, 100.0
Min, Max	45, 100	75, 100	45, 100
Week 96			
n (%)	14 (78)	7 (50)	21 (66)
Mean (SD)	86.1 (20.86)	94.3 (13.05)	88.8 (18.70)
Median	95.0	100.0	100.0
Q1,Q3	85.0, 100.0	95.0, 100.0	90.0, 100.0
Min, Max	40, 100	65, 100	40, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Work/Study/School Functioning

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	10 (56)	11 (79)	21 (66)
Mean (SD)	79.5 (23.62)	75.5 (18.50)	77.4 (20.65)
Median	90.0	75.0	85.0
Q1,Q3	50.0, 100.0	65.0, 90.0	65.0, 95.0
Min, Max	45, 100	40, 100	40, 100
Week 24			
n (%)	16 (89)	12 (86)	28 (88)
Mean (SD)	64.5 (28.43)	77.1 (15.59)	69.9 (24.26)
Median	67.5	77.5	72.5
Q1,Q3	47.5, 90.0	62.5, 90.0	55.6, 90.0
Min, Max	0, 100	55, 100	0, 100
Week 48			
n (%)	12 (67)	10 (71)	22 (69)
Mean (SD)	74.6 (23.69)	71.5 (22.74)	73.2 (22.76)
Median	77.5	80.0	77.5
Q1,Q3	57.5, 97.5	55.0, 90.0	55.0, 90.0
Min, Max	25, 100	30, 95	25, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	70.3 (20.66)	76.3 (20.66)	72.4 (20.39)
Median	70.0	80.0	75.0
Q1,Q3	55.0, 90.0	62.5, 92.5	55.0, 90.0
Min, Max	35, 100	40, 100	35, 100
Week 96			
n (%)	14 (78)	7 (50)	21 (66)
Mean (SD)	74.6 (23.73)	77.9 (17.99)	75.7 (21.58)
Median	65.0	75.0	75.0
Q1,Q3	60.0, 100.0	65.0, 100.0	60.0, 100.0
Min, Max	30, 100	50, 100	30, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE_age15to17

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Physical Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	37 (70)	42 (84)	79 (77)
Mean (SD)	72.3 (27.03)	74.1 (19.78)	73.3 (23.32)
Median	78.1	75.0	78.1
Q1,Q3	56.3, 93.8	65.6, 87.5	59.4, 93.8
Min, Max	0, 100	19, 100	0, 100
Week 24			
n (%)	40 (75)	45 (90)	85 (83)
Mean (SD)	77.7 (20.50)	75.0 (19.06)	76.3 (19.68)
Median	81.3	78.1	78.1
Q1,Q3	59.4, 96.9	68.8, 87.5	65.6, 93.8
Min, Max	22, 100	19, 100	19, 100
Week 48			
n (%)	39 (74)	34 (68)	73 (71)
Mean (SD)	74.9 (22.09)	73.8 (18.97)	74.4 (20.56)
Median	81.3	75.0	78.1
Q1,Q3	59.4, 93.8	62.5, 90.6	62.5, 90.6
Min, Max	13, 100	22, 100	13, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	31 (58)	21 (42)	52 (50)
Mean (SD)	70.6 (20.31)	76.0 (21.34)	72.8 (20.70)
Median	71.9	78.1	75.0
Q1,Q3	50.0, 87.5	65.6, 93.8	54.7, 90.6
Min, Max	28, 100	31, 100	28, 100
Week 96			
n (%)	15 (28)	15 (30)	30 (29)
Mean (SD)	75.0 (21.33)	81.3 (16.99)	78.1 (19.21)
Median	78.1	84.4	82.8
Q1,Q3	50.0, 96.9	65.6, 100.0	62.5, 96.9
Min, Max	44, 100	53, 100	44, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Emotional Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	37 (70)	42 (84)	79 (77)
Mean (SD)	60.7 (23.98)	67.6 (20.58)	64.4 (22.37)
Median	60.0	65.0	65.0
Q1,Q3	45.0, 80.0	55.0, 85.0	50.0, 80.0
Min, Max	0, 95	20, 100	0, 100
Week 24			
n (%)	40 (75)	45 (90)	85 (83)
Mean (SD)	66.8 (20.77)	67.2 (19.06)	67.0 (19.76)
Median	67.5	70.0	70.0
Q1,Q3	55.0, 80.0	50.0, 80.0	55.0, 80.0
Min, Max	20, 100	30, 100	20, 100
Week 48			
n (%)	39 (74)	34 (68)	73 (71)
Mean (SD)	70.5 (20.89)	68.1 (19.23)	69.4 (20.03)
Median	70.0	67.5	70.0
Q1,Q3	50.0, 90.0	60.0, 80.0	55.0, 90.0
Min, Max	30, 100	15, 100	15, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	31 (58)	21 (42)	52 (50)
Mean (SD)	65.9 (21.68)	69.0 (16.85)	67.1 (19.76)
Median	70.0	70.0	70.0
Q1,Q3	45.0, 80.0	60.0, 80.0	55.0, 80.0
Min, Max	25, 100	30, 100	25, 100
Week 96			
n (%)	15 (28)	15 (30)	30 (29)
Mean (SD)	58.0 (22.90)	66.0 (26.27)	62.0 (24.55)
Median	55.0	70.0	62.5
Q1,Q3	40.0, 80.0	45.0, 90.0	45.0, 80.0
Min, Max	15, 95	10, 100	10, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Social Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	37 (70)	42 (84)	79 (77)
Mean (SD)	81.1 (24.39)	86.4 (18.46)	83.9 (21.46)
Median	90.0	95.0	95.0
Q1,Q3	65.0, 100.0	80.0, 100.0	75.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 24			
n (%)	40 (75)	45 (90)	85 (83)
Mean (SD)	87.9 (14.09)	87.1 (15.02)	87.5 (14.51)
Median	90.0	90.0	90.0
Q1,Q3	80.0, 100.0	75.0, 100.0	80.0, 100.0
Min, Max	50, 100	50, 100	50, 100
Week 48			
n (%)	39 (74)	34 (68)	73 (71)
Mean (SD)	82.9 (20.51)	88.5 (17.60)	85.5 (19.29)
Median	90.0	95.0	95.0
Q1,Q3	65.0, 100.0	80.0, 100.0	75.0, 100.0
Min, Max	25, 100	15, 100	15, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	31 (58)	21 (42)	52 (50)
Mean (SD)	87.6 (18.39)	81.7 (24.05)	85.2 (20.84)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	70.0, 100.0	72.5, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 96			
n (%)	15 (28)	15 (30)	30 (29)
Mean (SD)	88.0 (18.97)	88.7 (17.16)	88.3 (17.78)
Median	95.0	100.0	100.0
Q1,Q3	80.0, 100.0	70.0, 100.0	80.0, 100.0
Min, Max	30, 100	50, 100	30, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Work/Study/School Functioning

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	36 (68)	42 (84)	78 (76)
Mean (SD)	61.0 (29.00)	68.0 (19.63)	64.7 (24.49)
Median	60.0	70.0	65.0
Q1,Q3	37.5, 87.5	55.0, 80.0	50.0, 85.0
Min, Max	5, 100	25, 100	5, 100
Week 24			
n (%)	40 (75)	44 (88)	84 (82)
Mean (SD)	67.8 (22.90)	64.1 (19.27)	65.8 (21.03)
Median	70.0	65.0	65.0
Q1,Q3	50.0, 85.0	50.0, 82.5	50.0, 85.0
Min, Max	25, 100	20, 100	20, 100
Week 48			
n (%)	39 (74)	34 (68)	73 (71)
Mean (SD)	65.5 (23.73)	71.6 (19.80)	68.4 (22.05)
Median	70.0	75.0	75.0
Q1,Q3	50.0, 85.0	55.0, 85.0	50.0, 85.0
Min, Max	15, 100	20, 100	15, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	31 (58)	21 (42)	52 (50)
Mean (SD)	65.6 (22.31)	67.6 (20.22)	66.4 (21.31)
Median	60.0	70.0	70.0
Q1,Q3	50.0, 90.0	55.0, 80.0	50.0, 85.0
Min, Max	15, 100	20, 100	15, 100
Week 96			
n (%)	15 (28)	15 (30)	30 (29)
Mean (SD)	66.7 (26.37)	74.7 (18.94)	70.7 (22.92)
Median	75.0	80.0	75.0
Q1,Q3	45.0, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	20, 100	45, 100	20, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE_female

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Physical Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	72.7 (24.80)	71.7 (19.59)	72.2 (22.03)
Median	81.3	71.9	78.1
Q1,Q3	57.8, 93.8	60.9, 87.5	59.4, 89.1
Min, Max	0, 100	19, 100	0, 100
Week 24			
n (%)	39 (78)	42 (91)	81 (84)
Mean (SD)	72.3 (23.17)	73.4 (20.01)	72.9 (21.46)
Median	71.9	71.9	71.9
Q1,Q3	56.3, 93.8	62.5, 90.6	59.4, 90.6
Min, Max	13, 100	19, 100	13, 100
Week 48			
n (%)	36 (72)	33 (72)	69 (72)
Mean (SD)	74.2 (20.06)	72.3 (21.55)	73.3 (20.66)
Median	75.0	78.1	75.0
Q1,Q3	62.5, 93.8	56.3, 90.6	59.4, 90.6
Min, Max	28, 97	16, 100	16, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	31 (62)	22 (48)	53 (55)
Mean (SD)	68.3 (18.15)	76.0 (20.80)	71.5 (19.48)
Median	71.9	79.7	75.0
Q1,Q3	46.9, 87.5	59.4, 93.8	56.3, 87.5
Min, Max	41, 100	31, 100	31, 100
Week 96			
n (%)	19 (38)	17 (37)	36 (38)
Mean (SD)	73.5 (21.41)	79.4 (15.90)	76.3 (18.98)
Median	78.1	81.3	79.7
Q1,Q3	50.0, 93.8	65.6, 93.8	62.5, 93.8
Min, Max	38, 97	53, 100	38, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_
SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	61.6 (24.38)	70.0 (20.74)	66.0 (22.75)
Median	60.0	70.0	70.0
Q1,Q3	42.5, 85.0	57.5, 90.0	50.0, 90.0
Min, Max	0, 95	20, 100	0, 100
Week 24			
n (%)	39 (78)	42 (91)	81 (84)
Mean (SD)	62.7 (23.39)	66.5 (18.85)	64.7 (21.11)
Median	60.0	70.0	65.0
Q1,Q3	50.0, 80.0	50.0, 80.0	50.0, 80.0
Min, Max	0, 100	30, 100	0, 100
Week 48			
n (%)	36 (72)	33 (72)	69 (72)
Mean (SD)	67.5 (24.07)	66.4 (18.43)	67.0 (21.41)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 90.0	60.0, 80.0	55.0, 80.0
Min, Max	0, 100	15, 100	0, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	31 (62)	22 (48)	53 (55)
Mean (SD)	65.4 (20.49)	71.8 (18.16)	68.1 (19.64)
Median	70.0	75.0	70.0
Q1,Q3	50.0, 80.0	60.0, 80.0	60.0, 80.0
Min, Max	20, 100	30, 100	20, 100
Week 96			
n (%)	19 (38)	17 (37)	36 (38)
Mean (SD)	58.7 (25.43)	64.1 (23.67)	61.3 (24.42)
Median	55.0	65.0	60.0
Q1,Q3	40.0, 80.0	50.0, 85.0	42.5, 82.5
Min, Max	15, 95	10, 95	10, 95

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	82.5 (24.10)	86.9 (17.78)	84.9 (20.95)
Median	100.0	95.0	95.0
Q1,Q3	67.5, 100.0	82.5, 100.0	75.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 24			
n (%)	39 (78)	42 (91)	81 (84)
Mean (SD)	84.7 (15.77)	85.2 (16.53)	85.0 (16.07)
Median	90.0	90.0	90.0
Q1,Q3	75.0, 100.0	75.0, 100.0	75.0, 100.0
Min, Max	45, 100	50, 100	45, 100
Week 48			
n (%)	36 (72)	33 (72)	69 (72)
Mean (SD)	82.5 (19.36)	86.8 (19.88)	84.6 (19.59)
Median	87.5	95.0	95.0
Q1,Q3	67.5, 100.0	80.0, 100.0	70.0, 100.0
Min, Max	30, 100	15, 100	15, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	31 (62)	22 (48)	53 (55)
Mean (SD)	86.8 (18.82)	83.2 (20.73)	85.3 (19.52)
Median	95.0	90.0	95.0
Q1,Q3	70.0, 100.0	75.0, 100.0	75.0, 100.0
Min, Max	30, 100	25, 100	25, 100
Week 96			
n (%)	19 (38)	17 (37)	36 (38)
Mean (SD)	87.1 (19.95)	90.6 (14.35)	88.8 (17.38)
Median	95.0	100.0	100.0
Q1,Q3	80.0, 100.0	90.0, 100.0	82.5, 100.0
Min, Max	30, 100	65, 100	30, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	31 (62)	36 (78)	67 (70)
Mean (SD)	65.3 (29.47)	69.2 (18.22)	67.4 (23.97)
Median	70.0	70.0	70.0
Q1,Q3	40.0, 95.0	57.5, 82.5	55.0, 85.0
Min, Max	5, 100	30, 100	5, 100
Week 24			
n (%)	39 (78)	41 (89)	80 (83)
Mean (SD)	64.5 (22.98)	66.7 (19.12)	65.6 (20.99)
Median	70.0	65.0	67.5
Q1,Q3	50.0, 80.0	55.0, 80.0	50.0, 80.0
Min, Max	0, 100	30, 100	0, 100
Week 48			
n (%)	36 (72)	33 (72)	69 (72)
Mean (SD)	65.8 (24.07)	71.5 (19.98)	68.6 (22.23)
Median	70.0	75.0	70.0
Q1,Q3	47.5, 85.0	55.0, 90.0	50.0, 85.0
Min, Max	15, 100	20, 100	15, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	31 (62)	22 (48)	53 (55)
Mean (SD)	66.6 (19.38)	68.9 (20.81)	67.5 (19.82)
Median	70.0	75.0	70.0
Q1,Q3	50.0, 85.0	55.0, 85.0	55.0, 85.0
Min, Max	35, 100	20, 100	20, 100
Week 96			
n (%)	19 (38)	17 (37)	36 (38)
Mean (SD)	66.8 (26.68)	74.1 (18.31)	70.3 (23.08)
Median	65.0	80.0	72.5
Q1,Q3	45.0, 90.0	60.0, 90.0	52.5, 90.0
Min, Max	20, 100	45, 100	20, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

109MS306_table46_48_CHG_DESCRIBE_male

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Physical Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	82.9 (25.55)	82.9 (18.98)	82.9 (21.93)
Median	93.8	87.5	92.2
Q1,Q3	75.0, 100.0	71.9, 100.0	71.9, 100.0
Min, Max	6, 100	38, 100	6, 100
Week 24			
n (%)	17 (81)	16 (89)	33 (85)
Mean (SD)	88.2 (15.21)	80.5 (18.42)	84.5 (17.04)
Median	90.6	81.3	87.5
Q1,Q3	81.3, 100.0	76.6, 95.3	78.1, 100.0
Min, Max	44, 100	31, 100	31, 100
Week 48			
n (%)	16 (76)	11 (61)	27 (69)
Mean (SD)	78.2 (27.02)	79.3 (15.20)	78.7 (22.59)
Median	89.1	71.9	87.5
Q1,Q3	60.9, 100.0	68.8, 96.9	68.8, 100.0
Min, Max	13, 100	59, 100	13, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	7 (39)	22 (56)
Mean (SD)	83.1 (21.61)	83.0 (18.39)	83.1 (20.20)
Median	90.6	90.6	90.6
Q1,Q3	71.9, 100.0	71.9, 100.0	71.9, 100.0
Min, Max	28, 100	50, 100	28, 100
Week 96			
n (%)	10 (48)	5 (28)	15 (38)
Mean (SD)	89.4 (13.60)	92.5 (11.18)	90.4 (12.53)
Median	96.9	100.0	100.0
Q1,Q3	75.0, 100.0	87.5, 100.0	75.0, 100.0
Min, Max	66, 100	75, 100	66, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Emotional Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Baseline			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	69.0 (25.65)	68.5 (21.20)	68.8 (23.00)
Median	75.0	70.0	72.5
Q1,Q3	60.0, 90.0	60.0, 85.0	60.0, 87.5
Min, Max	15, 100	25, 100	15, 100
Week 24			
n (%)	16 (76)	16 (89)	32 (82)
Mean (SD)	76.3 (18.39)	68.4 (21.96)	72.3 (20.32)
Median	72.5	72.5	72.5
Q1,Q3	65.0, 95.0	52.5, 82.5	57.5, 87.5
Min, Max	45, 100	25, 100	25, 100
Week 48			
n (%)	16 (76)	11 (61)	27 (69)
Mean (SD)	75.9 (21.85)	75.0 (21.56)	75.6 (21.32)
Median	80.0	80.0	80.0
Q1,Q3	55.0, 97.5	55.0, 95.0	55.0, 95.0
Min, Max	45, 100	40, 100	40, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	7 (39)	22 (56)
Mean (SD)	74.7 (26.89)	70.7 (15.66)	73.4 (23.57)
Median	80.0	70.0	75.0
Q1,Q3	45.0, 100.0	55.0, 80.0	55.0, 100.0
Min, Max	30, 100	55, 100	30, 100
Week 96			
n (%)	10 (48)	5 (28)	15 (38)
Mean (SD)	80.0 (18.86)	86.0 (19.49)	82.0 (18.59)
Median	82.5	100.0	85.0
Q1,Q3	65.0, 100.0	70.0, 100.0	65.0, 100.0
Min, Max	45, 100	60, 100	45, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_DESCRIBE_SubGr date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Social Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Baseline			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	86.7 (19.97)	86.2 (20.12)	86.4 (19.73)
Median	100.0	100.0	100.0
Q1,Q3	75.0, 100.0	80.0, 100.0	77.5, 100.0
Min, Max	30, 100	30, 100	30, 100
Week 24			
n (%)	17 (81)	16 (89)	33 (85)
Mean (SD)	90.3 (16.63)	90.6 (12.89)	90.5 (14.70)
Median	100.0	100.0	100.0
Q1,Q3	80.0, 100.0	80.0, 100.0	80.0, 100.0
Min, Max	50, 100	60, 100	50, 100
Week 48			
n (%)	16 (76)	11 (61)	27 (69)
Mean (SD)	82.5 (25.17)	92.3 (11.04)	86.5 (20.88)
Median	97.5	100.0	100.0
Q1,Q3	70.0, 100.0	80.0, 100.0	80.0, 100.0
Min, Max	25, 100	75, 100	25, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	7 (39)	22 (56)
Mean (SD)	88.7 (19.41)	86.4 (24.45)	88.0 (20.57)
Median	100.0	100.0	100.0
Q1,Q3	80.0, 100.0	75.0, 100.0	80.0, 100.0
Min, Max	45, 100	35, 100	35, 100
Week 96			
n (%)	10 (48)	5 (28)	15 (38)
Mean (SD)	87.0 (19.89)	90.0 (22.36)	88.0 (19.98)
Median	95.0	100.0	100.0
Q1,Q3	85.0, 100.0	100.0, 100.0	85.0, 100.0
Min, Max	40, 100	50, 100	40, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
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Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Work/Study/School Functioning

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	64.3 (28.15)	70.3 (22.46)	67.5 (25.05)
Median	65.0	75.0	65.0
Q1,Q3	45.0, 90.0	55.0, 90.0	52.5, 90.0
Min, Max	15, 100	25, 100	15, 100
Week 24			
n (%)	17 (81)	15 (83)	32 (82)
Mean (SD)	72.1 (27.33)	67.3 (19.99)	69.8 (23.91)
Median	80.0	65.0	75.0
Q1,Q3	50.0, 95.0	55.0, 85.0	52.5, 90.0
Min, Max	25, 100	20, 90	20, 100
Week 48			
n (%)	15 (71)	11 (61)	26 (67)
Mean (SD)	72.0 (23.36)	71.8 (21.94)	71.9 (22.32)
Median	75.0	75.0	75.0
Q1,Q3	55.0, 90.0	55.0, 95.0	55.0, 90.0
Min, Max	15, 100	35, 100	15, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	15 (71)	7 (39)	22 (56)
Mean (SD)	68.3 (26.50)	73.6 (19.94)	70.0 (24.25)
Median	65.0	70.0	70.0
Q1,Q3	50.0, 95.0	55.0, 95.0	55.0, 95.0
Min, Max	15, 100	45, 100	15, 100
Week 96			
n (%)	10 (48)	5 (28)	15 (38)
Mean (SD)	77.5 (20.98)	81.0 (19.17)	78.7 (19.77)
Median	80.0	75.0	75.0
Q1,Q3	55.0, 100.0	75.0, 100.0	55.0, 100.0
Min, Max	50, 100	55, 100	50, 100

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source:
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SubGr date: 09MAR2022

109MS306_table46_48_CHG_HEDGESCI_age13to14

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.658	-0.299	1.615
	48	0.571	-0.485	1.627
	72	-0.061	-1.076	0.953
	96	-0.142	-1.202	0.918
PHYSICAL FUNCTIONING	24	0.2	-0.733	1.132
	48	1.11	-0.008	2.228
	72	0.035	-0.980	1.049
	96	-0.185	-1.246	0.876
SCHOOL FUNCTIONING	24	-0.618	-1.572	0.336
	48	0.635	-0.427	1.696
	72	-0.18	-1.196	0.837
	96	0.336	-0.731	1.403
SOCIAL FUNCTIONING	24	-0.163	-1.094	0.769
	48	0.39	-0.654	1.434
	72	0.452	-0.577	1.481
	96	-0.313	-1.379	0.753

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table46_48_CHG_HEDGESCI_age15to17

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.202	-0.296	0.700
	48	0.545	-0.020	1.111
	72	0.127	-0.502	0.755
	96	-0.315	-1.185	0.555
PHYSICAL FUNCTIONING	24	0.011	-0.486	0.508
	48	0.207	-0.349	0.763
	72	-0.24	-0.871	0.390
	96	-0.392	-1.265	0.481
SCHOOL FUNCTIONING	24	0.657	0.147	1.167
	48	0.525	-0.040	1.089
	72	0.442	-0.194	1.078
	96	0.17	-0.696	1.036
SOCIAL FUNCTIONING	24	0.096	-0.402	0.593
	48	0.089	-0.466	0.644
	72	0.523	-0.116	1.162
	96	-0.228	-1.095	0.639

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table46_48_CHG_HEDGESCI_female

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.143	-0.390	0.677
	48	0.672	0.075	1.269
	72	0.124	-0.514	0.761
	96	0.109	-0.681	0.900
PHYSICAL FUNCTIONING	24	-0.323	-0.859	0.214
	48	0.401	-0.185	0.987
	72	-0.398	-1.042	0.245
	96	-0.295	-1.090	0.499
SCHOOL FUNCTIONING	24	0.223	-0.311	0.758
	48	0.41	-0.176	0.996
	72	0.409	-0.235	1.053
	96	0.468	-0.334	1.269
SOCIAL FUNCTIONING	24	0.116	-0.417	0.650
	48	0.311	-0.272	0.895
	72	0.617	-0.035	1.270
	96	-0.089	-0.879	0.701

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table46_48_CHG_HEDGESCI_male

Table 46.48: Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
EMOTIONAL FUNCTIONING	24	0.551	-0.236	1.337
	48	0.393	-0.517	1.303
	72	-0.015	-1.028	0.997
	96	-3.277	-5.321	-1.233
PHYSICAL FUNCTIONING	24	1.044	0.218	1.869
	48	0.269	-0.636	1.174
	72	0.387	-0.635	1.409
	96	-0.975	-2.327	0.377
SCHOOL FUNCTIONING	24	0.585	-0.204	1.374
	48	0.88	-0.068	1.828
	72	0	-1.012	1.012
	96	-0.51	-1.799	0.780
SOCIAL FUNCTIONING	24	-0.18	-0.953	0.593
	48	-0.289	-1.195	0.617
	72	0.124	-0.889	1.137
	96	-0.74	-2.056	0.576

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source:
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109MS306_table46_48_CHG_LSMEANS_age13to14

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Emotional Functioning

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	-0.80 (4.488)	-10.33 (3.826)
Lsmean_95 % CI	(-10.310, 8.719)	(-18.442, -2.219)
Diffrence (95% CI)	9.535 (-2.982, 22.052)	
SE_Difference	5.9045	
p-value	0.1259	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	7.21 (6.975)	-10.92 (5.655)
Lsmean_95 % CI	(-7.982, 22.411)	(-23.242, 1.400)
Diffrence (95% CI)	18.136 (-1.754, 38.025)	
SE_Difference	9.1284	
p-value	0.0703	
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	0.67 (5.755)	-3.62 (6.166)
Lsmean_95 % CI	(-11.867, 13.210)	(-17.059, 9.810)
Diffrence (95% CI)	4.296 (-14.387, 22.979)	
SE_Difference	8.5747	
p-value	0.6254	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	1.70 (5.751)	-3.94 (6.706)

	DMF (N= 18)	**IFN B-1a (N= 14)**
Lsmean_95 % CI	(-10.957, 14.361)	(-18.697, 10.824)
Diffrence (95% CI)	5.639 (-14.446, 25.723)	
SE_Difference	9.1252	
p-value	0.5492	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Physical Functioning

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	1.26 (5.082)	-4.04 (4.307)
Lsmean_95 % CI	(-9.517, 12.032)	(-13.171, 5.092)
Diffrence (95% CI)	5.297 (-9.095, 19.689)	
SE_Difference	6.7889	
p-value	0.4466	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	4.37 (4.758)	-8.12 (3.854)
Lsmean_95 % CI	(-6.000, 14.734)	(-16.518, 0.278)
Diffrence (95% CI)	12.487 (-1.105, 26.080)	
SE_Difference	6.2384	
p-value	0.0685	
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	-2.16 (4.545)	-4.68 (4.869)
Lsmean_95 % CI	(-12.060, 7.745)	(-15.285, 5.931)
Diffrence (95% CI)	2.519 (-12.215, 17.253)	
SE_Difference	6.7623	
p-value	0.7160	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	-0.39 (3.242)	-0.52 (3.768)

	DMF (N= 18)	**IFN B-1a (N= 14)**
Lsmean_95 % CI	(-7.529, 6.741)	(-8.811, 7.777)
Diffrence (95% CI)	0.123 (-11.065, 11.311)	
SE_Difference	5.0832	
p-value	0.9811	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Work/Study/School Functioning

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	-9.05 (5.241)	-0.69 (4.469)
Lsmean_95 % CI	(-20.162, 2.059)	(-10.164, 8.785)
Diffrence (95% CI)	-8.362 (-22.968, 6.244)	
SE_Difference	6.8899	
p-value	0.2425	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	7.85 (7.539)	-7.45 (6.151)
Lsmean_95 % CI	(-8.579, 24.274)	(-20.855, 5.947)
Diffrence (95% CI)	15.301 (-5.941, 36.543)	
SE_Difference	9.7494	
p-value	0.1425	
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	-4.20 (6.150)	-2.34 (6.576)
Lsmean_95 % CI	(-17.601, 9.198)	(-16.669, 11.987)
Diffrence (95% CI)	-1.860 (-21.513, 17.792)	
SE_Difference	9.0197	
p-value	0.8400	
Week 96		
n (%)	8 (44)	6 (43)

	DMF (N= 18)	**IFN B-1a (N= 14)**
Lsmean (SE)	6.45 (5.385)	-1.93 (6.222)
Lsmean_95 % CI	(-5.408, 18.298)	(-15.620, 11.767)
Diffrence (95% CI)	8.372 (-9.769, 26.513)	
SE_Difference	8.2419	
p-value	0.3316	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. Social Functioning

	DMF (N= 18)	IFN B-1a (N= 14)
Week 24		
n (%)	8 (44)	11 (79)
Lsmean (SE)	-1.72 (4.874)	-1.48 (4.149)
Lsmean_95 % CI	(-12.051, 8.613)	(-10.272, 7.318)
Diffrence (95% CI)	-0.242 (-13.887, 13.403)	
SE_Difference	6.4364	
p-value	0.9705	
Week 48		
n (%)	6 (33)	9 (64)
Lsmean (SE)	4.86 (5.603)	-3.24 (4.552)
Lsmean_95 % CI	(-7.349, 17.067)	(-13.157, 6.678)
Diffrence (95% CI)	8.098 (-7.821, 24.018)	
SE_Difference	7.3063	
p-value	0.2894	
Week 72		
n (%)	8 (44)	7 (50)
Lsmean (SE)	4.18 (3.025)	-3.35 (3.234)
Lsmean_95 % CI	(-2.408, 10.774)	(-10.399, 3.694)
Diffrence (95% CI)	7.535 (-2.118, 17.188)	
SE_Difference	4.4303	
p-value	0.1147	
Week 96		
n (%)	8 (44)	6 (43)
Lsmean (SE)	-2.78 (6.141)	2.05 (7.093)

	DMF (N= 18)	**IFN B-1a (N= 14)**
Lsmean_95 % CI	(-16.301, 10.731)	(-13.564, 17.658)
Diffrence (95% CI)	-4.832 (-25.500, 15.837)	
SE_Difference	9.3904	
p-value	0.6171	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table46_48_CHG_LSMEANS_age15to17

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Emotional Functioning

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	28 (53)	38 (76)
Lsmean (SE)	0.99 (3.225)	0.85 (2.768)
Lsmean_95 % CI	(-5.459, 7.431)	(-4.678, 6.383)
Diffrence (95% CI)	0.134 (-8.369, 8.636)	
SE_Difference	4.2548	
p-value	0.9750	
Week 48		
n (%)	27 (51)	28 (56)
Lsmean (SE)	8.21 (3.238)	-0.24 (3.179)
Lsmean_95 % CI	(1.714, 14.709)	(-6.620, 6.140)
Diffrence (95% CI)	8.452 (-0.685, 17.589)	
SE_Difference	4.5534	
p-value	0.0691	
Week 72		
n (%)	21 (40)	19 (38)
Lsmean (SE)	3.82 (3.578)	1.83 (3.763)
Lsmean_95 % CI	(-3.428, 11.072)	(-5.796, 9.452)
Diffrence (95% CI)	1.994 (-8.556, 12.544)	
SE_Difference	5.2067	
p-value	0.7040	
Week 96		
n (%)	10 (19)	13 (26)
Lsmean (SE)	-3.03 (6.631)	0.79 (5.808)

	DMF (N= 53)	**IFN B-1a (N= 50)**
Lsmean_95 % CI	(-16.862, 10.803)	(-11.324, 12.908)
Diffrence (95% CI)	-3.822 (-22.302, 14.658)	
SE_Difference	8.8590	
p-value	0.6708	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Physical Functioning

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	28 (53)	38 (76)
Lsmean (SE)	0.54 (2.751)	-0.40 (2.359)
Lsmean_95 % CI	(-4.956, 6.041)	(-5.115, 4.315)
Diffrence (95% CI)	0.943 (-6.325, 8.211)	
SE_Difference	3.6370	
p-value	0.7963	
Week 48		
n (%)	27 (51)	28 (56)
Lsmean (SE)	-0.43 (3.278)	-3.49 (3.219)
Lsmean_95 % CI	(-7.010, 6.144)	(-9.948, 2.969)
Diffrence (95% CI)	3.057 (-6.161, 12.275)	
SE_Difference	4.5937	
p-value	0.5087	
Week 72		
n (%)	21 (40)	19 (38)
Lsmean (SE)	-7.10 (3.416)	-2.85 (3.591)
Lsmean_95 % CI	(-14.018, -0.176)	(-10.123, 4.430)
Diffrence (95% CI)	-4.251 (-14.304, 5.803)	
SE_Difference	4.9617	
p-value	0.3971	
Week 96		
n (%)	10 (19)	13 (26)
Lsmean (SE)	-3.18 (4.985)	1.25 (4.370)

	DMF (N= 53)	**IFN B-1a (N= 50)**
Lsmean_95 % CI	(-13.582, 7.213)	(-7.868, 10.363)
Diffrence (95% CI)	-4.432 (-18.282, 9.419)	
SE_Difference	6.6396	
p-value	0.5121	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Work/Study/School Functioning

	DMF (N= 53)	IFN B-1a (N= 50)
Week 24		
n (%)	28 (53)	38 (76)
Lsmean (SE)	3.98 (2.840)	-3.32 (2.437)
Lsmean_95 % CI	(-1.701, 9.651)	(-8.193, 1.546)
Diffrence (95% CI)	7.299 (-0.192, 14.791)	
SE_Difference	3.7489	
p-value	0.0560	
Week 48		
n (%)	27 (51)	28 (56)
Lsmean (SE)	5.82 (3.149)	2.06 (3.092)
Lsmean_95 % CI	(-0.495, 12.145)	(-4.142, 8.266)
Diffrence (95% CI)	3.763 (-5.161, 12.688)	
SE_Difference	4.4475	
p-value	0.4014	
Week 72		
n (%)	21 (40)	19 (38)
Lsmean (SE)	2.74 (3.999)	-2.24 (4.211)
Lsmean_95 % CI	(-5.359, 10.846)	(-10.775, 6.289)
Diffrence (95% CI)	4.987 (-6.962, 16.936)	
SE_Difference	5.8972	
p-value	0.4032	
Week 96		
n (%)	10 (19)	12 (24)
Lsmean (SE)	4.92 (5.849)	2.98 (5.336)
Lsmean_95 % CI	(-7.319, 17.164)	(-8.186, 14.149)

	DMF (N= 53)	**IFN B-1a (N= 50)**
Diffrence (95% CI)	1.941 (-14.687, 18.569)	
SE_Difference	7.9443	
p-value	0.8096	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
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Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. Social Functioning

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	28 (53)	38 (76)
Lsmean (SE)	1.03 (2.091)	0.95 (1.795)
Lsmean_95 % CI	(-3.148, 5.209)	(-2.636, 4.538)
Diffrence (95% CI)	0.079 (-5.428, 5.587)	
SE_Difference	2.7560	
p-value	0.9771	
Week 48		
n (%)	27 (51)	28 (56)
Lsmean (SE)	-0.45 (3.241)	0.79 (3.182)
Lsmean_95 % CI	(-6.955, 6.051)	(-5.593, 7.179)
Diffrence (95% CI)	-1.245 (-10.368, 7.877)	
SE_Difference	4.5462	
p-value	0.7852	
Week 72		
n (%)	21 (40)	19 (38)
Lsmean (SE)	1.36 (3.840)	-7.03 (4.039)
Lsmean_95 % CI	(-6.419, 9.143)	(-15.216, 1.153)
Diffrence (95% CI)	8.394 (-2.957, 19.744)	
SE_Difference	5.6017	
p-value	0.1425	
Week 96		
n (%)	10 (19)	13 (26)
Lsmean (SE)	-0.23 (6.168)	3.64 (5.410)

	DMF (N= 53)	**IFN B-1a (N= 50)**
Lsmean_95 % CI	(-13.101, 12.632)	(-7.642, 14.926)
Diffrence (95% CI)	-3.876 (-20.991, 13.239)	
SE_Difference	8.2047	
p-value	0.6417	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table46_48_CHG_LSMEANS_female

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Emotional Functioning

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	24 (48)	34 (74)
Lsmean (SE)	-4.78 (3.821)	-3.62 (3.190)
Lsmean_95 % CI	(-12.437, 2.886)	(-10.014, 2.776)
Diffrence (95% CI)	-1.157 (-9.978, 7.664)	
SE_Difference	4.3998	
p-value	0.7936	
Week 48		
n (%)	22 (44)	26 (57)
Lsmean (SE)	3.18 (3.958)	-6.62 (3.477)
Lsmean_95 % CI	(-4.797, 11.157)	(-13.633, 0.383)
Diffrence (95% CI)	9.805 (0.668, 18.942)	
SE_Difference	4.5337	
p-value	0.0360	
Week 72		
n (%)	18 (36)	20 (43)
Lsmean (SE)	0.28 (3.949)	-0.049 (3.639)
Lsmean_95 % CI	(-7.751, 8.302)	(-7.444, 7.346)
Diffrence (95% CI)	0.325 (-9.231, 9.881)	
SE_Difference	4.7022	
p-value	0.9453	
Week 96		
n (%)	11 (22)	15 (33)
Lsmean (SE)	-3.47 (6.321)	-5.12 (5.436)

	DMF (N= 50)	**IFN B-1a (N= 46)**
Lsmean_95 % CI	(-16.578, 9.639)	(-16.396, 6.152)
Diffrence (95% CI)	1.652 (-14.416, 17.721)	
SE_Difference	7.7481	
p-value	0.8331	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Physical Functioning

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	24 (48)	34 (74)
Lsmean (SE)	-3.66 (3.777)	-0.46 (3.024)
Lsmean_95 % CI	(-11.231, 3.913)	(-6.527, 5.598)
Diffrence (95% CI)	-3.194 (-11.968, 5.580)	
SE_Difference	4.3762	
p-value	0.4686	
Week 48		
n (%)	22 (44)	26 (57)
Lsmean (SE)	2.58 (3.547)	-2.96 (3.054)
Lsmean_95 % CI	(-4.566, 9.729)	(-9.113, 3.198)
Diffrence (95% CI)	5.539 (-2.681, 13.760)	
SE_Difference	4.0790	
p-value	0.1814	
Week 72		
n (%)	18 (36)	20 (43)
Lsmean (SE)	-9.02 (4.280)	-2.22 (3.877)
Lsmean_95 % CI	(-17.720, -0.323)	(-10.095, 5.662)
Diffrence (95% CI)	-6.804 (-17.209, 3.600)	
SE_Difference	5.1198	
p-value	0.1927	
Week 96		
n (%)	11 (22)	15 (33)
Lsmean (SE)	-3.69 (4.810)	-0.19 (4.188)

	DMF (N= 50)	**IFN B-1a (N= 46)**
Lsmean_95 % CI	(-13.665, 6.285)	(-8.877, 8.493)
Diffrence (95% CI)	-3.498 (-15.879, 8.883)	
SE_Difference	5.9700	
p-value	0.5639	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Work/Study/School Functioning

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	24 (48)	34 (74)
Lsmean (SE)	-1.63 (3.503)	-3.29 (2.909)
Lsmean_95 % CI	(-8.653, 5.392)	(-9.125, 2.540)
Diffrence (95% CI)	1.662 (-6.444, 9.768)	
SE_Difference	4.0431	
p-value	0.6827	
Week 48		
n (%)	22 (44)	26 (57)
Lsmean (SE)	4.01 (4.206)	0.32 (3.686)
Lsmean_95 % CI	(-4.464, 12.490)	(-7.106, 7.753)
Diffrence (95% CI)	3.690 (-6.102, 13.481)	
SE_Difference	4.8584	
p-value	0.4517	
Week 72		
n (%)	18 (36)	20 (43)
Lsmean (SE)	0.99 (4.197)	-3.04 (3.873)
Lsmean_95 % CI	(-7.536, 9.523)	(-10.907, 4.836)
Diffrence (95% CI)	4.029 (-6.379, 14.437)	
SE_Difference	5.1213	
p-value	0.4369	
Week 96		
n (%)	11 (22)	14 (30)
Lsmean (SE)	4.37 (5.429)	-2.51 (4.896)
Lsmean_95 % CI	(-6.923, 15.658)	(-12.693, 7.671)

	DMF (N= 50)	**IFN B-1a (N= 46)**
Diffrence (95% CI)	6.879 (-7.504, 21.262)	
SE_Difference	6.9161	
p-value	0.3312	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. Social Functioning

	DMF (N= 50)	IFN B-1a (N= 46)
Week 24		
n (%)	24 (48)	34 (74)
Lsmean (SE)	-1.78 (2.751)	-2.45 (2.280)
Lsmean_95 % CI	(-7.293, 3.738)	(-7.024, 2.120)
Diffrence (95% CI)	0.674 (-5.698, 7.046)	
SE_Difference	3.1782	
p-value	0.8327	
Week 48		
n (%)	22 (44)	26 (57)
Lsmean (SE)	1.23 (4.380)	-1.97 (3.816)
Lsmean_95 % CI	(-7.600, 10.053)	(-9.660, 5.722)
Diffrence (95% CI)	3.195 (-6.973, 13.364)	
SE_Difference	5.0456	
p-value	0.5298	
Week 72		
n (%)	18 (36)	20 (43)
Lsmean (SE)	1.24 (4.485)	-7.47 (4.146)
Lsmean_95 % CI	(-7.877, 10.353)	(-15.898, 0.953)
Diffrence (95% CI)	8.710 (-2.391, 19.812)	
SE_Difference	5.4626	
p-value	0.1201	
Week 96		
n (%)	11 (22)	15 (33)
Lsmean (SE)	-1.71 (5.588)	2.36 (4.951)
Lsmean_95 % CI	(-13.302, 9.876)	(-7.909, 12.625)

	DMF (N= 50)	**IFN B-1a (N= 46)**
Diffrence (95% CI)	-4.071 (-18.587, 10.445)	
SE_Difference	6.9993	
p-value	0.5667	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

109MS306_table46_48_CHG_LSMEANS_male

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Emotional Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	12 (57)	15 (83)
Lsmean (SE)	8.83 (4.547)	-0.29 (4.461)
Lsmean_95 % CI	(-0.581, 18.231)	(-9.520, 8.937)
Diffrence (95% CI)	9.116 (-3.282, 21.515)	
SE_Difference	5.9932	
p-value	0.1419	
Week 48		
n (%)	11 (52)	11 (61)
Lsmean (SE)	13.68 (5.855)	4.71 (5.877)
Lsmean_95 % CI	(1.373, 25.977)	(-7.642, 17.053)
Diffrence (95% CI)	8.970 (-7.432, 25.371)	
SE_Difference	7.8066	
p-value	0.2656	
Week 72		
n (%)	11 (52)	6 (33)
Lsmean (SE)	4.28 (6.329)	0.89 (8.719)
Lsmean_95 % CI	(-9.397, 17.951)	(-17.946, 19.727)
Diffrence (95% CI)	3.386 (-19.777, 26.549)	
SE_Difference	0.7216	
p-value	0.7572	
Week 96		
n (%)	7 (33)	4 (22)

	DMF (N= 21)	**IFN B-1a (N= 18)**
Lsmean (SE)	3.03 (4.868)	21.98 (6.502)
Lsmean_95 % CI	(-8.482, 14.541)	(6.608, 37.356)
Diffrence (95% CI)	-18.953 (-39.824, 1.919)	
SE_Difference	8.8266	
p-value	0.0689	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Physical Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	12 (57)	15 (83)
Lsmean (SE)	7.81 (2.803)	-3.33 (2.745)
Lsmean_95 % CI	(2.014, 13.609)	(-9.013, 2.346)
Diffrence (95% CI)	11.145 (3.502, 18.788)	
SE_Difference	3.6948	
p-value	0.0061	
Week 48		
n (%)	11 (52)	11 (61)
Lsmean (SE)	-3.34 (6.884)	-6.87 (6.915)
Lsmean_95 % CI	(-17.803, 11.121)	(-21.396, 7.658)
Diffrence (95% CI)	3.528 (-15.815, 22.870)	
SE_Difference	9.2065	
p-value	0.7061	
Week 72		
n (%)	11 (52)	6 (33)
Lsmean (SE)	-0.39 (3.590)	-4.38 (4.952)
Lsmean_95 % CI	(-8.146, 7.365)	(-15.083, 6.313)
Diffrence (95% CI)	3.994 (-9.150, 17.138)	
SE_Difference	6.0839	
p-value	0.5230	
Week 96		
n (%)	7 (33)	4 (22)
Lsmean (SE)	1.86 (2.810)	5.87 (3.508)

	DMF (N= 21)	**IFN B-1a (N= 18)**
Lsmean_95 % CI	(-4.782, 8.505)	(-2.427, 14.163)
Diffrence (95% CI)	-4.006 (-15.117, 7.104)	
SE_Difference	4.6986	
p-value	0.4220	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Work/Study/School Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	12 (57)	15 (83)
Lsmean (SE)	5.95 (4.714)	-2.85 (4.665)
Lsmean_95 % CI	(-3.804, 15.700)	(-12.504, 6.797)
Diffrence (95% CI)	8.801 (-4.220, 21.822)	
SE_Difference	6.2942	
p-value	0.1754	
Week 48		
n (%)	11 (52)	11 (61)
Lsmean (SE)	8.86 (5.791)	-2.22 (5.945)
Lsmean_95 % CI	(-3.309, 21.025)	(-14.709, 10.271)
Diffrence (95% CI)	11.077 (-5.660, 27.814)	
SE_Difference	7.9665	
p-value	0.1813	
Week 72		
n (%)	11 (52)	6 (33)
Lsmean (SE)	0.81 (7.270)	2.02 (10.12)
Lsmean_95 % CI	(-14.893, 16.519)	(-19.830, 23.880)
Diffrence (95% CI)	-1.212 (-28.083, 25.659)	
SE_Difference	2.4380	
p-value	0.9239	
Week 96		
n (%)	7 (33)	4 (22)
Lsmean (SE)	7.64 (6.949)	13.52 (8.727)

	DMF (N= 21)	**IFN B-1a (N= 18)**
Lsmean_95 % CI	(-8.790, 24.074)	(-7.118, 34.152)
Diffrence (95% CI)	-5.876 (-32.363, 20.612)	
SE_Difference	1.2017	
p-value	0.6161	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

Table 46.48:Summary of PedsQL Quality of Life Scale Scores, Parent's Assessment-mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. Social Functioning

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	12 (57)	15 (83)
Lsmean (SE)	3.31 (3.076)	6.08 (3.000)
Lsmean_95 % CI	(-3.049, 9.679)	(-0.124, 12.287)
Diffrence (95% CI)	-2.767 (-11.133, 5.600)	
SE_Difference	4.0444	
p-value	0.5008	
Week 48		
n (%)	11 (52)	11 (61)
Lsmean (SE)	0.055 (4.526)	4.83 (4.527)
Lsmean_95 % CI	(-9.455, 9.564)	(-4.680, 14.344)
Diffrence (95% CI)	-4.777 (-17.442, 7.887)	
SE_Difference	6.0281	
p-value	0.4384	
Week 72		
n (%)	11 (52)	6 (33)
Lsmean (SE)	4.18 (4.692)	2.39 (6.466)
Lsmean_95 % CI	(-5.955, 14.317)	(-11.576, 16.361)
Diffrence (95% CI)	1.789 (-15.349, 18.927)	
SE_Difference	7.9327	
p-value	0.8251	
Week 96		
n (%)	7 (33)	4 (22)

	DMF (N= 21)	**IFN B-1a (N= 18)**
Lsmean (SE)	-1.21 (10.32)	7.57 (13.39)
Lsmean_95 % CI	(-25.615, 23.191)	(-24.090, 39.233)
Diffrence (95% CI)	-8.783 (-51.294, 33.727)	
SE_Difference	7.9775	
p-value	0.6401	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T46_48/109MS306_table46_48_CHG_LSMEANS_SubGr.sas date: 09MAR2022

MCID_15percent

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135)

OR, RR, RD FOR HAVING A MCID OF 15% TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
PHYSICAL scale Week 24 >=15% decrease from baseline	Effect measure	0.326	0.369	-0.109
	95% CI	(0.083, 1.285)	(0.106, 1.282)	(-0.234, 0.015)
	p-value	0.1092	0.1165	0.0850
PHYSICAL scale Week 48 >=15% decrease from baseline	Effect measure	0.347	0.402	-0.126
	95% CI	(0.102, 1.176)	(0.137, 1.178)	(-0.263, 0.010)
	p-value	0.0893	0.0967	0.0699
PHYSICAL scale Week 72 >=15% decrease from baseline	Effect measure	1.645	1.549	0.053
	95% CI	(0.484, 5.587)	(0.527, 4.551)	(-0.077, 0.182)
	p-value	0.4249	0.4262	0.4245
PHYSICAL scale Week 96 >=15% decrease from baseline	Effect measure	1.705	1.660	0.025
	95% CI	(0.272, 10.674)	(0.290, 9.504)	(-0.062, 0.113)
	p-value	0.5688	0.5694	0.5689

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% decrease from baseline	Effect measure	0.506	0.590	-0.118
	95% CI	(0.192, 1.333)	(0.275, 1.264)	(-0.282, 0.045)
	p-value	0.1681	0.1748	0.1561
EMOTIONAL scale Week 48 >=15% decrease from baseline	Effect measure	0.397	0.461	-0.124
	95% CI	(0.128, 1.228)	(0.175, 1.211)	(-0.269, 0.020)
	p-value	0.1088	0.1161	0.0916
EMOTIONAL scale Week 72 >=15% decrease from baseline	Effect measure	0.913	0.922	-0.009
	95% CI	(0.259, 3.212)	(0.301, 2.824)	(-0.133, 0.115)
	p-value	0.8869	0.8869	0.8866
EMOTIONAL scale Week 96 >=15% decrease from baseline	Effect measure	0.523	0.553	-0.052
	95% CI	(0.123, 2.220)	(0.147, 2.089)	(-0.163, 0.060)
	p-value	0.3793	0.3824	0.3647

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
SOCIAL scale Week 24 >=15% decrease from baseline	Effect measure	0.941	0.948	-0.007
	95% CI	(0.292, 3.030)	(0.343, 2.621)	(-0.140, 0.126)
	p-value	0.9185	0.9185	0.9184
SOCIAL scale Week 48 >=15% decrease from baseline	Effect measure	0.765	0.790	-0.028
	95% CI	(0.225, 2.598)	(0.269, 2.322)	(-0.156, 0.100)
	p-value	0.6680	0.6686	0.6654
SOCIAL scale Week 72 >=15% decrease from baseline	Effect measure	0.104	0.123	-0.152
	95% CI	(0.013, 0.854)	(0.016, 0.934)	(-0.263, -0.041)
	p-value	0.0352	0.0428	0.0072
SOCIAL scale Week 96 >=15% decrease from baseline	Effect measure	0.818	0.830	-0.013
	95% CI	(0.173, 3.862)	(0.196, 3.516)	(-0.114, 0.088)
	p-value	0.7999	0.8001	0.7987

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
School scale Week 24 >=15% decrease from baseline	Effect measure	0.404	0.495	-0.156
	95% CI	(0.149, 1.095)	(0.223, 1.095)	(-0.318, 0.007)
	p-value	0.0747	0.0825	0.0612
School scale Week 48 >=15% decrease from baseline	Effect measure	0.400	0.452	-0.105
	95% CI	(0.116, 1.377)	(0.152, 1.344)	(-0.240, 0.029)
	p-value	0.1462	0.1534	0.1249
School scale Week 72 >=15% decrease from baseline	Effect measure	1.154	1.130	0.018
	95% CI	(0.372, 3.579)	(0.429, 2.981)	(-0.122, 0.157)
	p-value	0.8043	0.8043	0.8047
School scale Week 96 >=15% decrease from baseline	Effect measure	0.116	0.125	-0.077
	95% CI	(0.006, 2.213)	(0.007, 2.268)	(-0.170, 0.016)
	p-value	0.1521	0.1599	0.1267

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
PHYSICAL scale Week 24 >=15% increase from baseline	Effect measure	0.941	0.948	-0.007
	95% CI	(0.292, 3.030)	(0.343, 2.621)	(-0.140, 0.126)
	p-value	0.9185	0.9185	0.9184
PHYSICAL scale Week 48 >=15% increase from baseline	Effect measure	1.376	1.328	0.032
	95% CI	(0.391, 4.843)	(0.433, 4.066)	(-0.093, 0.156)
	p-value	0.6194	0.6197	0.6202
PHYSICAL scale Week 72 >=15% increase from baseline	Effect measure	0.533	0.553	-0.034
	95% CI	(0.093, 3.055)	(0.106, 2.883)	(-0.127, 0.058)
	p-value	0.4803	0.4821	0.4670
PHYSICAL scale Week 96 >=15% increase from baseline	Effect measure	0.261	0.277	-0.056
	95% CI	(0.028, 2.422)	(0.032, 2.388)	(-0.139, 0.028)
	p-value	0.2372	0.2426	0.1907

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% increase from baseline	Effect measure	0.765	0.805	-0.041
	95% CI	(0.278, 2.101)	(0.354, 1.828)	(-0.196, 0.113)
	p-value	0.6027	0.6038	0.6001
EMOTIONAL scale Week 48 >=15% increase from baseline	Effect measure	3.594	2.877	0.180
	95% CI	(1.171, 11.036)	(1.109, 7.460)	(0.030, 0.331)
	p-value	0.0254	0.0298	0.0191
EMOTIONAL scale Week 72 >=15% increase from baseline	Effect measure	3.243	2.766	0.136
	95% CI	(0.942, 11.166)	(0.930, 8.230)	(-0.002, 0.273)
	p-value	0.0621	0.0674	0.0530
EMOTIONAL scale Week 96 >=15% increase from baseline	Effect measure	0.341	0.369	-0.073
	95% CI	(0.065, 1.778)	(0.078, 1.739)	(-0.177, 0.031)
	p-value	0.2015	0.2075	0.1710

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
SOCIAL scale Week 24 >=15% increase from baseline	Effect measure	1.125	1.106	0.014
	95% CI	(0.363, 3.486)	(0.419, 2.920)	(-0.123, 0.152)
	p-value	0.8383	0.8382	0.8385
SOCIAL scale Week 48 >=15% increase from baseline	Effect measure	1.645	1.549	0.053
	95% CI	(0.484, 5.587)	(0.527, 4.551)	(-0.077, 0.182)
	p-value	0.4249	0.4262	0.4245
SOCIAL scale Week 72 >=15% increase from baseline	Effect measure	3.659	3.319	0.089
	95% CI	(0.701, 19.102)	(0.704, 15.653)	(-0.020, 0.198)
	p-value	0.1240	0.1295	0.1080
SOCIAL scale Week 96 >=15% increase from baseline	Effect measure	1.114	1.106	0.006
	95% CI	(0.214, 5.806)	(0.235, 5.218)	(-0.088, 0.100)
	p-value	0.8983	0.8983	0.8985

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	Result	OR	RR	ARR
School scale Week 24 >=15% increase from baseline	Effect measure	1.376	1.319	0.037
	95% CI	(0.427, 4.438)	(0.478, 3.642)	(-0.099, 0.172)
	p-value	0.5931	0.5933	0.5942
School scale Week 48 >=15% increase from baseline	Effect measure	1.528	1.413	0.064
	95% CI	(0.546, 4.274)	(0.610, 3.276)	(-0.091, 0.218)
	p-value	0.4194	0.4203	0.4197
School scale Week 72 >=15% increase from baseline	Effect measure	4.537	3.768	0.160
	95% CI	(1.164, 17.678)	(1.104, 12.862)	(0.025, 0.295)
	p-value	0.0293	0.0342	0.0204
School scale Week 96 >=15% increase from baseline	Effect measure	0.612	0.646	-0.048
	95% CI	(0.167, 2.243)	(0.202, 2.066)	(-0.171, 0.076)
	p-value	0.4589	0.4613	0.4492

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR EVENTS AT EACH TIMEPOINT BY STUDY ARM. ANALYSIS NOT USING SUBGROUPS

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
PHYSICAL scale Week 24 >=15% decrease from baseline				
	Yes	3 (4)	9 (14)	12 (9)
	No	44 (62)	43 (67)	87 (64)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 48 >=15% decrease from baseline				
	Yes	4 (6)	11 (17)	15 (11)
	No	43 (61)	41 (64)	84 (62)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 72 >=15% decrease from baseline				
	Yes	7 (10)	5 (8)	12 (9)
	No	40 (56)	47 (73)	87 (64)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 96 >=15% decrease from baseline				
	Yes	3 (4)	2 (3)	5 (4)
	No	44 (62)	50 (78)	94 (70)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
EMOTIONAL scale Week 24 >=15% decrease from baseline				
	Yes	8 (11)	15 (23)	23 (17)
	No	39 (55)	37 (58)	76 (56)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 48 >=15% decrease from baseline				
	Yes	5 (7)	12 (19)	17 (13)
	No	42 (59)	40 (63)	82 (61)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 72 >=15% decrease from baseline				
	Yes	5 (7)	6 (9)	11 (8)
	No	42 (59)	46 (72)	88 (65)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 96 >=15% decrease from baseline				
	Yes	3 (4)	6 (9)	9 (7)
	No	44 (62)	46 (72)	90 (67)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SOCIAL scale Week 24 >=15% decrease from baseline				
	Yes	6 (8)	7 (11)	13 (10)
	No	41 (58)	45 (70)	86 (64)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 48 >=15% decrease from baseline				
	Yes	5 (7)	7 (11)	12 (9)
	No	42 (59)	45 (70)	87 (64)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 72 >=15% decrease from baseline				
	Yes	1 (1)	9 (14)	10 (7)
	No	46 (65)	43 (67)	89 (66)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 96 >=15% decrease from baseline				
	Yes	3 (4)	4 (6)	7 (5)
	No	44 (62)	48 (75)	92 (68)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 24 >=15% decrease from baseline				
	Yes	7 (10)	16 (25)	23 (17)
	No	39 (55)	36 (56)	75 (56)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 48 >=15% decrease from baseline				
	Yes	4 (6)	10 (16)	14 (10)
	No	42 (59)	42 (66)	84 (62)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 72 >=15% decrease from baseline				
	Yes	7 (10)	7 (11)	14 (10)
	No	39 (55)	45 (70)	84 (62)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 96 >=15% decrease from baseline				
	Yes	0 (0)	4 (6)	4 (3)
	No	46 (65)	48 (75)	94 (70)
	Missing	25 (35)	12 (19)	37 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
PHYSICAL scale Week 24 >=15% increase from baseline				
	Yes	6 (8)	7 (11)	13 (10)
	No	41 (58)	45 (70)	86 (64)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 48 >=15% increase from baseline				
	Yes	6 (8)	5 (8)	11 (8)
	No	41 (58)	47 (73)	88 (65)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 72 >=15% increase from baseline				
	Yes	2 (3)	4 (6)	6 (4)
	No	45 (63)	48 (75)	93 (69)
	Missing	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 96 >=15% increase from baseline				
	Yes	1 (1)	4 (6)	5 (4)
	No	46 (65)	48 (75)	94 (70)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
EMOTIONAL scale Week 24 >=15% increase from baseline				
	Yes	8 (11)	11 (17)	19 (14)
	No	39 (55)	41 (64)	80 (59)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 48 >=15% increase from baseline				
	Yes	13 (18)	5 (8)	18 (13)
	No	34 (48)	47 (73)	81 (60)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 72 >=15% increase from baseline				
	Yes	10 (14)	4 (6)	14 (10)
	No	37 (52)	48 (75)	85 (63)
	Missing	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 96 >=15% increase from baseline				
	Yes	2 (3)	6 (9)	8 (6)
	No	45 (63)	46 (72)	91 (67)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SOCIAL scale Week 24 >=15% increase from baseline				
	Yes	7 (10)	7 (11)	14 (10)
	No	40 (56)	45 (70)	85 (63)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 48 >=15% increase from baseline				
	Yes	7 (10)	5 (8)	12 (9)
	No	40 (56)	47 (73)	87 (64)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 72 >=15% increase from baseline				
	Yes	6 (8)	2 (3)	8 (6)
	No	41 (58)	50 (78)	91 (67)
	Missing	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 96 >=15% increase from baseline				
	Yes	3 (4)	3 (5)	6 (4)
	No	44 (62)	49 (77)	93 (69)
	Missing	24 (34)	12 (19)	36 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

	EVENT	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 24 >=15% increase from baseline				
	Yes	7 (10)	6 (9)	13 (10)
	No	39 (55)	46 (72)	85 (63)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 48 >=15% increase from baseline				
	Yes	10 (14)	8 (13)	18 (13)
	No	36 (51)	44 (69)	80 (59)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 72 >=15% increase from baseline				
	Yes	10 (14)	3 (5)	13 (10)
	No	36 (51)	49 (77)	85 (63)
	Missing	25 (35)	12 (19)	37 (27)
School scale Week 96 >=15% increase from baseline				
	Yes	4 (6)	7 (11)	11 (8)
	No	42 (59)	45 (70)	87 (64)
	Missing	25 (35)	12 (19)	37 (27)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_ban020622.sas date: 06FEB2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent>s Assessment - mITT Population (n=135)

N(%) FOR HAVING NON-MISSING RESPONSES AT BASELINE AND EACH TIMEPOINT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
PHYSICAL scale Week 0				
	Yes	47 (66)	52 (81)	99 (73)
	No	24 (34)	12 (19)	36 (27)
PHYSICAL scale Week 24				
	Yes	56 (79)	58 (91)	114 (84)
	No	15 (21)	6 (9)	21 (16)
PHYSICAL scale Week 48				
	Yes	52 (73)	43 (67)	95 (70)
	No	19 (27)	21 (33)	40 (30)
PHYSICAL scale Week 72				
	Yes	46 (65)	29 (45)	75 (56)
	No	25 (35)	35 (55)	60 (44)
PHYSICAL scale Week 96				
	Yes	29 (41)	22 (34)	51 (38)
	No	42 (59)	42 (66)	84 (62)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15PCT_Newmethod_ALL_MEASURES_3Pvalues_ban020622.sas date: 06FEB2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
EMOTIONAL scale Week 0				
	Yes	47 (66)	52 (81)	99 (73)
	No	24 (34)	12 (19)	36 (27)
EMOTIONAL scale Week 24				
	Yes	55 (77)	58 (91)	113 (84)
	No	16 (23)	6 (9)	22 (16)
EMOTIONAL scale Week 48				
	Yes	52 (73)	43 (67)	95 (70)
	No	19 (27)	21 (33)	40 (30)
EMOTIONAL scale Week 72				
	Yes	46 (65)	29 (45)	75 (56)
	No	25 (35)	35 (55)	60 (44)
EMOTIONAL scale Week 96				
	Yes	29 (41)	22 (34)	51 (38)
	No	42 (59)	42 (66)	84 (62)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15PCT_Newmethod_ALL_MEASURES_3Pvalues_ban020622.sas date: 06FEB2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
SOCIAL scale Week 0				
	Yes	47 (66)	52 (81)	99 (73)
	No	24 (34)	12 (19)	36 (27)
SOCIAL scale Week 24				
	Yes	56 (79)	58 (91)	114 (84)
	No	15 (21)	6 (9)	21 (16)
SOCIAL scale Week 48				
	Yes	52 (73)	43 (67)	95 (70)
	No	19 (27)	21 (33)	40 (30)
SOCIAL scale Week 72				
	Yes	46 (65)	29 (45)	75 (56)
	No	25 (35)	35 (55)	60 (44)
SOCIAL scale Week 96				
	Yes	29 (41)	22 (34)	51 (38)
	No	42 (59)	42 (66)	84 (62)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15PCT_Newmethod_ALL_MEASURES_3Pvalues_ban020622.sas date: 06FEB2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 0				
	Yes	46 (65)	52 (81)	98 (73)
	No	25 (35)	12 (19)	37 (27)
School scale Week 24				
	Yes	56 (79)	56 (88)	112 (83)
	No	15 (21)	8 (13)	23 (17)
School scale Week 48				
	Yes	51 (72)	43 (67)	94 (70)
	No	20 (28)	21 (33)	41 (30)
School scale Week 72				
	Yes	46 (65)	29 (45)	75 (56)
	No	25 (35)	35 (55)	60 (44)
School scale Week 96				
	Yes	29 (41)	22 (34)	51 (38)
	No	42 (59)	42 (66)	84 (62)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table46_48_MCID15PCT_Newmethod_ALL_MEASURES_3Pvalues_ban020622.sas date: 06FEB2022

Sub groups

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_age13to14

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD FOR HAVING A MCID OF 15% TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% decrease from baseline	Effect measure	0.133	0.220	-0.355
	95% CI	(0.012, 1.444)	(0.031, 1.576)	(-0.703, -0.006)
	p-value	0.0974	0.1317	0.0459
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	1.143	1.100	0.027
	95% CI	(0.172, 7.601)	(0.285, 4.251)	(-0.360, 0.414)
	p-value	0.8901	0.8901	0.8902
EMOTIONAL scale Week 24 >=15% increase from baseline	Effect measure	0.333	0.365	-0.091
	95% CI	(0.012, 9.155)	(0.017, 8.018)	(-0.356, 0.174)
	p-value	0.5157	0.5226	0.9582
EMOTIONAL scale Week 48 >=15% increase from baseline	Effect measure	0.296	0.367	-0.173
	95% CI	(0.025, 3.452)	(0.045, 2.979)	(-0.495, 0.150)
	p-value	0.3316	0.3479	0.2935

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_age15to17

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD FOR HAVING A MCID OF 15% TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% decrease from baseline	Effect measure	0.723	0.776	-0.055
	95% CI	(0.244, 2.148)	(0.329, 1.829)	(-0.237, 0.128)
	p-value	0.5598	0.5615	0.5562
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	0.269	0.350	-0.206
	95% CI	(0.079, 0.921)	(0.125, 0.979)	(-0.382, -0.030)
	p-value	0.0365	0.0454	0.0215
EMOTIONAL scale Week 24 >=15% increase from baseline	Effect measure	0.855	0.886	-0.028
	95% CI	(0.297, 2.465)	(0.392, 2.006)	(-0.214, 0.159)
	p-value	0.7721	0.7724	0.7714
EMOTIONAL scale Week 48 >=15% increase from baseline	Effect measure	9.360	6.649	0.276
	95% CI	(1.930, 45.394)	(1.592, 27.767)	(0.111, 0.440)
	p-value	0.0055	0.0094	0.0010

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a

NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_female

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD FOR HAVING A MCID OF 15% TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% decrease from baseline	Effect measure	0.636	0.716	-0.087
	95% CI	(0.212, 1.908)	(0.316, 1.624)	(-0.295, 0.121)
	p-value	0.4197	0.4240	0.4128
EMOTIONAL scale Week 48 >=15% decrease from baseline	Effect measure	0.269	0.338	-0.184
	95% CI	(0.067, 1.085)	(0.102, 1.120)	(-0.362, -0.006)
	p-value	0.0650	0.0758	0.0425
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	0.545	0.633	-0.112
	95% CI	(0.175, 1.703)	(0.265, 1.514)	(-0.317, 0.093)
	p-value	0.2968	0.3043	0.2840

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA. Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_EFFECTMEASURES_male

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). OR, RR, RD FOR HAVING A MCID OF 15% TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
EMOTIONAL scale Week 24 >=15% decrease from baseline	Effect measure	0.214	0.267	-0.183
	95% CI	(0.021, 2.187)	(0.033, 2.124)	(-0.430, 0.064)
	p-value	0.1937	0.2119	0.1455
EMOTIONAL scale Week 48 >=15% decrease from baseline	Effect measure	1.077	1.067	0.008
	95% CI	(0.132, 8.797)	(0.171, 6.643)	(-0.228, 0.245)
	p-value	0.9449	0.9449	0.9449
SCHOOL scale Week 24 >=15% decrease from baseline	Effect measure	0.157	0.213	-0.246
	95% CI	(0.016, 1.548)	(0.028, 1.621)	(-0.506, 0.014)
	p-value	0.1128	0.1355	0.0637

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE5: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA. Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_age13to14

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	EVENT	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
EMOTIONAL scale Week 24 >=15% decrease from baseline				
	Yes	1 (6)	5 (36)	6 (19)
	No	9 (50)	6 (43)	15 (47)
	Missing	8 (44)	3 (21)	11 (34)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	3 (17)	3 (21)	6 (19)
	No	7 (39)	8 (57)	15 (47)
	Missing	8 (44)	3 (21)	11 (34)
EMOTIONAL scale Week 24 >=15% increase from baseline				
	Yes	0 (0)	1 (7)	1 (3)
	No	10 (56)	10 (71)	20 (63)
	Missing	8 (44)	3 (21)	11 (34)
EMOTIONAL scale Week 48 >=15% increase from baseline				
	Yes	1 (6)	3 (21)	4 (13)
	No	9 (50)	8 (57)	17 (53)
	Missing	8 (44)	3 (21)	11 (34)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores. Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_ MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_age15to17

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	EVENT	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
EMOTIONAL scale Week 24 >=15% decrease from baseline				
	Yes	7 (13)	10 (20)	17 (17)
	No	30 (57)	31 (62)	61 (59)
	Missing	16 (30)	9 (18)	25 (24)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	4 (8)	13 (26)	17 (17)
	No	32 (60)	28 (56)	60 (58)
	Missing	17 (32)	9 (18)	26 (25)
EMOTIONAL scale Week 24 >=15% increase from baseline				
	Yes	8 (15)	10 (20)	18 (17)
	No	29 (55)	31 (62)	60 (58)
	Missing	16 (30)	9 (18)	25 (24)
EMOTIONAL scale Week 48 >=15% increase from baseline				
	Yes	12 (23)	2 (4)	14 (14)
	No	25 (47)	39 (78)	64 (62)
	Missing	16 (30)	9 (18)	25 (24)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_female

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	EVENT	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
EMOTIONAL scale Week 24 >=15% decrease from baseline				
	Yes	7 (14)	11 (24)	18 (19)
	No	25 (50)	25 (54)	50 (52)
	Missing	18 (36)	10 (22)	28 (29)
EMOTIONAL scale Week 48 >=15% decrease from baseline				
	Yes	3 (6)	10 (22)	13 (14)
	No	29 (58)	26 (57)	55 (57)
	Missing	18 (36)	10 (22)	28 (29)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	6 (12)	11 (24)	17 (18)
	No	25 (50)	25 (54)	50 (52)
	Missing	19 (38)	10 (22)	29 (30)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_EVENT_male

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	EVENT	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
EMOTIONAL scale Week 24 >=15% decrease from baseline				
	Yes	1 (5)	4 (22)	5 (13)
	No	14 (67)	12 (67)	26 (67)
	Missing	6 (29)	2 (11)	8 (21)
EMOTIONAL scale Week 48 >=15% decrease from baseline				
	Yes	2 (10)	2 (11)	4 (10)
	No	13 (62)	14 (78)	27 (69)
	Missing	6 (29)	2 (11)	8 (21)
SCHOOL scale Week 24 >=15% decrease from baseline				
	Yes	1 (5)	5 (28)	6 (15)
	No	14 (67)	11 (61)	25 (64)
	Missing	6 (29)	2 (11)	8 (21)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups032722.sas date: 27MAR2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_Age13_14

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT BASELINE AND EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Age13_14

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
PHYSICAL scale Week 0				
	Yes	10 (56)	11 (79)	21 (66)
	No	8 (44)	3 (21)	11 (34)
PHYSICAL scale Week 24				
	Yes	16 (89)	13 (93)	29 (91)
	No	2 (11)	1 (7)	3 (9)
PHYSICAL scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
PHYSICAL scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
PHYSICAL scale Week 96				
	Yes	14 (78)	7 (50)	21 (66)
	No	4 (22)	7 (50)	11 (34)

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
EMOTIONAL scale Week 0				
	Yes	10 (56)	11 (79)	21 (66)
	No	8 (44)	3 (21)	11 (34)
EMOTIONAL scale Week 24				
	Yes	15 (83)	13 (93)	28 (88)
	No	3 (17)	1 (7)	4 (13)
EMOTIONAL scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
EMOTIONAL scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
EMOTIONAL scale Week 96				
	Yes	14 (78)	7 (50)	21 (66)
	No	4 (22)	7 (50)	11 (34)

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
SOCIAL scale Week 0				
	Yes	10 (56)	11 (79)	21 (66)
	No	8 (44)	3 (21)	11 (34)
SOCIAL scale Week 24				
	Yes	16 (89)	13 (93)	29 (91)
	No	2 (11)	1 (7)	3 (9)
SOCIAL scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
SOCIAL scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
SOCIAL scale Week 96				
	Yes	14 (78)	7 (50)	21 (66)
	No	4 (22)	7 (50)	11 (34)

	Response (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
School scale Week 0				
	Yes	10 (56)	11 (79)	21 (66)
	No	8 (44)	3 (21)	11 (34)
School scale Week 24				
	Yes	16 (89)	12 (86)	28 (88)
	No	2 (11)	2 (14)	4 (13)
School scale Week 48				
	Yes	12 (67)	10 (71)	22 (69)
	No	6 (33)	4 (29)	10 (31)
School scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
School scale Week 96				
	Yes	14 (78)	7 (50)	21 (66)
	No	4 (22)	7 (50)	11 (34)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups020622.sas date: 07FEB2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_Age15_17

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT BASELINE AND EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Age15_17

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
PHYSICAL scale Week 0				
	Yes	37 (70)	41 (82)	78 (76)
	No	16 (30)	9 (18)	25 (24)
PHYSICAL scale Week 24				
	Yes	40 (75)	45 (90)	85 (83)
	No	13 (25)	5 (10)	18 (17)
PHYSICAL scale Week 48				
	Yes	39 (74)	33 (66)	72 (70)
	No	14 (26)	17 (34)	31 (30)
PHYSICAL scale Week 72				
	Yes	31 (58)	21 (42)	52 (50)
	No	22 (42)	29 (58)	51 (50)
PHYSICAL scale Week 96				
	Yes	15 (28)	15 (30)	30 (29)
	No	38 (72)	35 (70)	73 (71)

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
EMOTIONAL scale Week 0				
	Yes	37 (70)	41 (82)	78 (76)
	No	16 (30)	9 (18)	25 (24)
EMOTIONAL scale Week 24				
	Yes	40 (75)	45 (90)	85 (83)
	No	13 (25)	5 (10)	18 (17)
EMOTIONAL scale Week 48				
	Yes	39 (74)	33 (66)	72 (70)
	No	14 (26)	17 (34)	31 (30)
EMOTIONAL scale Week 72				
	Yes	31 (58)	21 (42)	52 (50)
	No	22 (42)	29 (58)	51 (50)
EMOTIONAL scale Week 96				
	Yes	15 (28)	15 (30)	30 (29)
	No	38 (72)	35 (70)	73 (71)

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
SOCIAL scale Week 0				
	Yes	37 (70)	41 (82)	78 (76)
	No	16 (30)	9 (18)	25 (24)
SOCIAL scale Week 24				
	Yes	40 (75)	45 (90)	85 (83)
	No	13 (25)	5 (10)	18 (17)
SOCIAL scale Week 48				
	Yes	39 (74)	33 (66)	72 (70)
	No	14 (26)	17 (34)	31 (30)
SOCIAL scale Week 72				
	Yes	31 (58)	21 (42)	52 (50)
	No	22 (42)	29 (58)	51 (50)
SOCIAL scale Week 96				
	Yes	15 (28)	15 (30)	30 (29)
	No	38 (72)	35 (70)	73 (71)

	Response (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
School scale Week 0				
	Yes	36 (68)	41 (82)	77 (75)
	No	17 (32)	9 (18)	26 (25)
School scale Week 24				
	Yes	40 (75)	44 (88)	84 (82)
	No	13 (25)	6 (12)	19 (18)
School scale Week 48				
	Yes	39 (74)	33 (66)	72 (70)
	No	14 (26)	17 (34)	31 (30)
School scale Week 72				
	Yes	31 (58)	21 (42)	52 (50)
	No	22 (42)	29 (58)	51 (50)
School scale Week 96				
	Yes	15 (28)	15 (30)	30 (29)
	No	38 (72)	35 (70)	73 (71)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups020622.sas date: 07FEB2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_Female

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT BASELINE AND EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
PHYSICAL scale Week 0				
	Yes	32 (64)	36 (78)	68 (71)
	No	18 (36)	10 (22)	28 (29)
PHYSICAL scale Week 24				
	Yes	39 (78)	42 (91)	81 (84)
	No	11 (22)	4 (9)	15 (16)
PHYSICAL scale Week 48				
	Yes	36 (72)	32 (70)	68 (71)
	No	14 (28)	14 (30)	28 (29)
PHYSICAL scale Week 72				
	Yes	31 (62)	22 (48)	53 (55)
	No	19 (38)	24 (52)	43 (45)
PHYSICAL scale Week 96				
	Yes	19 (38)	17 (37)	36 (38)
	No	31 (62)	29 (63)	60 (63)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
EMOTIONAL scale Week 0				
	Yes	32 (64)	36 (78)	68 (71)
	No	18 (36)	10 (22)	28 (29)
EMOTIONAL scale Week 24				
	Yes	39 (78)	42 (91)	81 (84)
	No	11 (22)	4 (9)	15 (16)
EMOTIONAL scale Week 48				
	Yes	36 (72)	32 (70)	68 (71)
	No	14 (28)	14 (30)	28 (29)
EMOTIONAL scale Week 72				
	Yes	31 (62)	22 (48)	53 (55)
	No	19 (38)	24 (52)	43 (45)
EMOTIONAL scale Week 96				
	Yes	19 (38)	17 (37)	36 (38)
	No	31 (62)	29 (63)	60 (63)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
SOCIAL scale Week 0				
	Yes	32 (64)	36 (78)	68 (71)
	No	18 (36)	10 (22)	28 (29)
SOCIAL scale Week 24				
	Yes	39 (78)	42 (91)	81 (84)
	No	11 (22)	4 (9)	15 (16)
SOCIAL scale Week 48				
	Yes	36 (72)	32 (70)	68 (71)
	No	14 (28)	14 (30)	28 (29)
SOCIAL scale Week 72				
	Yes	31 (62)	22 (48)	53 (55)
	No	19 (38)	24 (52)	43 (45)
SOCIAL scale Week 96				
	Yes	19 (38)	17 (37)	36 (38)
	No	31 (62)	29 (63)	60 (63)

	Response (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
School scale Week 0				
	Yes	31 (62)	36 (78)	67 (70)
	No	19 (38)	10 (22)	29 (30)
School scale Week 24				
	Yes	39 (78)	41 (89)	80 (83)
	No	11 (22)	5 (11)	16 (17)
School scale Week 48				
	Yes	36 (72)	32 (70)	68 (71)
	No	14 (28)	14 (30)	28 (29)
School scale Week 72				
	Yes	31 (62)	22 (48)	53 (55)
	No	19 (38)	24 (52)	43 (45)
School scale Week 96				
	Yes	19 (38)	17 (37)	36 (38)
	No	31 (62)	29 (63)	60 (63)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups020622.sas date: 07FEB2022

109MS306_Table46_48_MCID_15PCT_NPERCENT_RESPONSE_Male

Tables 46/48: Summary of PedsQL Quality of Life Scale Scores, Parent Assessment - mITT Population (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT BASELINE AND EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
PHYSICAL scale Week 0				
	Yes	15 (71)	16 (89)	31 (79)
	No	6 (29)	2 (11)	8 (21)
PHYSICAL scale Week 24				
	Yes	17 (81)	16 (89)	33 (85)
	No	4 (19)	2 (11)	6 (15)
PHYSICAL scale Week 48				
	Yes	16 (76)	11 (61)	27 (69)
	No	5 (24)	7 (39)	12 (31)
PHYSICAL scale Week 72				
	Yes	15 (71)	7 (39)	22 (56)
	No	6 (29)	11 (61)	17 (44)
PHYSICAL scale Week 96				
	Yes	10 (48)	5 (28)	15 (38)
	No	11 (52)	13 (72)	24 (62)

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
EMOTIONAL scale Week 0				
	Yes	15 (71)	16 (89)	31 (79)
	No	6 (29)	2 (11)	8 (21)
EMOTIONAL scale Week 24				
	Yes	16 (76)	16 (89)	32 (82)
	No	5 (24)	2 (11)	7 (18)
EMOTIONAL scale Week 48				
	Yes	16 (76)	11 (61)	27 (69)
	No	5 (24)	7 (39)	12 (31)
EMOTIONAL scale Week 72				
	Yes	15 (71)	7 (39)	22 (56)
	No	6 (29)	11 (61)	17 (44)
EMOTIONAL scale Week 96				
	Yes	10 (48)	5 (28)	15 (38)
	No	11 (52)	13 (72)	24 (62)

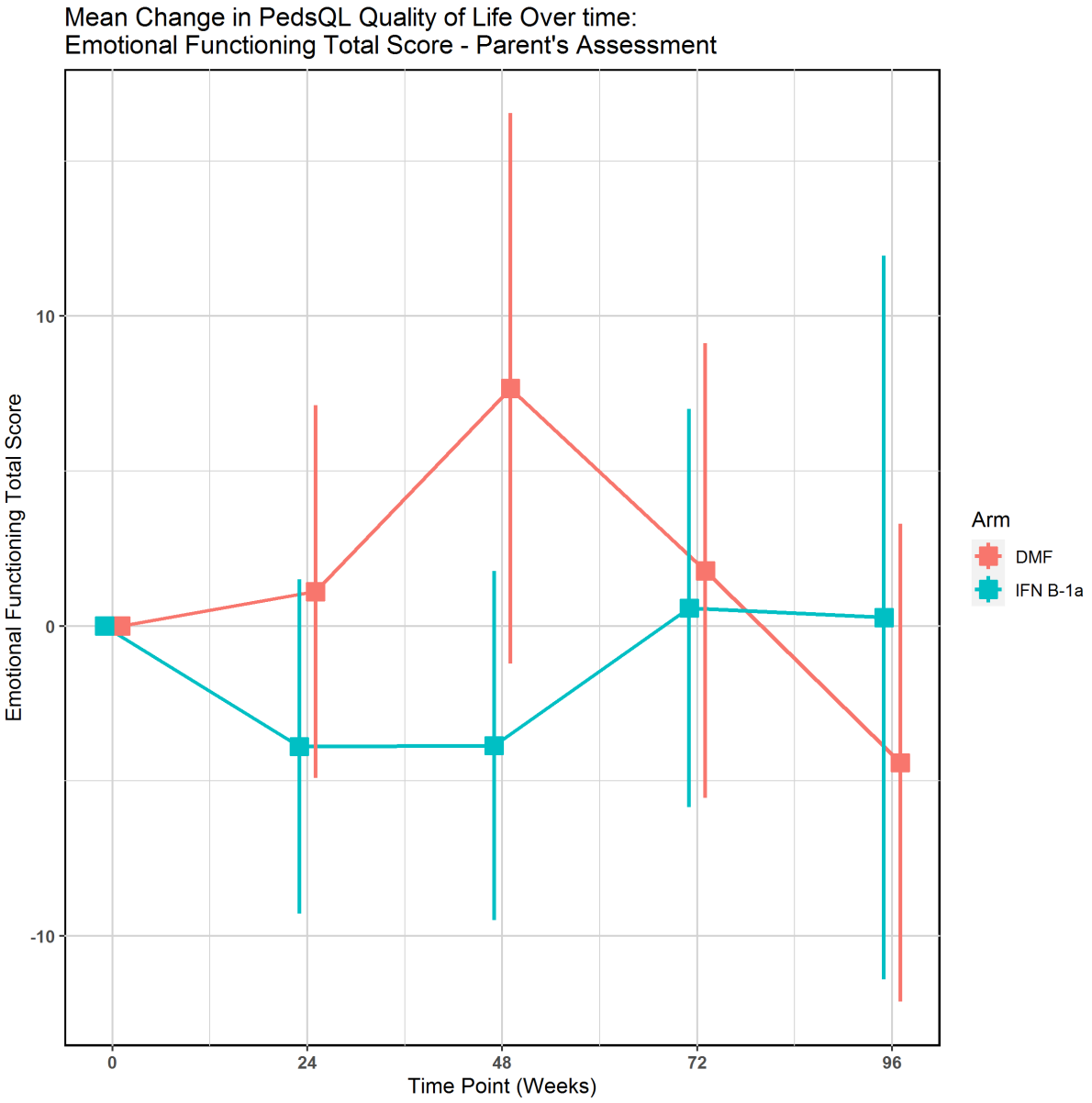
	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
SOCIAL scale Week 0				
	Yes	15 (71)	16 (89)	31 (79)
	No	6 (29)	2 (11)	8 (21)
SOCIAL scale Week 24				
	Yes	17 (81)	16 (89)	33 (85)
	No	4 (19)	2 (11)	6 (15)
SOCIAL scale Week 48				
	Yes	16 (76)	11 (61)	27 (69)
	No	5 (24)	7 (39)	12 (31)
SOCIAL scale Week 72				
	Yes	15 (71)	7 (39)	22 (56)
	No	6 (29)	11 (61)	17 (44)
SOCIAL scale Week 96				
	Yes	10 (48)	5 (28)	15 (38)
	No	11 (52)	13 (72)	24 (62)

	Response (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
School scale Week 0				
	Yes	15 (71)	16 (89)	31 (79)
	No	6 (29)	2 (11)	8 (21)
School scale Week 24				
	Yes	17 (81)	15 (83)	32 (82)
	No	4 (19)	3 (17)	7 (18)
School scale Week 48				
	Yes	15 (71)	11 (61)	26 (67)
	No	6 (29)	7 (39)	13 (33)
School scale Week 72				
	Yes	15 (71)	7 (39)	22 (56)
	No	6 (29)	11 (61)	17 (44)
School scale Week 96				
	Yes	10 (48)	5 (28)	15 (38)
	No	11 (52)	13 (72)	24 (62)

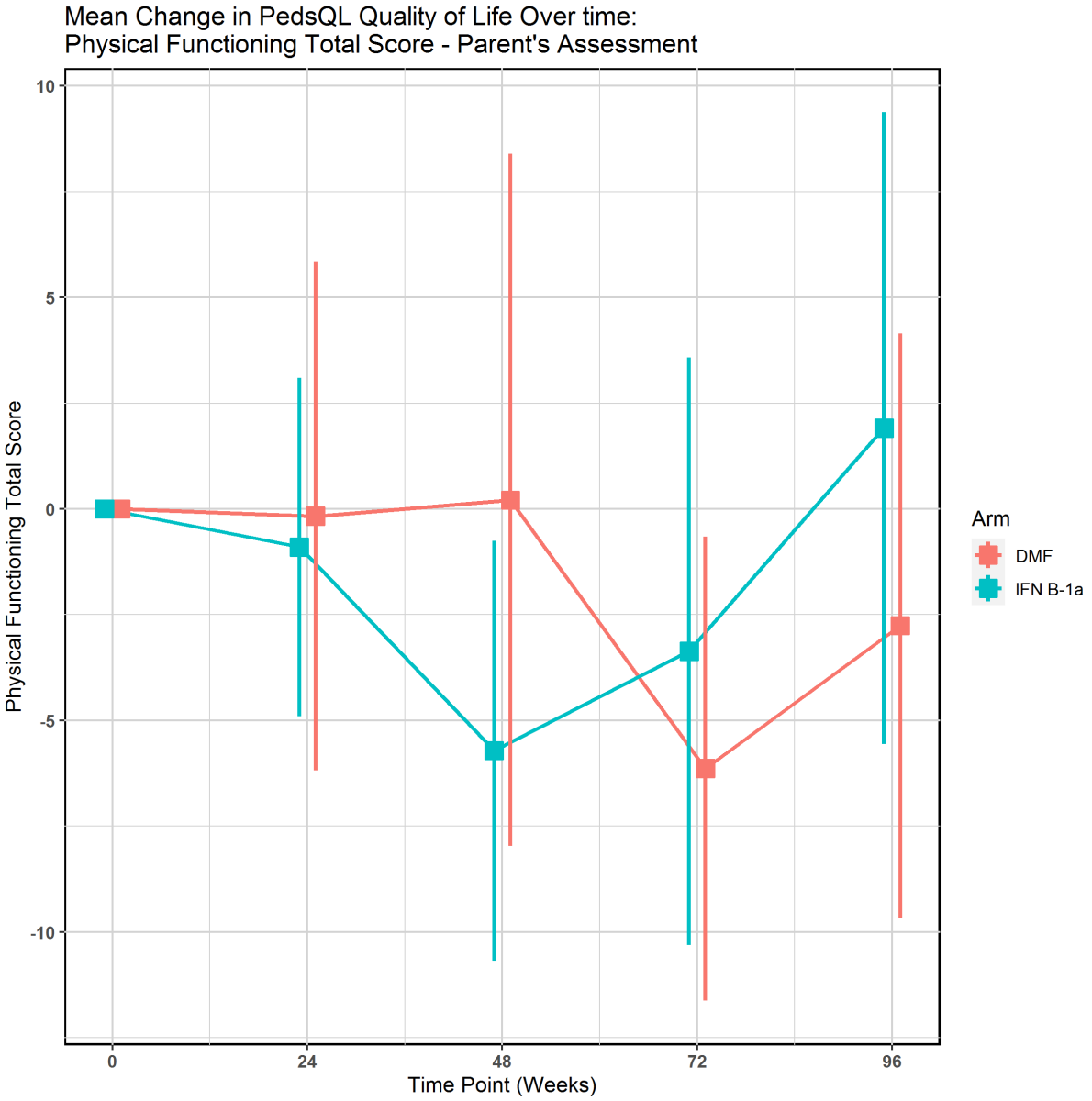
NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/table46_48_MCID15pct_NewMethod_ALL_MEASURES_3pvalues_subgroups020622.sas date: 07FEB2022

Graphics

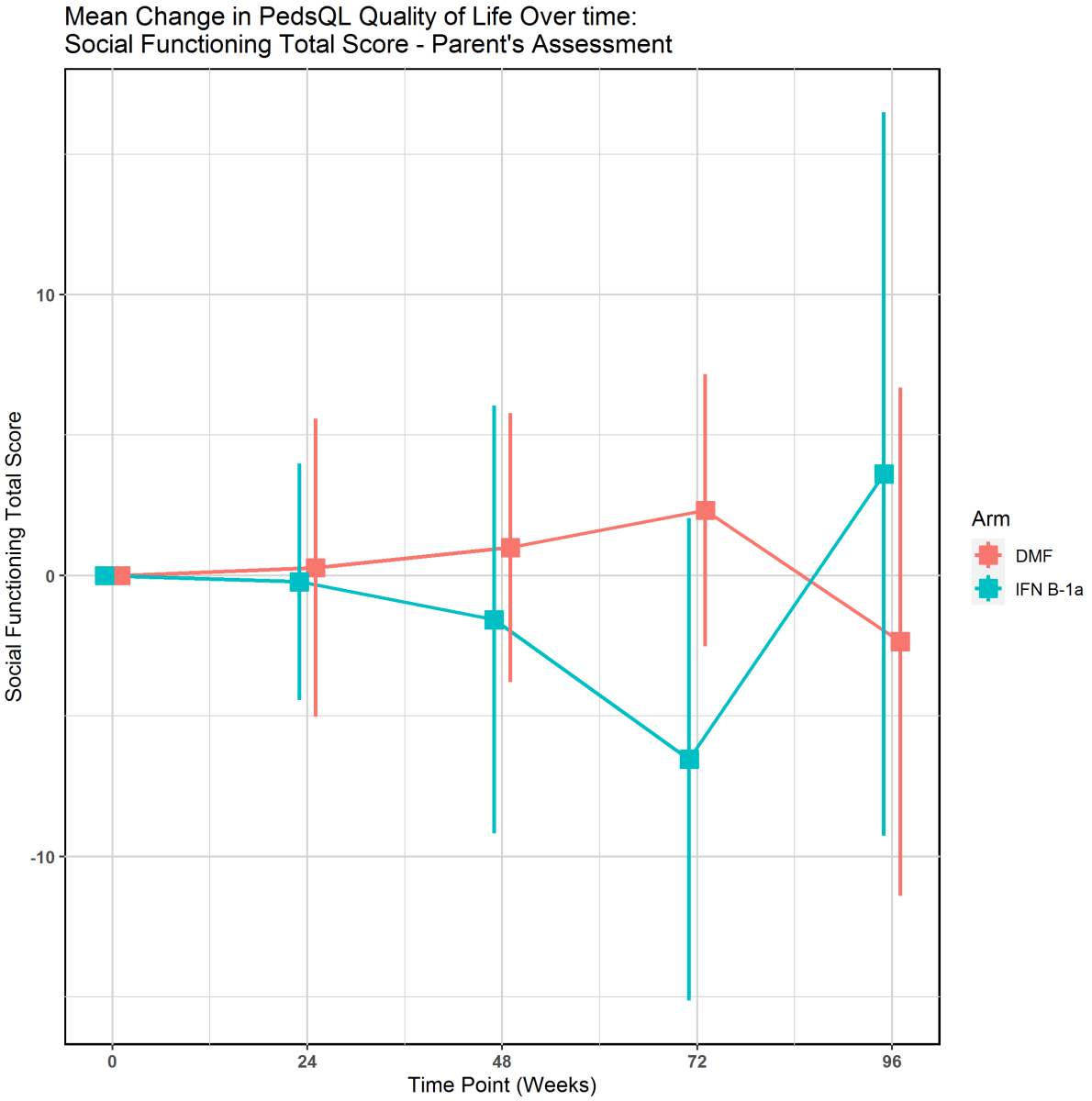
Change from baselineEmotional Functioning Total Score Parent's Assessment



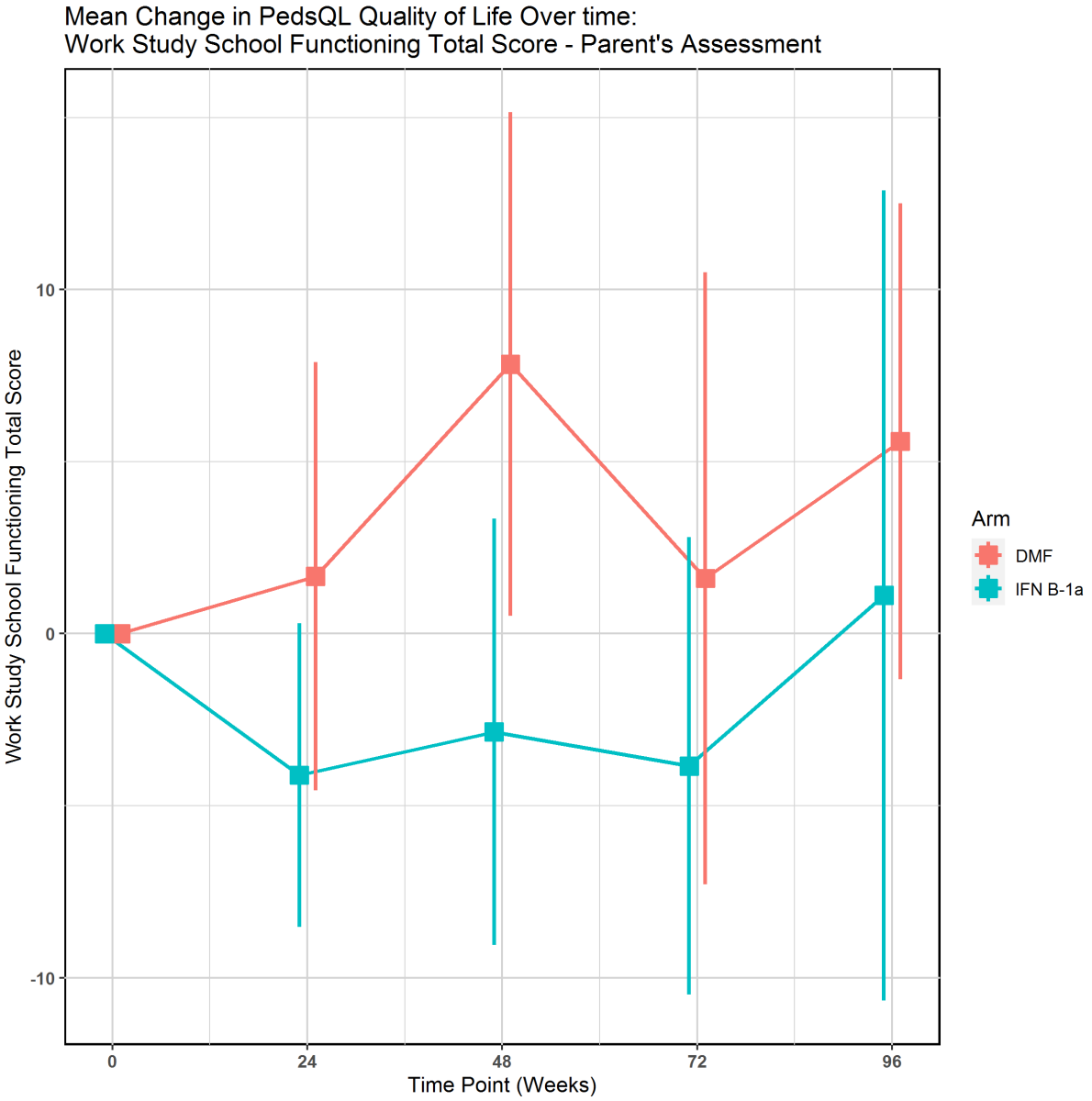
Change from baselinePhysical Functioning Total Score Parent's Assessment



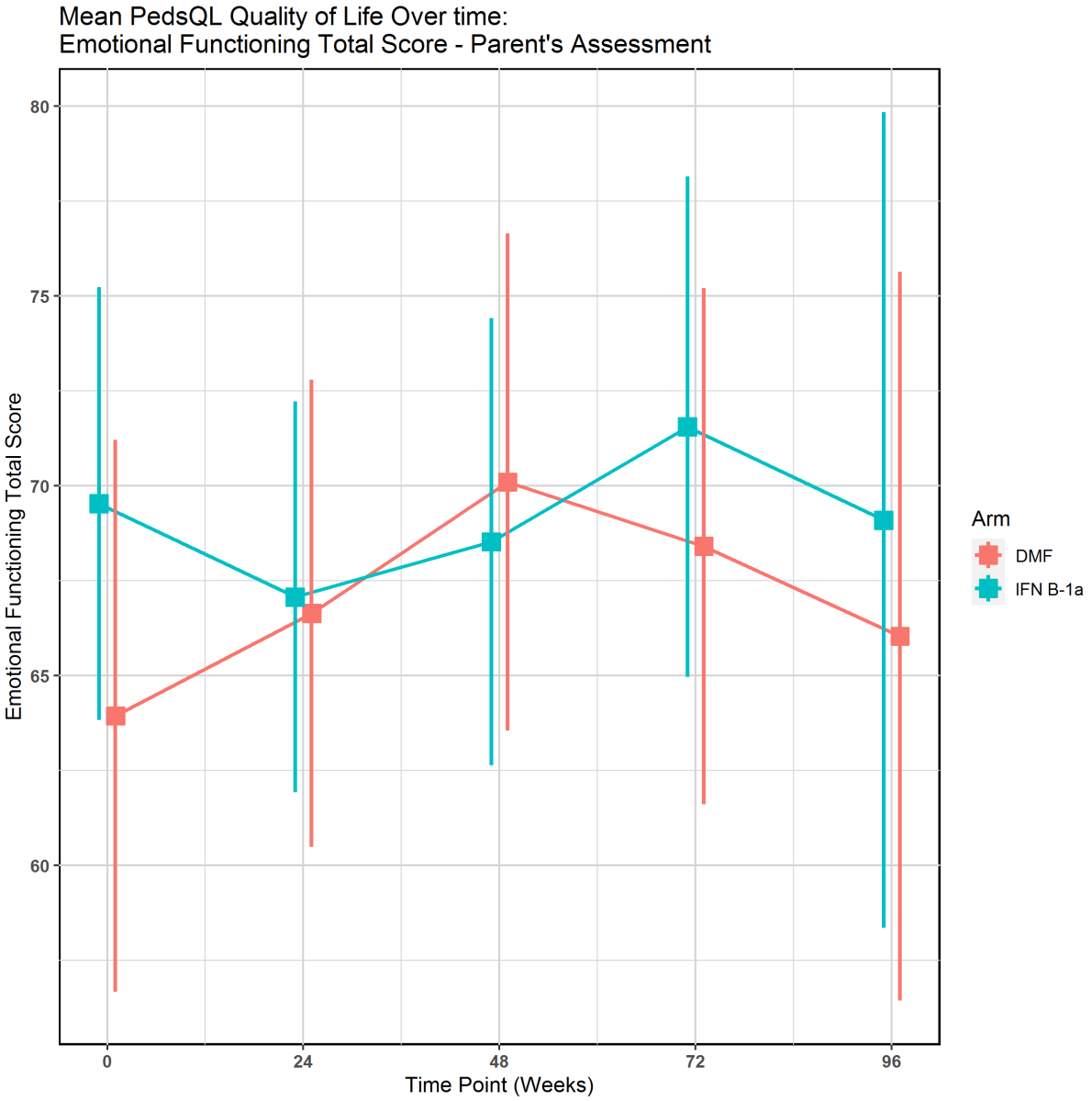
Change from baselineSocial Functioning Total Score Parent's Assessment



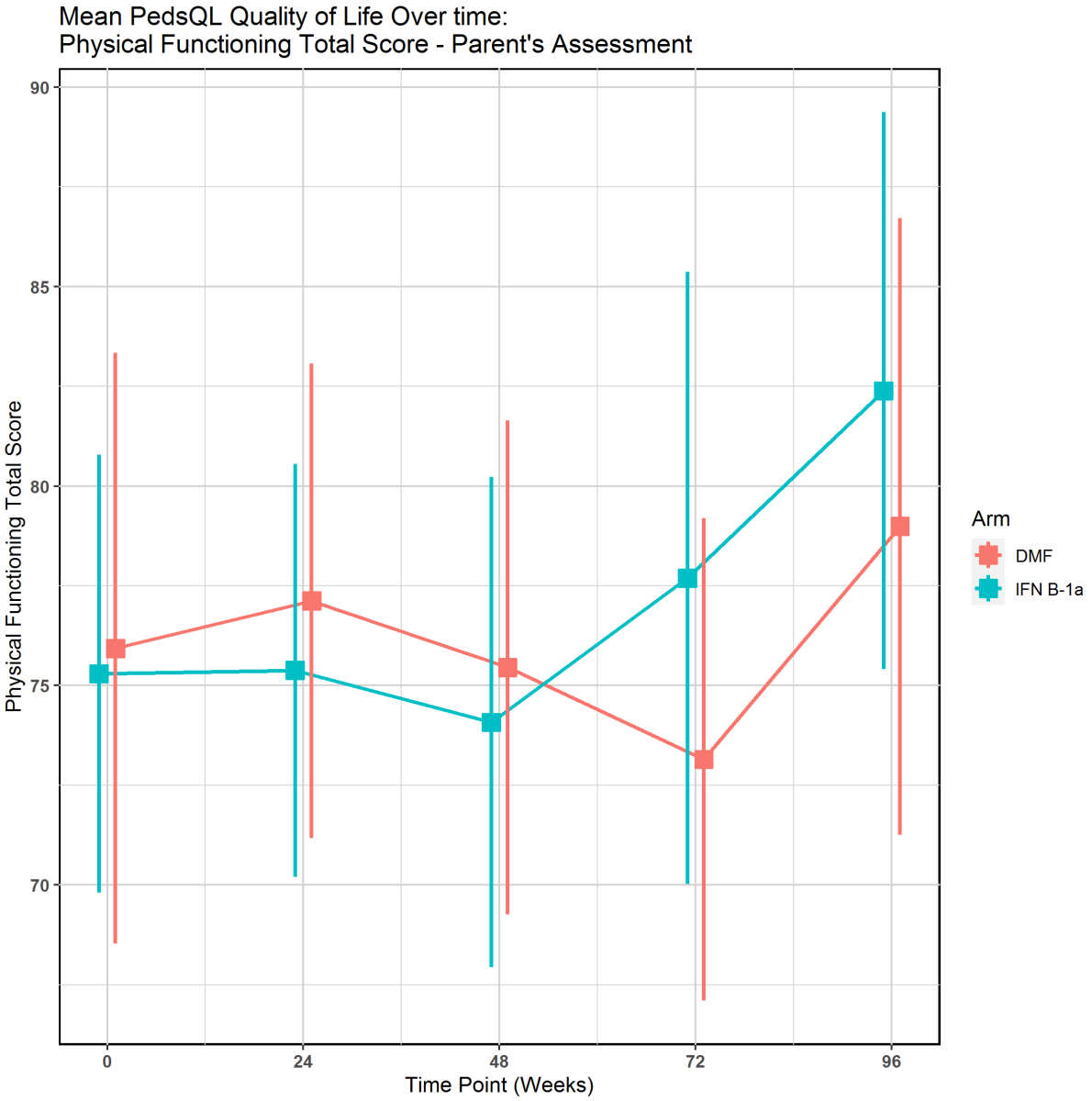
Change from baselineWork Study School Functioning Total Score Parent's Assessment



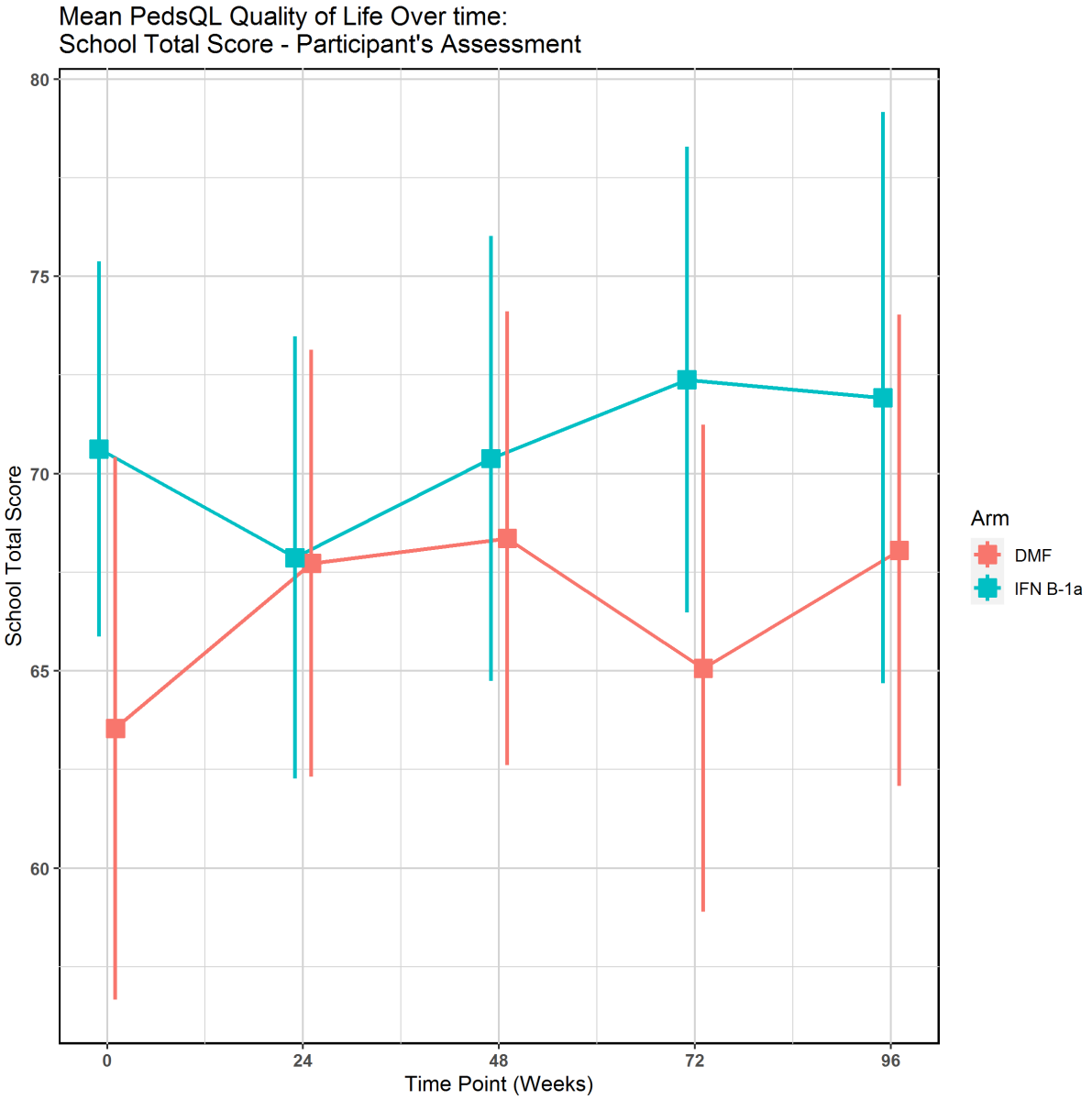
Emotional Functioning Total Score Parent's Assessment



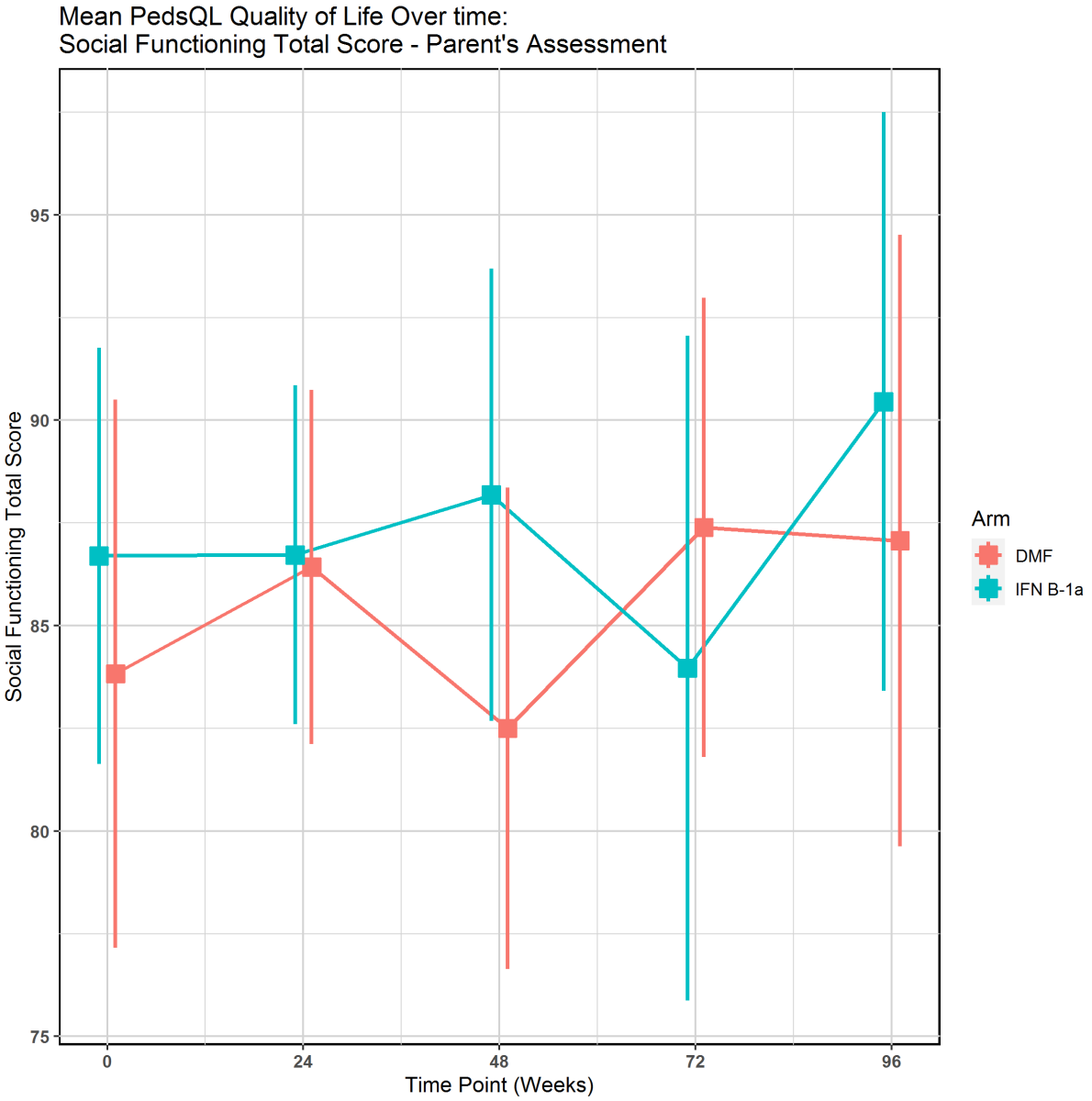
Physical Functioning Total Score Parent's Assessment



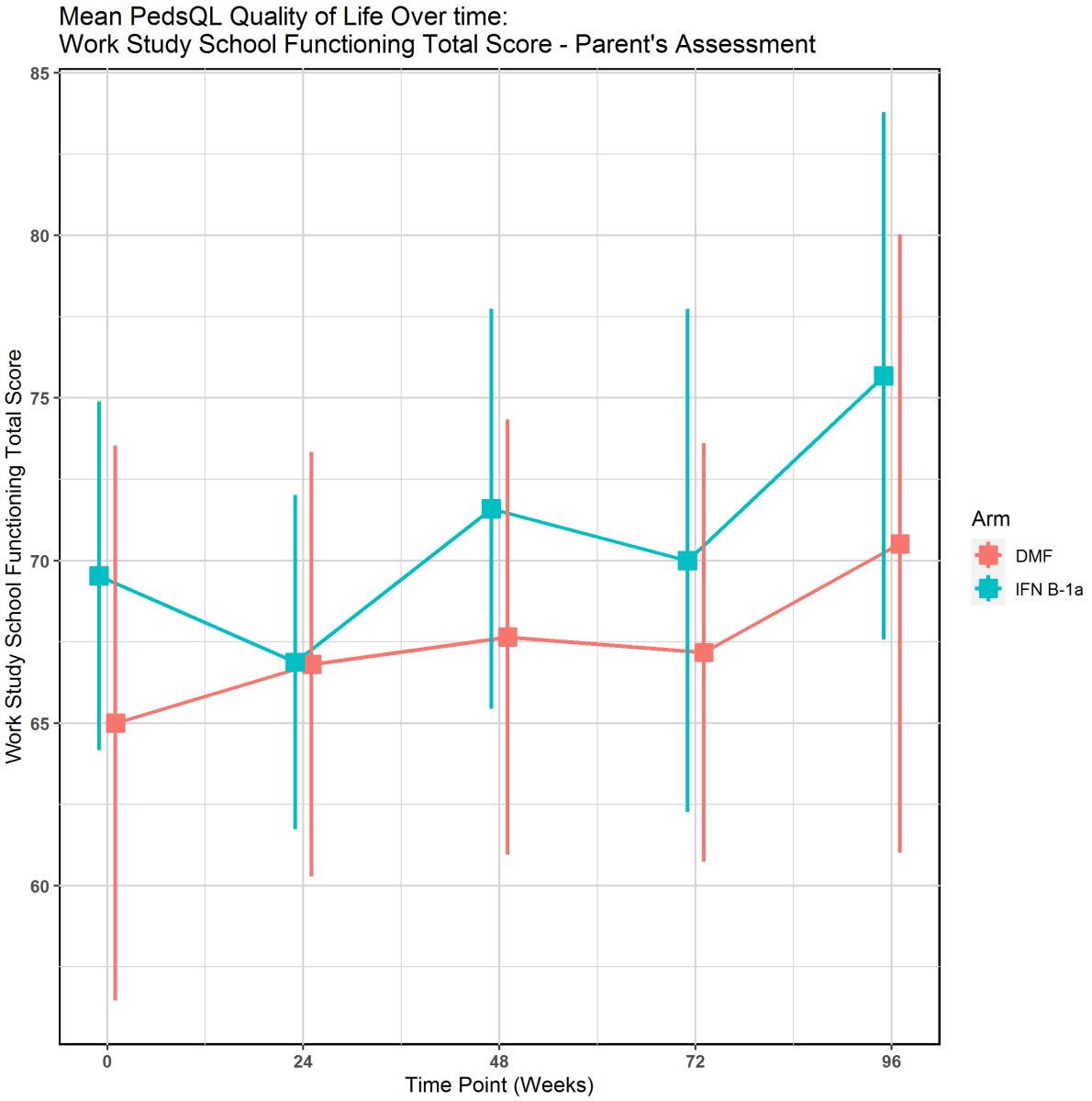
School Total Score Participant's Assessment



Social Functioning Total Score Parent's Assessment



Work Study School Functioning Total Score Parent's Assessment



PedsQL Participant

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
About My Health and Activities

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	2.5 (14.23)	-0.4 (11.59)	1.0 (12.91)
Median	0.0	0.0	0.0
Q1,Q3	-6.3, 9.4	-6.3, 3.1	-6.3, 7.8
Min, Max	-34, 34	-31, 28	-34, 34
Week 48			
n (%)	40 (56)	41 (64)	81 (60)
Mean (SD)	0.5 (13.53)	0.2 (12.54)	0.3 (12.96)
Median	3.1	0.0	3.1
Q1,Q3	-4.7, 7.8	-3.1, 6.3	-3.1, 6.3
Min, Max	-38, 28	-31, 19	-38, 28

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	36 (51)	30 (47)	66 (49)
Mean (SD)	-1.3 (15.82)	-1.5 (14.16)	-1.4 (14.97)
Median	-1.6	0.0	0.0
Q1,Q3	-10.9, 7.8	-9.4, 6.3	-9.4, 6.3
Min, Max	-41, 38	-28, 22	-41, 38
Week 96			
n (%)	24 (34)	22 (34)	46 (34)
Mean (SD)	-7.2 (17.37)	3.6 (15.86)	-2.0 (17.35)
Median	-4.7	3.1	0.0
Q1,Q3	-20.3, 4.7	0.0, 12.5	-15.6, 6.3
Min, Max	-50, 25	-31, 44	-50, 44

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
About My Feelings

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	3.7 (17.83)	-1.8 (18.52)	0.8 (18.32)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-10.0, 10.0	-5.0, 10.0
Min, Max	-45, 55	-60, 35	-60, 55
Week 48			
n (%)	40 (56)	41 (64)	81 (60)
Mean (SD)	6.5 (22.51)	-1.3 (17.09)	2.6 (20.21)
Median	2.5	0.0	0.0
Q1,Q3	-5.0, 17.5	-15.0, 10.0	-10.0, 15.0
Min, Max	-40, 65	-45, 35	-45, 65

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	36 (51)	30 (47)	66 (49)
Mean (SD)	2.5 (18.84)	3.4 (16.38)	2.9 (17.64)
Median	5.0	2.5	5.0
Q1,Q3	-7.5, 15.0	-10.0, 15.0	-10.0, 15.0
Min, Max	-35, 45	-25, 40	-35, 45
Week 96			
n (%)	24 (34)	22 (34)	46 (34)
Mean (SD)	-4.8 (21.14)	7.8 (16.41)	1.3 (19.87)
Median	-5.0	7.5	0.0
Q1,Q3	-20.0, 12.5	-5.0, 22.5	-10.0, 15.0
Min, Max	-50, 35	-20, 40	-50, 40

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
How I get Along With Others

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	0.1 (11.59)	0.4 (9.81)	0.2 (10.63)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 5.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-35, 25	-35, 25	-35, 25
Week 48			
n (%)	40 (56)	41 (64)	81 (60)
Mean (SD)	-0.4 (10.15)	0.4 (10.86)	0.0 (10.46)
Median	0.0	0.0	0.0
Q1,Q3	-2.5, 5.0	0.0, 5.0	0.0, 5.0
Min, Max	-30, 25	-25, 35	-30, 35

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	36 (51)	30 (47)	66 (49)
Mean (SD)	1.0 (11.39)	1.5 (8.52)	1.2 (10.12)
Median	0.0	2.5	0.0
Q1,Q3	-5.0, 5.0	0.0, 5.0	-5.0, 5.0
Min, Max	-30, 30	-20, 15	-30, 30
Week 96			
n (%)	24 (34)	22 (34)	46 (34)
Mean (SD)	-4.8 (15.84)	5.9 (13.68)	0.3 (15.65)
Median	0.0	5.0	0.0
Q1,Q3	-7.5, 0.0	0.0, 15.0	-5.0, 5.0
Min, Max	-45, 35	-25, 35	-45, 35

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
About Work or School

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Week 24			
n (%)	47 (66)	53 (83)	100 (74)
Mean (SD)	3.5 (16.84)	-1.9 (13.67)	0.7 (15.40)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-10.0, 5.0	-10.0, 7.5
Min, Max	-20, 50	-40, 30	-40, 50
Week 48			
n (%)	40 (56)	41 (64)	81 (60)
Mean (SD)	5.5 (18.29)	-0.2 (16.16)	2.6 (17.38)
Median	5.0	5.0	5.0
Q1,Q3	-5.0, 10.0	-10.0, 10.0	-10.0, 10.0
Min, Max	-30, 55	-45, 30	-45, 55

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	36 (51)	30 (47)	66 (49)
Mean (SD)	0.3 (16.86)	1.2 (14.42)	0.7 (15.69)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-5.0, 10.0	-10.0, 10.0
Min, Max	-25, 40	-35, 30	-35, 40
Week 96			
n (%)	24 (34)	22 (34)	46 (34)
Mean (SD)	-1.7 (28.58)	-0.5 (17.79)	-1.1 (23.78)
Median	0.0	0.0	0.0
Q1,Q3	-20.0, 22.5	-15.0, 10.0	-15.0, 15.0
Min, Max	-75, 55	-35, 35	-75, 55

109MS306_table45_47_CHG_DESCRIBE

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

About My Health and Activities

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	56 (79)	56 (88)	112 (83)
Mean (SD)	76.9 (22.64)	79.6 (18.52)	78.2 (20.64)
Median	82.8	87.5	84.4
Q1,Q3	68.8, 93.8	65.6, 93.8	67.2, 93.8
Min, Max	0, 100	28, 100	0, 100
Week 24			
n (%)	67 (94)	62 (97)	129 (96)
Mean (SD)	78.9 (17.29)	78.5 (19.70)	78.7 (18.42)
Median	81.3	84.4	84.4
Q1,Q3	68.8, 93.8	71.9, 93.8	68.8, 93.8
Min, Max	34, 100	22, 100	22, 100
Week 48			
n (%)	62 (87)	52 (81)	114 (84)
Mean (SD)	77.1 (19.58)	81.5 (17.76)	79.1 (18.82)
Median	81.3	87.5	81.7
Q1,Q3	65.6, 90.6	75.0, 93.8	68.8, 93.8
Min, Max	0, 100	13, 100	0, 100

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	42 (66)	101 (75)
Mean (SD)	77.0 (20.82)	80.8 (16.46)	78.6 (19.13)
Median	84.4	87.5	87.5
Q1,Q3	59.4, 93.8	68.8, 93.8	68.8, 93.8
Min, Max	22, 100	44, 100	22, 100
Week 96			
n (%)	54 (76)	39 (61)	93 (69)
Mean (SD)	78.6 (19.28)	82.9 (17.05)	80.4 (18.41)
Median	84.4	87.5	84.4
Q1,Q3	68.8, 93.8	71.9, 100.0	71.9, 93.8
Min, Max	9, 100	28, 100	9, 100

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

About My Feelings

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	56 (79)	56 (88)	112 (83)
Mean (SD)	64.6 (25.41)	74.2 (18.29)	69.4 (22.57)
Median	65.0	75.0	75.0
Q1,Q3	50.0, 87.5	60.0, 87.5	55.0, 87.5
Min, Max	0, 100	30, 100	0, 100
Week 24			
n (%)	67 (94)	62 (97)	129 (96)
Mean (SD)	69.3 (22.46)	71.1 (20.65)	70.2 (21.55)
Median	70.0	75.0	75.0
Q1,Q3	55.0, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	15, 100	25, 100	15, 100
Week 48			
n (%)	62 (87)	52 (81)	114 (84)
Mean (SD)	70.3 (25.06)	71.6 (21.87)	70.9 (23.56)
Median	72.5	75.0	75.0
Q1,Q3	55.0, 95.0	57.5, 90.0	55.0, 90.0
Min, Max	10, 100	15, 100	10, 100

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	42 (66)	101 (75)
Mean (SD)	69.0 (24.74)	72.6 (20.64)	70.5 (23.08)
Median	75.0	72.5	75.0
Q1,Q3	50.0, 90.0	60.0, 90.0	55.0, 90.0
Min, Max	15, 100	25, 100	15, 100
Week 96			
n (%)	54 (76)	39 (61)	93 (69)
Mean (SD)	66.5 (24.98)	73.2 (21.87)	69.3 (23.84)
Median	70.0	75.0	70.0
Q1,Q3	45.0, 90.0	60.0, 95.0	55.0, 90.0
Min, Max	15, 100	20, 100	15, 100

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

How I get Along With Others

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	56 (79)	56 (88)	112 (83)
Mean (SD)	85.9 (19.93)	89.1 (14.77)	87.5 (17.54)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	20, 100	45, 100	20, 100
Week 24			
n (%)	67 (94)	62 (97)	129 (96)
Mean (SD)	87.1 (16.65)	89.7 (13.71)	88.4 (15.31)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	25, 100	50, 100	25, 100
Week 48			
n (%)	62 (87)	52 (81)	114 (84)
Mean (SD)	84.9 (20.54)	90.0 (16.18)	87.2 (18.77)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	30, 100	20, 100	20, 100

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	42 (66)	101 (75)
Mean (SD)	86.7 (16.98)	92.4 (11.80)	89.1 (15.24)
Median	95.0	100.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	30, 100	50, 100	30, 100
Week 96			
n (%)	54 (76)	39 (61)	93 (69)
Mean (SD)	86.7 (17.80)	93.6 (10.76)	89.6 (15.56)
Median	95.0	100.0	100.0
Q1,Q3	75.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	30, 100	60, 100	30, 100

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

About Work or School

	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Baseline			
n (%)	55 (77)	56 (88)	111 (82)
Mean (SD)	63.5 (25.43)	70.6 (17.76)	67.1 (22.09)
Median	65.0	75.0	70.0
Q1,Q3	50.0, 85.0	57.5, 85.0	55.0, 85.0
Min, Max	0, 100	25, 100	0, 100
Week 24			
n (%)	66 (93)	61 (95)	127 (94)
Mean (SD)	67.7 (22.02)	67.9 (21.88)	67.8 (21.86)
Median	65.0	70.0	70.0
Q1,Q3	55.0, 90.0	50.0, 85.0	50.0, 85.0
Min, Max	25, 100	10, 100	10, 100
Week 48			
n (%)	61 (86)	52 (81)	113 (84)
Mean (SD)	68.4 (22.45)	70.4 (20.26)	69.3 (21.40)
Median	65.0	75.0	70.0
Q1,Q3	55.0, 85.0	50.0, 85.0	55.0, 85.0
Min, Max	0, 100	30, 100	0, 100

	DMF (N= 71)	**IFN B-1a (N= 64)**	**Total (N= 135)**
Week 72			
n (%)	59 (83)	42 (66)	101 (75)
Mean (SD)	65.1 (23.69)	72.4 (18.94)	68.1 (22.04)
Median	70.0	75.0	70.0
Q1,Q3	45.0, 80.0	60.0, 90.0	55.0, 85.0
Min, Max	5, 100	25, 100	5, 100
Week 96			
n (%)	54 (76)	39 (61)	93 (69)
Mean (SD)	68.1 (21.90)	71.9 (22.32)	69.7 (22.04)
Median	70.0	75.0	70.0
Q1,Q3	55.0, 85.0	55.0, 95.0	55.0, 90.0
Min, Max	15, 100	15, 100	15, 100

109MS306_table45_47_CHG_LSMEANS

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
About My Health and Activities

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	47 (66)	53 (83)
Lsmean (SE)	3.11 (1.837)	0.35 (1.801)
Lsmean_95 % CI	(-0.539, 6.754)	(-3.223, 3.928)
Diffrence (95% CI)	2.755 (-1.902, 7.411)	
SE_Difference	2.3459	
p-value	0.2432	
Week 48		
n (%)	40 (56)	41 (64)
Lsmean (SE)	0.039 (2.133)	-0.010 (2.124)
Lsmean_95 % CI	(-4.208, 4.286)	(-4.238, 4.219)
Diffrence (95% CI)	0.049 (-5.362, 5.460)	
SE_Difference	2.7174	
p-value	0.9857	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	36 (51)	30 (47)
Lsmean (SE)	0.28 (2.327)	1.43 (2.598)
Lsmean_95 % CI	(-4.370, 4.933)	(-3.767, 6.619)
Diffrence (95% CI)	-1.145 (-7.623, 5.334)	
SE_Difference	3.2409	
p-value	0.7251	
Week 96		
n (%)	24 (34)	22 (34)
Lsmean (SE)	-5.75 (3.170)	3.48 (3.453)
Lsmean_95 % CI	(-12.147, 0.649)	(-3.489, 10.450)
Diffrence (95% CI)	-9.230 (-18.547, 0.088)	
SE_Difference	4.6170	
p-value	0.0521	

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)

About My Feelings

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	47 (66)	53 (83)
Lsmean (SE)	3.43 (2.621)	1.20 (2.595)
Lsmean_95 % CI	(-1.775, 8.632)	(-3.954, 6.347)
Diffrence (95% CI)	2.232 (-4.526, 8.990)	
SE_Difference	3.4047	
p-value	0.5137	
Week 48		
n (%)	40 (56)	41 (64)
Lsmean (SE)	4.98 (3.242)	-0.31 (3.267)
Lsmean_95 % CI	(-1.480, 11.430)	(-6.812, 6.200)
Diffrence (95% CI)	5.281 (-3.054, 13.616)	
SE_Difference	4.1856	
p-value	0.2109	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	36 (51)	30 (47)
Lsmean (SE)	2.54 (2.936)	6.00 (3.320)
Lsmean_95 % CI	(-3.328, 8.408)	(-0.638, 12.633)
Diffrence (95% CI)	-3.458 (-11.737, 4.821)	
SE_Difference	4.1417	
p-value	0.4070	
Week 96		
n (%)	24 (34)	22 (34)
Lsmean (SE)	-4.82 (3.586)	10.88 (3.944)
Lsmean_95 % CI	(-12.056, 2.419)	(2.925, 18.842)
Diffrence (95% CI)	-15.703 (-26.283, -5.123)	
SE_Difference	5.2426	
p-value	0.0046	

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)

How I get Along With Others

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	47 (66)	53 (83)
Lsmean (SE)	1.14 (1.483)	1.61 (1.454)
Lsmean_95 % CI	(-1.801, 4.086)	(-1.273, 4.499)
Diffrence (95% CI)	-0.471 (-4.232, 3.290)	
SE_Difference	1.8948	
p-value	0.8043	
Week 48		
n (%)	40 (56)	41 (64)
Lsmean (SE)	-0.81 (1.791)	-0.16 (1.778)
Lsmean_95 % CI	(-4.380, 2.751)	(-3.699, 3.382)
Diffrence (95% CI)	-0.656 (-5.199, 3.886)	
SE_Difference	2.2811	
p-value	0.7743	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	36 (51)	30 (47)
Lsmean (SE)	1.52 (1.525)	2.58 (1.696)
Lsmean_95 % CI	(-1.530, 4.566)	(-0.812, 5.968)
Diffrence (95% CI)	-1.059 (-5.298, 3.179)	
SE_Difference	2.1205	
p-value	0.6191	
Week 96		
n (%)	24 (34)	22 (34)
Lsmean (SE)	-3.61 (2.648)	5.07 (2.881)
Lsmean_95 % CI	(-8.950, 1.739)	(-0.749, 10.881)
Diffrence (95% CI)	-8.672 (-16.440, -0.903)	
SE_Difference	3.8494	
p-value	0.0296	

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Scale Scores, Subject's Assessment - mITT Population, , Aged 13 years and older (n=135)
About Work or School

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 24		
n (%)	47 (66)	53 (83)
Lsmean (SE)	3.10 (2.261)	-0.63 (2.245)
Lsmean_95 % CI	(-1.388, 7.588)	(-5.087, 3.826)
Diffrence (95% CI)	3.730 (-2.070, 9.531)	
SE_Difference	2.9221	
p-value	0.2048	
Week 48		
n (%)	40 (56)	41 (64)
Lsmean (SE)	3.67 (2.758)	0.048 (2.811)
Lsmean_95 % CI	(-1.818, 9.167)	(-5.550, 5.645)
Diffrence (95% CI)	3.627 (-3.467, 10.720)	
SE_Difference	3.5625	
p-value	0.3119	

	DMF (N= 71)	**IFN B-1a (N= 64)**
Week 72		
n (%)	36 (51)	30 (47)
Lsmean (SE)	0.74 (2.590)	4.35 (2.976)
Lsmean_95 % CI	(-4.434, 5.919)	(-1.599, 10.300)
Diffrence (95% CI)	-3.607 (-10.947, 3.732)	
SE_Difference	3.6716	
p-value	0.3297	
Week 96		
n (%)	24 (34)	22 (34)
Lsmean (SE)	-2.69 (4.579)	1.11 (5.077)
Lsmean_95 % CI	(-11.933, 6.550)	(-9.133, 11.360)
Diffrence (95% CI)	-3.805 (-17.385, 9.775)	
SE_Difference	6.7292	
p-value	0.5748	

109MS306_Table45_47_MCID_15PCT_EFFECTMEASURES

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135)

OR, RR, ARR FOR HAVING A MCID OF 15% OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.324	0.385	-0.143
	95% CI	(0.107, 0.982)	(0.147, 1.007)	(-0.276, -0.009)
	p-value	0.0464	0.0517	0.0359
Feelings scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.500	0.571	-0.107
	95% CI	(0.191, 1.309)	(0.260, 1.254)	(-0.253, 0.039)
	p-value	0.1580	0.1627	0.1498
Feelings scale Week 72 >=4.4 point decrease from baseline	Effect measure	0.783	0.818	-0.036
	95% CI	(0.297, 2.069)	(0.368, 1.820)	(-0.177, 0.106)
	p-value	0.6222	0.6227	0.6213
Feelings scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.277	1.222	0.036
	95% CI	(0.483, 3.371)	(0.550, 2.718)	(-0.106, 0.177)
	p-value	0.6222	0.6227	0.6213

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point decrease from baseline	Effect measure	2.120	2.000	0.054
	95% CI	(0.503, 8.937)	(0.526, 7.604)	(-0.047, 0.154)
	p-value	0.3060	0.3090	0.2947
Get along scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.857	1.750	0.054
	95% CI	(0.512, 6.740)	(0.542, 5.646)	(-0.056, 0.163)
	p-value	0.3465	0.3491	0.3389
Get along scale Week 72 >=4.4 point decrease from baseline	Effect measure	2.077	2.000	0.036
	95% CI	(0.365, 11.828)	(0.382, 10.482)	(-0.047, 0.119)
	p-value	0.4102	0.4121	0.3998
Get along scale Week 96 >=4.4 point decrease from baseline	Effect measure	2.944	2.667	0.089
	95% CI	(0.738, 11.741)	(0.746, 9.535)	(-0.020, 0.198)
	p-value	0.1259	0.1314	0.1083

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point decrease from baseline	Effect measure	1.000	1.000	0.000
	95% CI	(0.302, 3.312)	(0.343, 2.913)	(-0.115, 0.115)
	p-value	>0.99	>0.99	>0.99
Health scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.700	1.600	0.054
	95% CI	(0.520, 5.559)	(0.558, 4.591)	(-0.065, 0.172)
	p-value	0.3801	0.3822	0.3745
Health scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.190	1.167	0.018
	95% CI	(0.373, 3.795)	(0.418, 3.254)	(-0.101, 0.136)
	p-value	0.7682	0.7683	0.7679
Health scale Week 96 >=4.4 point decrease from baseline	Effect measure	2.037	1.833	0.089
	95% CI	(0.697, 5.958)	(0.728, 4.615)	(-0.043, 0.221)
	p-value	0.1938	0.1981	0.1845

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.501	0.555	-0.087
	95% CI	(0.171, 1.466)	(0.221, 1.397)	(-0.220, 0.045)
	p-value	0.2071	0.2115	0.1971
School scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.563	0.611	-0.069
	95% CI	(0.190, 1.674)	(0.238, 1.566)	(-0.199, 0.060)
	p-value	0.3016	0.3048	0.2941
School scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.370	1.309	0.039
	95% CI	(0.471, 3.979)	(0.524, 3.268)	(-0.092, 0.169)
	p-value	0.5633	0.5640	0.5621
School scale Week 96 >=4.4 point decrease from baseline	Effect measure	0.909	0.926	-0.015
	95% CI	(0.351, 2.353)	(0.428, 2.002)	(-0.160, 0.131)
	p-value	0.8442	0.8443	0.8441

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
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	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point increase from baseline	Effect measure	1.000	1.000	0.000
	95% CI	(0.405, 2.466)	(0.492, 2.032)	(-0.152, 0.152)
	p-value	>0.99	>0.99	>0.99
Feelings scale Week 48 >=4.4 point increase from baseline	Effect measure	1.840	1.600	0.107
	95% CI	(0.751, 4.510)	(0.796, 3.215)	(-0.048, 0.262)
	p-value	0.1825	0.1868	0.1758
Feelings scale Week 72 >=4.4 point increase from baseline	Effect measure	2.615	2.125	0.161
	95% CI	(1.021, 6.699)	(0.999, 4.518)	(0.009, 0.312)
	p-value	0.0451	0.0502	0.0374
Feelings scale Week 96 >=4.4 point increase from baseline	Effect measure	1.109	1.083	0.018
	95% CI	(0.455, 2.700)	(0.542, 2.163)	(-0.136, 0.172)
	p-value	0.8205	0.8206	0.8204

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
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	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point increase from baseline	Effect measure	1.000	1.000	0.000
	95% CI	(0.302, 3.312)	(0.343, 2.913)	(-0.115, 0.115)
	p-value	>0.99	>0.99	>0.99
Get along scale Week 48 >=4.4 point increase from baseline	Effect measure	1.359	1.333	0.018
	95% CI	(0.290, 6.371)	(0.313, 5.686)	(-0.072, 0.107)
	p-value	0.6972	0.6975	0.6961
Get along scale Week 72 >=4.4 point increase from baseline	Effect measure	1.275	1.250	0.018
	95% CI	(0.324, 5.017)	(0.354, 4.414)	(-0.083, 0.118)
	p-value	0.7286	0.7288	0.7280
Get along scale Week 96 >=4.4 point increase from baseline	Effect measure	0.538	0.571	-0.054
	95% CI	(0.148, 1.954)	(0.177, 1.844)	(-0.163, 0.056)
	p-value	0.3465	0.3491	0.3389

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point increase from baseline	Effect measure	2.273	2.000	0.107
	95% CI	(0.787, 6.563)	(0.807, 4.955)	(-0.027, 0.242)
	p-value	0.1292	0.1343	0.1187
Health scale Week 48 >=4.4 point increase from baseline	Effect measure	0.720	0.750	-0.036
	95% CI	(0.233, 2.229)	(0.278, 2.022)	(-0.158, 0.087)
	p-value	0.5689	0.5696	0.5671
Health scale Week 72 >=4.4 point increase from baseline	Effect measure	1.304	1.250	0.036
	95% CI	(0.473, 3.595)	(0.533, 2.933)	(-0.100, 0.172)
	p-value	0.6075	0.6080	0.6064
Health scale Week 96 >=4.4 point increase from baseline	Effect measure	1.857	1.750	0.054
	95% CI	(0.512, 6.740)	(0.542, 5.646)	(-0.056, 0.163)
	p-value	0.3465	0.3491	0.3389

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point increase from baseline	Effect measure	2.267	2.036	0.093
	95% CI	(0.721, 7.129)	(0.744, 5.574)	(-0.034, 0.219)
	p-value	0.1616	0.1663	0.1512
School scale Week 48 >=4.4 point increase from baseline	Effect measure	1.852	1.697	0.075
	95% CI	(0.623, 5.504)	(0.662, 4.350)	(-0.056, 0.205)
	p-value	0.2676	0.2708	0.2610
School scale Week 72 >=4.4 point increase from baseline	Effect measure	1.953	1.745	0.093
	95% CI	(0.706, 5.407)	(0.743, 4.103)	(-0.046, 0.233)
	p-value	0.1974	0.2015	0.1900
School scale Week 96 >=4.4 point increase from baseline	Effect measure	2.049	1.782	0.112
	95% CI	(0.782, 5.369)	(0.813, 3.906)	(-0.035, 0.259)
	p-value	0.1445	0.1492	0.1368

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=15 (CODED AS YES). SCALES ARE 0 TO 100, SO 15%=15)
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARAIBLE=0
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

109MS306_Table45_47_MCID_15PCT_NPERCENT_EVENT

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment - ITT Population, Aged 13 years and older (n=135)

N(%) FOR EVENTS (>=15% MCID) AT EACH TIMEPOINT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Feelings scale Week 24 >=15% decrease from baseline				
	Yes	5 (7)	13 (20)	18 (13)
	No	51 (72)	43 (67)	94 (70)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 48 >=15% decrease from baseline				
	Yes	8 (11)	14 (22)	22 (16)
	No	48 (68)	42 (66)	90 (67)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 72 >=15% decrease from baseline				
	Yes	9 (13)	11 (17)	20 (15)
	No	47 (66)	45 (70)	92 (68)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 96 >=15% decrease from baseline				
	Yes	11 (15)	9 (14)	20 (15)
	No	45 (63)	47 (73)	92 (68)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Get along scale Week 24 >=15% decrease from baseline				
	Yes	6 (8)	3 (5)	9 (7)
	No	50 (70)	53 (83)	103 (76)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 48 >=15% decrease from baseline				
	Yes	7 (10)	4 (6)	11 (8)
	No	49 (69)	52 (81)	101 (75)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 72 >=15% decrease from baseline				
	Yes	4 (6)	2 (3)	6 (4)
	No	52 (73)	54 (84)	106 (79)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 96 >=15% decrease from baseline				
	Yes	8 (11)	3 (5)	11 (8)
	No	48 (68)	53 (83)	101 (75)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Health scale Week 24 >=15% decrease from baseline				
	Yes	6 (8)	6 (9)	12 (9)
	No	50 (70)	50 (78)	100 (74)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 48 >=15% decrease from baseline				
	Yes	8 (11)	5 (8)	13 (10)
	No	48 (68)	51 (80)	99 (73)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 72 >=15% decrease from baseline				
	Yes	7 (10)	6 (9)	13 (10)
	No	49 (69)	50 (78)	99 (73)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 96 >=15% decrease from baseline				
	Yes	11 (15)	6 (9)	17 (13)
	No	45 (63)	50 (78)	95 (70)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 24 >=15% decrease from baseline				
	Yes	6 (8)	11 (17)	17 (13)
	No	49 (69)	45 (70)	94 (70)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 48 >=15% decrease from baseline				
	Yes	6 (8)	10 (16)	16 (12)
	No	49 (69)	46 (72)	95 (70)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 72 >=15% decrease from baseline				
	Yes	9 (13)	7 (11)	16 (12)
	No	46 (65)	49 (77)	95 (70)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 96 >=15% decrease from baseline				
	Yes	10 (14)	11 (17)	21 (16)
	No	45 (63)	45 (70)	90 (67)
	Missing	16 (23)	8 (13)	24 (18)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Feelings scale Week 24 >=15% increase from baseline				
	Yes	12 (17)	12 (19)	24 (18)
	No	44 (62)	44 (69)	88 (65)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 48 >=15% increase from baseline				
	Yes	16 (23)	10 (16)	26 (19)
	No	40 (56)	46 (72)	86 (64)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 72 >=15% increase from baseline				
	Yes	17 (24)	8 (13)	25 (19)
	No	39 (55)	48 (75)	87 (64)
	Missing	15 (21)	8 (13)	23 (17)
Feelings scale Week 96 >=15% increase from baseline				
	Yes	13 (18)	12 (19)	25 (19)
	No	43 (61)	44 (69)	87 (64)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Get along scale Week 24 >=15% increase from baseline				
	Yes	6 (8)	6 (9)	12 (9)
	No	50 (70)	50 (78)	100 (74)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 48 >=15% increase from baseline				
	Yes	4 (6)	3 (5)	7 (5)
	No	52 (73)	53 (83)	105 (78)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 72 >=15% increase from baseline				
	Yes	5 (7)	4 (6)	9 (7)
	No	51 (72)	52 (81)	103 (76)
	Missing	15 (21)	8 (13)	23 (17)
Get along scale Week 96 >=15% increase from baseline				
	Yes	4 (6)	7 (11)	11 (8)
	No	52 (73)	49 (77)	101 (75)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Health scale Week 24 >=15% increase from baseline				
	Yes	12 (17)	6 (9)	18 (13)
	No	44 (62)	50 (78)	94 (70)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 48 >=15% increase from baseline				
	Yes	6 (8)	8 (13)	14 (10)
	No	50 (70)	48 (75)	98 (73)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 72 >=15% increase from baseline				
	Yes	10 (14)	8 (13)	18 (13)
	No	46 (65)	48 (75)	94 (70)
	Missing	15 (21)	8 (13)	23 (17)
Health scale Week 96 >=15% increase from baseline				
	Yes	7 (10)	4 (6)	11 (8)
	No	49 (69)	52 (81)	101 (75)
	Missing	15 (21)	8 (13)	23 (17)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Event (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 24 >=15% increase from baseline				
	Yes	10 (14)	5 (8)	15 (11)
	No	45 (63)	51 (80)	96 (71)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 48 >=15% increase from baseline				
	Yes	10 (14)	6 (9)	16 (12)
	No	45 (63)	50 (78)	95 (70)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 72 >=15% increase from baseline				
	Yes	12 (17)	7 (11)	19 (14)
	No	43 (61)	49 (77)	92 (68)
	Missing	16 (23)	8 (13)	24 (18)
School scale Week 96 >=15% increase from baseline				
	Yes	14 (20)	8 (13)	22 (16)
	No	41 (58)	48 (75)	89 (66)
	Missing	16 (23)	8 (13)	24 (18)

NOTE1: An event is yes when the MCID is >=15%. Scale is 0 to 100, which translates to >=15 total score.
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana_pedsqos-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

109MS306_Table45_47_MCID_15PCT_NPERCENT_RESPONSE

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135)

N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Feelings scale Week 0				
	Yes	56 (79)	56 (88)	112 (83)
	No	15 (21)	8 (13)	23 (17)
Feelings scale Week 24				
	Yes	67 (94)	62 (97)	129 (96)
	No	4 (6)	2 (3)	6 (4)
Feelings scale Week 48				
	Yes	62 (87)	52 (81)	114 (84)
	No	9 (13)	12 (19)	21 (16)
Feelings scale Week 72				
	Yes	59 (83)	41 (64)	100 (74)
	No	12 (17)	23 (36)	35 (26)
Feelings scale Week 96				
	Yes	54 (76)	38 (59)	92 (68)
	No	17 (24)	26 (41)	43 (32)

NOTE1: Response rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Get along scale Week 0				
	Yes	56 (79)	56 (88)	112 (83)
	No	15 (21)	8 (13)	23 (17)
Get along scale Week 24				
	Yes	67 (94)	62 (97)	129 (96)
	No	4 (6)	2 (3)	6 (4)
Get along scale Week 48				
	Yes	62 (87)	52 (81)	114 (84)
	No	9 (13)	12 (19)	21 (16)
Get along scale Week 72				
	Yes	59 (83)	41 (64)	100 (74)
	No	12 (17)	23 (36)	35 (26)
Get along scale Week 96				
	Yes	54 (76)	38 (59)	92 (68)
	No	17 (24)	26 (41)	43 (32)

NOTE1: Response rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Health scale Week 0				
	Yes	56 (79)	56 (88)	112 (83)
	No	15 (21)	8 (13)	23 (17)
Health scale Week 24				
	Yes	67 (94)	62 (97)	129 (96)
	No	4 (6)	2 (3)	6 (4)
Health scale Week 48				
	Yes	62 (87)	52 (81)	114 (84)
	No	9 (13)	12 (19)	21 (16)
Health scale Week 72				
	Yes	59 (83)	41 (64)	100 (74)
	No	12 (17)	23 (36)	35 (26)
Health scale Week 96				
	Yes	54 (76)	38 (59)	92 (68)
	No	17 (24)	26 (41)	43 (32)

NOTE1: Response rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

	Response (n (%))	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
School scale Week 0				
	Yes	55 (77)	56 (88)	111 (82)
	No	16 (23)	8 (13)	24 (18)
School scale Week 24				
	Yes	66 (93)	61 (95)	127 (94)
	No	5 (7)	3 (5)	8 (6)
School scale Week 48				
	Yes	61 (86)	52 (81)	113 (84)
	No	10 (14)	12 (19)	22 (16)
School scale Week 72				
	Yes	59 (83)	41 (64)	100 (74)
	No	12 (17)	23 (36)	35 (26)
School scale Week 96				
	Yes	54 (76)	38 (59)	92 (68)
	No	17 (24)	26 (41)	43 (32)

NOTE1: Response rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID15pct_NewMethod_3pvalues_n=135_ban012822.sas date: 28JAN2022

109MS306_table45_47CHG_HEDGESCI

Table 45.47: PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Participant's Assessment - mITTPopulation, Aged 13 years and older (n=135)

Summary of PedsQL Quality of Life Multidimensional Fatigue Scale Scores, Subject's Assessment - mITT Population, Aged 13 years and older (n=135)

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24 Weeks	0.306	-0.089	0.701
	48 Weeks	0.39	-0.050	0.830
	72 Weeks	-0.052	-0.536	0.433
	96 Weeks	-0.664	-1.259	-0.069
GET ALON	24 Weeks	-0.023	-0.416	0.370
	48 Weeks	-0.07	-0.506	0.365
	72 Weeks	-0.052	-0.536	0.433
	96 Weeks	-0.72	-1.318	-0.123
HEALTH A	24 Weeks	0.218	-0.176	0.612
	48 Weeks	0.024	-0.411	0.460
	72 Weeks	0.01	-0.474	0.495
	96 Weeks	-0.643	-1.237	-0.049
SCHOOL	24 Weeks	0.354	-0.042	0.750
	48 Weeks	0.333	-0.106	0.772
	72 Weeks	-0.056	-0.541	0.428
	96 Weeks	-0.05	-0.629	0.528

Note 1: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note 2: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\MainQCd\T45_47/109MS306_table45_47_CHG_HEDGESCI.sas date: 16FEB2022

Sub groups

Change

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_age13to14

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Health and Activities

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	12 (67)	11 (79)	23 (72)
Mean (SD)	1.0 (14.80)	3.4 (7.05)	2.2 (11.56)
Median	1.6	0.0	0.0
Q1,Q3	-10.9, 9.4	0.0, 9.4	-6.3, 9.4
Min, Max	-19, 28	-6, 16	-19, 28
Week 48			
n (%)	9 (50)	9 (64)	18 (56)
Mean (SD)	-2.8 (10.42)	-0.7 (15.84)	-1.7 (13.05)
Median	3.1	0.0	1.6
Q1,Q3	-9.4, 3.1	-3.1, 6.3	-9.4, 6.3
Min, Max	-22, 9	-31, 19	-31, 19

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	0.6 (10.70)	5.4 (11.37)	2.6 (10.89)
Median	1.6	3.1	3.1
Q1,Q3	-9.4, 6.3	-3.1, 18.8	-3.1, 6.3
Min, Max	-13, 22	-9, 22	-13, 22
Week 96			
n (%)	10 (56)	6 (43)	16 (50)
Mean (SD)	-2.5 (15.15)	2.1 (13.06)	-0.8 (14.14)
Median	3.1	4.7	3.1
Q1,Q3	-18.8, 6.3	0.0, 12.5	-15.6, 9.4
Min, Max	-22, 22	-22, 13	-22, 22

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Feelings

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	12 (67)	11 (79)	23 (72)
Mean (SD)	2.5 (6.22)	5.2 (14.25)	3.8 (10.66)
Median	5.0	2.5	5.0
Q1,Q3	-2.5, 5.0	-5.0, 15.0	-5.0, 10.0
Min, Max	-10, 10	-15, 30	-15, 30
Week 48			
n (%)	9 (50)	9 (64)	18 (56)
Mean (SD)	-1.7 (15.41)	0.8 (20.92)	-0.4 (17.87)
Median	0.0	-10.0	0.0
Q1,Q3	0.0, 5.0	-15.0, 15.0	-12.5, 10.0
Min, Max	-40, 15	-25, 35	-40, 35

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	0.5 (12.79)	8.2 (21.73)	3.7 (16.87)
Median	2.5	7.5	5.0
Q1,Q3	-5.0, 10.0	-15.0, 25.0	-5.0, 15.0
Min, Max	-25, 15	-20, 40	-25, 40
Week 96			
n (%)	10 (56)	6 (43)	16 (50)
Mean (SD)	-1.5 (20.01)	13.8 (21.55)	4.2 (21.29)
Median	2.5	21.3	10.0
Q1,Q3	-10.0, 15.0	-10.0, 25.0	-10.0, 20.0
Min, Max	-45, 20	-15, 40	-45, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. How I get Along With Others

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	12 (67)	11 (79)	23 (72)
Mean (SD)	2.5 (6.91)	4.4 (7.06)	3.4 (6.89)
Median	0.0	5.0	0.0
Q1,Q3	0.0, 5.0	0.0, 10.0	0.0, 5.0
Min, Max	-5, 20	-6, 15	-6, 20
Week 48			
n (%)	9 (50)	9 (64)	18 (56)
Mean (SD)	-2.8 (5.07)	-0.6 (12.36)	-1.7 (9.24)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 0.0	0.0, 5.0	-5.0, 5.0
Min, Max	-10, 5	-25, 15	-25, 15

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	0.5 (3.69)	4.3 (9.76)	2.1 (6.86)
Median	0.0	5.0	0.0
Q1,Q3	0.0, 0.0	0.0, 10.0	0.0, 5.0
Min, Max	-5, 10	-15, 15	-15, 15
Week 96			
n (%)	10 (56)	6 (43)	16 (50)
Mean (SD)	-5.0 (11.06)	5.8 (9.70)	-0.9 (11.58)
Median	0.0	7.5	0.0
Q1,Q3	-5.0, 0.0	0.0, 15.0	-2.5, 2.5
Min, Max	-35, 0	-10, 15	-35, 15

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About Work or School

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Week 24			
n (%)	12 (67)	11 (79)	23 (72)
Mean (SD)	-0.8 (13.11)	2.3 (13.30)	0.7 (13.00)
Median	0.0	5.0	0.0
Q1,Q3	-10.0, 5.0	-10.0, 10.0	-10.0, 10.0
Min, Max	-20, 30	-20, 25	-20, 30
Week 48			
n (%)	9 (50)	9 (64)	18 (56)
Mean (SD)	-5.6 (13.10)	-0.6 (13.10)	-3.1 (12.96)
Median	0.0	5.0	2.5
Q1,Q3	-15.0, 5.0	-10.0, 10.0	-15.0, 5.0
Min, Max	-30, 5	-20, 15	-30, 15

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	10 (56)	7 (50)	17 (53)
Mean (SD)	-1.0 (11.50)	5.0 (14.72)	1.5 (12.84)
Median	-2.5	10.0	0.0
Q1,Q3	-10.0, 5.0	-5.0, 15.0	-5.0, 10.0
Min, Max	-20, 20	-20, 25	-20, 25
Week 96			
n (%)	10 (56)	6 (43)	16 (50)
Mean (SD)	-4.5 (29.58)	-4.2 (20.60)	-4.4 (25.81)
Median	0.0	0.0	0.0
Q1,Q3	-15.0, 20.0	-25.0, 5.0	-17.5, 12.5
Min, Max	-75, 25	-30, 25	-75, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_age15to17

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Health and Activities

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	35 (66)	42 (84)	77 (75)
Mean (SD)	2.9 (14.22)	-1.3 (12.39)	0.6 (13.34)
Median	0.0	0.0	0.0
Q1,Q3	-3.1, 15.6	-9.4, 3.1	-6.3, 6.3
Min, Max	-34, 34	-31, 28	-34, 34
Week 48			
n (%)	31 (58)	32 (64)	63 (61)
Mean (SD)	1.4 (14.32)	0.4 (11.74)	0.9 (12.98)
Median	3.1	0.0	3.1
Q1,Q3	-3.1, 12.5	-3.1, 6.3	-3.1, 6.3
Min, Max	-38, 28	-31, 19	-38, 28

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	26 (49)	23 (46)	49 (48)
Mean (SD)	-2.0 (17.52)	-3.5 (14.48)	-2.7 (16.02)
Median	-3.1	-3.1	-3.1
Q1,Q3	-12.5, 12.5	-15.6, 3.1	-12.5, 6.3
Min, Max	-41, 38	-28, 22	-41, 38
Week 96			
n (%)	14 (26)	16 (32)	30 (29)
Mean (SD)	-10.5 (18.61)	4.1 (17.14)	-2.7 (19.03)
Median	-7.8	3.1	0.0
Q1,Q3	-21.9, 0.0	-3.1, 14.1	-15.6, 6.3
Min, Max	-50, 25	-31, 44	-50, 44

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Feelings

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	35 (66)	42 (84)	77 (75)
Mean (SD)	4.1 (20.42)	-3.7 (19.19)	-0.1 (20.02)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 15.0	-20.0, 10.0	-10.0, 10.0
Min, Max	-45, 55	-60, 35	-60, 55
Week 48			
n (%)	31 (58)	32 (64)	63 (61)
Mean (SD)	8.9 (23.86)	-1.9 (16.20)	3.4 (20.88)
Median	5.0	0.0	0.0
Q1,Q3	-10.0, 25.0	-15.0, 10.0	-10.0, 15.0
Min, Max	-25, 65	-45, 25	-45, 65

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	26 (49)	23 (46)	49 (48)
Mean (SD)	3.3 (20.88)	2.0 (14.67)	2.7 (18.06)
Median	7.5	0.0	5.0
Q1,Q3	-10.0, 20.0	-10.0, 10.0	-10.0, 15.0
Min, Max	-35, 45	-25, 35	-35, 45
Week 96			
n (%)	14 (26)	16 (32)	30 (29)
Mean (SD)	-7.1 (22.34)	5.6 (14.24)	-0.3 (19.25)
Median	-5.0	2.5	0.0
Q1,Q3	-25.0, 10.0	-5.0, 17.5	-15.0, 15.0
Min, Max	-50, 35	-20, 25	-50, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. How I get Along With Others

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	35 (66)	42 (84)	77 (75)
Mean (SD)	-0.7 (12.78)	-0.7 (10.22)	-0.7 (11.38)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 5.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-35, 25	-35, 25	-35, 25
Week 48			
n (%)	31 (58)	32 (64)	63 (61)
Mean (SD)	0.3 (11.18)	0.6 (10.61)	0.5 (10.80)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 5.0	-2.5, 5.0	0.0, 5.0
Min, Max	-30, 25	-25, 35	-30, 35

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	26 (49)	23 (46)	49 (48)
Mean (SD)	1.2 (13.29)	0.7 (8.16)	0.9 (11.07)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-30, 30	-20, 15	-30, 30
Week 96			
n (%)	14 (26)	16 (32)	30 (29)
Mean (SD)	-4.6 (18.96)	5.9 (15.19)	1.0 (17.59)
Median	0.0	5.0	0.0
Q1,Q3	-15.0, 5.0	0.0, 12.5	-5.0, 5.0
Min, Max	-45, 35	-25, 35	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About Work or School

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Week 24			
n (%)	35 (66)	42 (84)	77 (75)
Mean (SD)	5.0 (17.86)	-3.0 (13.71)	0.6 (16.13)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 10.0	-10.0, 5.0	-10.0, 5.0
Min, Max	-20, 50	-40, 30	-40, 50
Week 48			
n (%)	31 (58)	32 (64)	63 (61)
Mean (SD)	8.7 (18.48)	-0.2 (17.11)	4.2 (18.21)
Median	5.0	5.0	5.0
Q1,Q3	-5.0, 15.0	-10.0, 10.0	-5.0, 10.0
Min, Max	-20, 55	-45, 30	-45, 55

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	26 (49)	23 (46)	49 (48)
Mean (SD)	0.8 (18.69)	0.0 (14.46)	0.4 (16.67)
Median	0.0	0.0	0.0
Q1,Q3	-15.0, 15.0	-10.0, 10.0	-10.0, 10.0
Min, Max	-25, 40	-35, 30	-35, 40
Week 96			
n (%)	14 (26)	16 (32)	30 (29)
Mean (SD)	0.4 (28.79)	0.9 (17.15)	0.7 (22.88)
Median	-2.5	0.0	0.0
Q1,Q3	-20.0, 25.0	-12.5, 12.5	-15.0, 15.0
Min, Max	-45, 55	-35, 35	-45, 55

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_female

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Health and Activities

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	1.3 (15.75)	-0.3 (11.88)	0.4 (13.75)
Median	0.0	0.0	0.0
Q1,Q3	-9.4, 12.5	-6.3, 6.3	-9.4, 9.4
Min, Max	-34, 34	-31, 28	-34, 34
Week 48			
n (%)	27 (54)	28 (61)	55 (57)
Mean (SD)	-1.5 (14.49)	-1.7 (13.91)	-1.6 (14.06)
Median	3.1	0.0	3.1
Q1,Q3	-12.5, 6.3	-3.1, 6.3	-9.4, 6.3
Min, Max	-38, 25	-31, 19	-38, 25

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	24 (48)	22 (48)	46 (48)
Mean (SD)	-2.9 (18.52)	-2.7 (14.98)	-2.8 (16.73)
Median	-6.3	0.0	-3.1
Q1,Q3	-14.1, 12.5	-12.5, 6.3	-12.5, 6.3
Min, Max	-41, 38	-28, 22	-41, 38
Week 96			
n (%)	16 (32)	16 (35)	32 (33)
Mean (SD)	-10.9 (18.33)	1.6 (15.18)	-4.7 (17.73)
Median	-14.1	3.1	0.0
Q1,Q3	-21.9, 3.1	-6.3, 12.5	-18.8, 6.3
Min, Max	-50, 25	-31, 22	-50, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Feelings

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	1.6 (18.47)	0.1 (15.36)	0.8 (16.78)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-7.5, 10.0	-5.0, 10.0
Min, Max	-45, 55	-40, 35	-45, 55
Week 48			
n (%)	27 (54)	28 (61)	55 (57)
Mean (SD)	5.0 (20.66)	-3.1 (17.28)	0.9 (19.28)
Median	5.0	-5.0	0.0
Q1,Q3	-10.0, 20.0	-15.0, 15.0	-15.0, 15.0
Min, Max	-40, 45	-45, 25	-45, 45

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	24 (48)	22 (48)	46 (48)
Mean (SD)	4.4 (20.23)	3.1 (15.20)	3.8 (17.82)
Median	10.0	5.0	5.0
Q1,Q3	-5.0, 17.5	-10.0, 15.0	-5.0, 15.0
Min, Max	-35, 45	-20, 35	-35, 45
Week 96			
n (%)	16 (32)	16 (35)	32 (33)
Mean (SD)	-4.1 (22.75)	4.5 (15.44)	0.2 (19.62)
Median	-5.0	2.5	0.0
Q1,Q3	-15.0, 12.5	-7.5, 20.0	-10.0, 15.0
Min, Max	-50, 35	-20, 25	-50, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. How I get Along With Others

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	0.5 (12.60)	0.7 (10.10)	0.6 (11.26)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 5.0	-5.0, 5.0	-2.5, 5.0
Min, Max	-35, 25	-35, 25	-35, 25
Week 48			
n (%)	27 (54)	28 (61)	55 (57)
Mean (SD)	-1.3 (10.71)	-0.4 (11.22)	-0.8 (10.88)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 5.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-30, 20	-25, 35	-30, 35

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	24 (48)	22 (48)	46 (48)
Mean (SD)	-0.2 (12.89)	1.1 (8.58)	0.4 (10.95)
Median	0.0	5.0	0.0
Q1,Q3	-5.0, 0.0	0.0, 5.0	-5.0, 5.0
Min, Max	-30, 30	-20, 15	-30, 30
Week 96			
n (%)	16 (32)	16 (35)	32 (33)
Mean (SD)	-5.3 (19.19)	6.3 (13.48)	0.5 (17.34)
Median	0.0	5.0	0.0
Q1,Q3	-12.5, 2.5	0.0, 12.5	-2.5, 7.5
Min, Max	-45, 35	-25, 35	-45, 35

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About Work or School

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Week 24			
n (%)	32 (64)	36 (78)	68 (71)
Mean (SD)	2.3 (16.66)	-0.7 (13.26)	0.7 (14.92)
Median	0.0	0.0	0.0
Q1,Q3	-10.0, 7.5	-10.0, 7.5	-10.0, 7.5
Min, Max	-20, 45	-30, 30	-30, 45
Week 48			
n (%)	27 (54)	28 (61)	55 (57)
Mean (SD)	3.9 (19.03)	0.7 (15.38)	2.3 (17.18)
Median	0.0	5.0	5.0
Q1,Q3	-10.0, 10.0	-10.0, 10.0	-10.0, 10.0
Min, Max	-30, 50	-45, 30	-45, 50

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	24 (48)	22 (48)	46 (48)
Mean (SD)	2.3 (19.56)	0.7 (14.90)	1.5 (17.32)
Median	0.0	0.0	0.0
Q1,Q3	-15.0, 20.0	-5.0, 10.0	-10.0, 15.0
Min, Max	-25, 40	-35, 30	-35, 40
Week 96			
n (%)	16 (32)	16 (35)	32 (33)
Mean (SD)	-3.1 (33.16)	-1.6 (20.06)	-2.3 (26.97)
Median	-7.5	-2.5	-5.0
Q1,Q3	-20.0, 25.0	-15.0, 15.0	-20.0, 17.5
Min, Max	-75, 55	-35, 35	-75, 55

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_male

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About My Health and Activities

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	5.0 (10.28)	-0.4 (11.32)	2.1 (11.01)
Median	3.1	0.0	0.0
Q1,Q3	0.0, 9.4	0.0, 3.1	0.0, 4.7
Min, Max	-16, 25	-31, 16	-31, 25
Week 48			
n (%)	13 (62)	13 (72)	26 (67)
Mean (SD)	4.6 (10.64)	4.1 (8.01)	4.3 (9.23)
Median	0.0	3.1	1.6
Q1,Q3	0.0, 9.4	-3.1, 12.5	-3.1, 12.5
Min, Max	-9, 28	-6, 16	-9, 28

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	8 (44)	20 (51)
Mean (SD)	1.8 (7.93)	2.0 (11.80)	1.9 (9.37)
Median	0.0	-1.6	0.0
Q1,Q3	-1.6, 6.3	-3.1, 9.4	-3.1, 6.3
Min, Max	-13, 19	-16, 22	-16, 22
Week 96			
n (%)	8 (38)	6 (33)	14 (36)
Mean (SD)	0.4 (13.20)	8.9 (17.83)	4.0 (15.33)
Median	1.6	3.1	3.1
Q1,Q3	-7.8, 7.8	0.0, 9.4	-6.3, 9.4
Min, Max	-22, 22	-6, 44	-22, 44

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX About My Feelings

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	8.3 (16.00)	-5.9 (23.93)	0.8 (21.52)
Median	5.0	-5.0	0.0
Q1,Q3	0.0, 10.0	-25.0, 10.0	-7.5, 10.0
Min, Max	-10, 50	-60, 30	-60, 50
Week 48			
n (%)	13 (62)	13 (72)	26 (67)
Mean (SD)	9.6 (26.57)	2.7 (16.66)	6.2 (22.01)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 15.0	-10.0, 10.0	-5.0, 10.0
Min, Max	-25, 65	-25, 35	-25, 65

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	8 (44)	20 (51)
Mean (SD)	-1.3 (15.83)	4.4 (20.43)	1.0 (17.52)
Median	2.5	0.0	0.0
Q1,Q3	-12.5, 10.0	-7.5, 17.5	-10.0, 12.5
Min, Max	-30, 20	-25, 40	-30, 40
Week 96			
n (%)	8 (38)	6 (33)	14 (36)
Mean (SD)	-6.3 (18.85)	16.7 (16.93)	3.6 (20.98)
Median	-12.5	20.0	5.0
Q1,Q3	-22.5, 12.5	0.0, 25.0	-20.0, 20.0
Min, Max	-25, 20	-5, 40	-25, 40

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. How I get Along With Others

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	-0.7 (9.42)	-0.3 (9.43)	-0.5 (9.28)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 5.0	-5.0, 5.0	-5.0, 5.0
Min, Max	-25, 10	-20, 15	-25, 15
Week 48			
n (%)	13 (62)	13 (72)	26 (67)
Mean (SD)	1.5 (8.99)	1.9 (10.32)	1.7 (9.48)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 0.0	0.0, 5.0	0.0, 5.0
Min, Max	-15, 25	-20, 25	-20, 25

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	8 (44)	20 (51)
Mean (SD)	3.3 (7.49)	2.5 (8.86)	3.0 (7.85)
Median	0.0	0.0	0.0
Q1,Q3	0.0, 10.0	-2.5, 10.0	0.0, 10.0
Min, Max	-5, 20	-10, 15	-10, 20
Week 96			
n (%)	8 (38)	6 (33)	14 (36)
Mean (SD)	-3.8 (5.82)	5.0 (15.49)	0.0 (11.44)
Median	0.0	0.0	0.0
Q1,Q3	-7.5, 0.0	0.0, 15.0	-5.0, 0.0
Min, Max	-15, 0	-15, 30	-15, 30

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About Work or School

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Week 24			
n (%)	15 (71)	17 (94)	32 (82)
Mean (SD)	6.0 (17.55)	-4.4 (14.56)	0.5 (16.62)
Median	0.0	0.0	0.0
Q1,Q3	-5.0, 10.0	-5.0, 5.0	-5.0, 7.5
Min, Max	-15, 50	-40, 15	-40, 50
Week 48			
n (%)	13 (62)	13 (72)	26 (67)
Mean (SD)	8.8 (16.85)	-2.3 (18.21)	3.3 (18.11)
Median	5.0	0.0	5.0
Q1,Q3	5.0, 10.0	-10.0, 10.0	-5.0, 10.0
Min, Max	-10, 55	-45, 25	-45, 55

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	12 (57)	8 (44)	20 (51)
Mean (SD)	-3.8 (8.82)	2.5 (13.89)	-1.3 (11.22)
Median	-2.5	7.5	0.0
Q1,Q3	-10.0, 2.5	-5.0, 12.5	-10.0, 7.5
Min, Max	-20, 10	-25, 15	-25, 15
Week 96			
n (%)	8 (38)	6 (33)	14 (36)
Mean (SD)	1.3 (17.68)	2.5 (10.37)	1.8 (14.49)
Median	5.0	7.5	5.0
Q1,Q3	-10.0, 12.5	-5.0, 10.0	-10.0, 10.0
Min, Max	-30, 25	-15, 10	-30, 25

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: This is based on calculated Change variable (CHG), CHG is calculated from follow up AVAL value minus baseline AVAL value.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE (CHG FROM BL)_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE_age13to14

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Health and Activities

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	13 (72)	12 (86)	25 (78)
Mean (SD)	84.9 (21.61)	81.5 (18.68)	83.3 (19.91)
Median	90.6	89.1	90.6
Q1,Q3	87.5, 96.9	64.1, 95.3	75.0, 96.9
Min, Max	19, 100	44, 100	19, 100
Week 24			
n (%)	16 (89)	13 (93)	29 (91)
Mean (SD)	80.5 (16.56)	81.3 (19.97)	80.8 (17.83)
Median	79.7	87.5	84.4
Q1,Q3	71.9, 95.3	75.0, 96.9	75.0, 96.9
Min, Max	47, 100	41, 100	41, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	83.5 (12.84)	80.9 (25.87)	82.4 (19.11)
Median	81.3	90.6	82.1
Q1,Q3	78.1, 93.8	78.1, 96.9	78.1, 96.9
Min, Max	59, 100	13, 100	13, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	83.5 (19.42)	88.7 (7.27)	85.3 (16.22)
Median	90.6	89.1	90.6
Q1,Q3	75.0, 96.9	82.8, 93.8	78.1, 96.9
Min, Max	28, 100	78, 100	28, 100
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	84.2 (11.30)	85.7 (14.64)	84.7 (12.12)
Median	81.3	87.5	84.4
Q1,Q3	75.0, 93.8	71.9, 100.0	75.0, 96.9
Min, Max	66, 100	69, 100	66, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Feelings

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	13 (72)	12 (86)	25 (78)
Mean (SD)	72.7 (23.86)	74.8 (17.53)	73.7 (20.65)
Median	80.0	77.5	80.0
Q1,Q3	65.0, 90.0	65.0, 85.0	65.0, 90.0
Min, Max	20, 100	38, 100	20, 100
Week 24			
n (%)	16 (89)	13 (93)	29 (91)
Mean (SD)	70.6 (27.13)	78.1 (21.75)	74.0 (24.73)
Median	80.0	90.0	80.0
Q1,Q3	57.5, 92.5	65.0, 90.0	60.0, 90.0
Min, Max	15, 100	35, 100	15, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	72.7 (29.20)	78.0 (27.61)	75.0 (28.00)
Median	85.0	90.0	85.0
Q1,Q3	55.0, 95.0	65.0, 100.0	55.0, 100.0
Min, Max	25, 100	25, 100	25, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	72.0 (29.99)	85.0 (18.71)	76.5 (26.90)
Median	85.0	87.5	85.0
Q1,Q3	50.0, 100.0	80.0, 100.0	55.0, 100.0
Min, Max	15, 100	45, 100	15, 100
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	70.7 (25.97)	85.7 (16.69)	75.5 (24.10)
Median	75.0	95.0	80.0
Q1,Q3	60.0, 90.0	65.0, 100.0	65.0, 95.0
Min, Max	20, 100	60, 100	20, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. How I get Along With Others

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	13 (72)	12 (86)	25 (78)
Mean (SD)	92.7 (13.79)	86.7 (16.70)	89.8 (15.24)
Median	100.0	95.0	95.0
Q1,Q3	95.0, 100.0	75.0, 100.0	85.0, 100.0
Min, Max	60, 100	45, 100	45, 100
Week 24			
n (%)	16 (89)	13 (93)	29 (91)
Mean (SD)	88.8 (14.20)	91.1 (12.95)	89.8 (13.46)
Median	95.0	95.0	95.0
Q1,Q3	77.5, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	55, 100	60, 100	55, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	90.8 (14.27)	86.5 (24.39)	88.9 (18.95)
Median	95.0	95.0	95.0
Q1,Q3	90.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	60, 100	20, 100	20, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	92.3 (11.93)	94.4 (6.78)	93.0 (10.31)
Median	100.0	97.5	100.0
Q1,Q3	90.0, 100.0	87.5, 100.0	90.0, 100.0
Min, Max	60, 100	85, 100	60, 100
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	91.3 (12.46)	95.0 (6.45)	92.5 (10.88)
Median	100.0	100.0	100.0
Q1,Q3	85.0, 100.0	90.0, 100.0	90.0, 100.0
Min, Max	65, 100	85, 100	65, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About Work or School

	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Baseline			
n (%)	13 (72)	12 (86)	25 (78)
Mean (SD)	74.2 (27.22)	74.2 (15.05)	74.2 (21.78)
Median	90.0	72.5	80.0
Q1,Q3	60.0, 90.0	67.5, 90.0	65.0, 90.0
Min, Max	5, 95	50, 95	5, 95
Week 24			
n (%)	16 (89)	12 (86)	28 (88)
Mean (SD)	66.3 (25.79)	78.3 (16.70)	71.4 (22.81)
Median	65.0	80.0	72.5
Q1,Q3	47.5, 95.0	67.5, 92.5	55.0, 95.0
Min, Max	25, 100	45, 100	25, 100
Week 48			
n (%)	13 (72)	10 (71)	23 (72)
Mean (SD)	73.8 (18.50)	75.5 (22.17)	74.6 (19.71)
Median	70.0	82.5	75.0
Q1,Q3	60.0, 95.0	70.0, 90.0	60.0, 95.0
Min, Max	50, 100	30, 100	30, 100

	DMF (N= 18)	**IFN B-1a (N= 14)**	**Total (N= 32)**
Week 72			
n (%)	15 (83)	8 (57)	23 (72)
Mean (SD)	72.6 (21.96)	81.9 (17.51)	75.8 (20.61)
Median	80.0	87.5	80.0
Q1,Q3	55.0, 90.0	75.0, 92.5	65.0, 90.0
Min, Max	35, 100	45, 100	35, 100
Week 96			
n (%)	15 (83)	7 (50)	22 (69)
Mean (SD)	70.7 (22.90)	76.4 (22.31)	72.5 (22.35)
Median	65.0	80.0	67.5
Q1,Q3	65.0, 90.0	60.0, 95.0	65.0, 95.0
Min, Max	15, 100	40, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE_age15to17

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Health and Activities

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	43 (81)	44 (88)	87 (84)
Mean (SD)	74.5 (22.64)	79.0 (18.66)	76.8 (20.73)
Median	78.1	82.8	81.3
Q1,Q3	62.5, 93.8	68.8, 93.8	65.6, 93.8
Min, Max	0, 100	28, 100	0, 100
Week 24			
n (%)	51 (96)	49 (98)	100 (97)
Mean (SD)	78.4 (17.64)	77.7 (19.77)	78.1 (18.62)
Median	84.4	81.3	82.8
Q1,Q3	65.6, 93.8	71.9, 93.8	67.2, 93.8
Min, Max	34, 100	22, 100	22, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	75.4 (20.78)	81.6 (15.67)	78.3 (18.76)
Median	81.3	85.9	81.3
Q1,Q3	59.4, 90.6	71.9, 93.8	65.6, 90.6
Min, Max	0, 100	34, 100	0, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	44 (83)	34 (68)	78 (76)
Mean (SD)	74.8 (21.03)	79.0 (17.51)	76.6 (19.56)
Median	79.7	87.5	84.4
Q1,Q3	56.3, 92.2	68.8, 93.8	62.5, 93.8
Min, Max	22, 100	44, 100	22, 100
Week 96			
n (%)	39 (74)	32 (64)	71 (69)
Mean (SD)	76.4 (21.31)	82.3 (17.69)	79.1 (19.85)
Median	84.4	85.9	84.4
Q1,Q3	59.4, 90.6	75.0, 96.9	68.8, 93.8
Min, Max	9, 100	28, 100	9, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Feelings

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	43 (81)	44 (88)	87 (84)
Mean (SD)	62.1 (25.62)	74.1 (18.69)	68.2 (23.05)
Median	65.0	75.0	70.0
Q1,Q3	45.0, 85.0	57.5, 87.5	55.0, 85.0
Min, Max	0, 100	30, 100	0, 100
Week 24			
n (%)	51 (96)	49 (98)	100 (97)
Mean (SD)	68.9 (21.08)	69.3 (20.18)	69.1 (20.54)
Median	70.0	70.0	70.0
Q1,Q3	55.0, 85.0	55.0, 85.0	55.0, 85.0
Min, Max	20, 100	25, 100	20, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	69.7 (24.14)	70.1 (20.38)	69.9 (22.36)
Median	70.0	70.0	70.0
Q1,Q3	60.0, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	10, 100	15, 100	10, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	44 (83)	34 (68)	78 (76)
Mean (SD)	68.0 (22.98)	69.7 (20.22)	68.7 (21.70)
Median	75.0	65.0	65.0
Q1,Q3	52.5, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	20, 100	25, 100	20, 100
Week 96			
n (%)	39 (74)	32 (64)	71 (69)
Mean (SD)	64.9 (24.75)	70.5 (22.12)	67.4 (23.60)
Median	70.0	72.5	70.0
Q1,Q3	45.0, 85.0	55.0, 90.0	50.0, 85.0
Min, Max	15, 100	20, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. How I get Along With Others

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	43 (81)	44 (88)	87 (84)
Mean (SD)	83.8 (21.15)	89.8 (14.34)	86.8 (18.17)
Median	95.0	95.0	95.0
Q1,Q3	70.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	20, 100	45, 100	20, 100
Week 24			
n (%)	51 (96)	49 (98)	100 (97)
Mean (SD)	86.6 (17.45)	89.4 (14.02)	88.0 (15.84)
Median	90.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	25, 100	50, 100	25, 100
Week 48			
n (%)	49 (92)	42 (84)	91 (88)
Mean (SD)	83.4 (21.76)	90.8 (13.83)	86.8 (18.80)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	30, 100	45, 100	30, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	44 (83)	34 (68)	78 (76)
Mean (SD)	84.8 (18.11)	91.9 (12.73)	87.9 (16.29)
Median	90.0	100.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	30, 100	50, 100	30, 100
Week 96			
n (%)	39 (74)	32 (64)	71 (69)
Mean (SD)	84.9 (19.31)	93.3 (11.54)	88.7 (16.71)
Median	95.0	100.0	95.0
Q1,Q3	75.0, 100.0	90.0, 100.0	80.0, 100.0
Min, Max	30, 100	60, 100	30, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About Work or School

	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Baseline			
n (%)	42 (79)	44 (88)	86 (83)
Mean (SD)	60.2 (24.24)	69.7 (18.47)	65.1 (21.88)
Median	60.0	75.0	67.5
Q1,Q3	50.0, 80.0	55.0, 85.0	50.0, 80.0
Min, Max	0, 100	25, 100	0, 100
Week 24			
n (%)	50 (94)	49 (98)	99 (96)
Mean (SD)	68.2 (20.94)	65.3 (22.37)	66.8 (21.60)
Median	65.0	65.0	65.0
Q1,Q3	55.0, 85.0	50.0, 85.0	50.0, 85.0
Min, Max	25, 100	10, 100	10, 100
Week 48			
n (%)	48 (91)	42 (84)	90 (87)
Mean (SD)	66.9 (23.35)	69.2 (19.88)	67.9 (21.71)
Median	65.0	70.0	70.0
Q1,Q3	50.0, 85.0	50.0, 85.0	50.0, 85.0
Min, Max	0, 100	30, 100	0, 100

	DMF (N= 53)	**IFN B-1a (N= 50)**	**Total (N= 103)**
Week 72			
n (%)	44 (83)	34 (68)	78 (76)
Mean (SD)	62.5 (23.95)	70.1 (18.81)	65.8 (22.06)
Median	67.5	67.5	67.5
Q1,Q3	42.5, 80.0	60.0, 85.0	50.0, 80.0
Min, Max	5, 100	25, 100	5, 100
Week 96			
n (%)	39 (74)	32 (64)	71 (69)
Mean (SD)	67.1 (21.73)	70.9 (22.56)	68.8 (22.03)
Median	70.0	72.5	70.0
Q1,Q3	55.0, 85.0	55.0, 90.0	55.0, 90.0
Min, Max	25, 100	15, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE_female

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Health and Activities

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	74.6 (22.38)	76.6 (19.21)	75.6 (20.76)
Median	78.1	84.4	81.3
Q1,Q3	62.5, 90.6	65.6, 90.6	65.6, 90.6
Min, Max	0, 100	28, 100	0, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	76.4 (16.67)	75.7 (19.27)	76.1 (17.88)
Median	79.7	81.3	81.3
Q1,Q3	65.6, 89.1	65.6, 87.5	65.6, 87.5
Min, Max	38, 100	22, 100	22, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	73.4 (19.51)	77.7 (18.72)	75.4 (19.16)
Median	75.0	81.3	79.7
Q1,Q3	59.4, 89.1	71.9, 90.6	62.5, 90.6
Min, Max	0, 100	13, 100	0, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	40 (80)	31 (67)	71 (74)
Mean (SD)	73.5 (20.92)	77.7 (17.23)	75.4 (19.38)
Median	75.0	87.5	81.3
Q1,Q3	56.3, 92.2	65.6, 90.6	56.3, 90.6
Min, Max	22, 100	44, 100	22, 100
Week 96			
n (%)	38 (76)	29 (63)	67 (70)
Mean (SD)	75.5 (20.47)	82.2 (14.99)	78.4 (18.48)
Median	79.7	84.4	81.3
Q1,Q3	62.5, 90.6	71.9, 93.8	68.8, 93.8
Min, Max	9, 100	50, 100	9, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Feelings

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	62.3 (24.57)	71.0 (18.21)	66.6 (21.96)
Median	65.0	75.0	70.0
Q1,Q3	45.0, 80.0	55.0, 85.0	55.0, 80.0
Min, Max	0, 100	30, 100	0, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	65.5 (23.25)	69.7 (20.68)	67.5 (22.03)
Median	67.5	70.0	70.0
Q1,Q3	50.0, 80.0	60.0, 90.0	55.0, 85.0
Min, Max	15, 100	25, 100	15, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	66.6 (26.08)	67.4 (21.68)	67.0 (24.00)
Median	70.0	70.0	70.0
Q1,Q3	52.5, 92.5	55.0, 80.0	55.0, 90.0
Min, Max	10, 100	15, 100	10, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	40 (80)	31 (67)	71 (74)
Mean (SD)	66.4 (25.22)	70.5 (21.03)	68.2 (23.41)
Median	70.0	70.0	70.0
Q1,Q3	50.0, 90.0	55.0, 90.0	55.0, 90.0
Min, Max	15, 100	25, 100	15, 100
Week 96			
n (%)	38 (76)	29 (63)	67 (70)
Mean (SD)	66.4 (25.70)	70.9 (20.96)	68.4 (23.70)
Median	67.5	70.0	70.0
Q1,Q3	45.0, 90.0	60.0, 90.0	50.0, 90.0
Min, Max	15, 100	20, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. How I get Along With Others

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	39 (78)	38 (83)	77 (80)
Mean (SD)	85.6 (20.81)	87.5 (16.06)	86.6 (18.52)
Median	95.0	95.0	95.0
Q1,Q3	70.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	20, 100	45, 100	20, 100
Week 24			
n (%)	48 (96)	45 (98)	93 (97)
Mean (SD)	87.5 (16.98)	89.0 (14.52)	88.2 (15.77)
Median	95.0	95.0	95.0
Q1,Q3	77.5, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	25, 100	50, 100	25, 100
Week 48			
n (%)	44 (88)	38 (83)	82 (85)
Mean (SD)	85.5 (20.02)	87.9 (17.69)	86.6 (18.90)
Median	95.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	30, 100	20, 100	20, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	40 (80)	31 (67)	71 (74)
Mean (SD)	87.6 (15.93)	91.0 (13.13)	89.1 (14.77)
Median	95.0	100.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	85.0, 100.0
Min, Max	35, 100	50, 100	35, 100
Week 96			
n (%)	38 (76)	29 (63)	67 (70)
Mean (SD)	88.4 (17.60)	94.3 (9.89)	91.0 (14.96)
Median	95.0	100.0	100.0
Q1,Q3	80.0, 100.0	95.0, 100.0	85.0, 100.0
Min, Max	30, 100	65, 100	30, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About Work or School

	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Baseline			
n (%)	38 (76)	38 (83)	76 (79)
Mean (SD)	61.7 (26.13)	69.1 (18.99)	65.4 (22.99)
Median	60.0	75.0	70.0
Q1,Q3	50.0, 80.0	50.0, 85.0	50.0, 85.0
Min, Max	0, 100	25, 100	0, 100
Week 24			
n (%)	47 (94)	44 (96)	91 (95)
Mean (SD)	66.2 (20.70)	67.2 (22.06)	66.6 (21.25)
Median	65.0	65.0	65.0
Q1,Q3	55.0, 80.0	50.0, 85.0	50.0, 85.0
Min, Max	25, 100	15, 100	15, 100
Week 48			
n (%)	43 (86)	38 (83)	81 (84)
Mean (SD)	65.8 (22.09)	68.7 (20.26)	67.2 (21.17)
Median	65.0	70.0	70.0
Q1,Q3	50.0, 85.0	50.0, 85.0	50.0, 85.0
Min, Max	0, 100	30, 100	0, 100

	DMF (N= 50)	**IFN B-1a (N= 46)**	**Total (N= 96)**
Week 72			
n (%)	40 (80)	31 (67)	71 (74)
Mean (SD)	64.8 (24.55)	69.8 (20.23)	67.0 (22.75)
Median	70.0	70.0	70.0
Q1,Q3	42.5, 80.0	55.0, 90.0	50.0, 85.0
Min, Max	5, 100	25, 100	5, 100
Week 96			
n (%)	38 (76)	29 (63)	67 (70)
Mean (SD)	67.2 (22.41)	71.4 (21.54)	69.0 (21.97)
Median	70.0	75.0	70.0
Q1,Q3	55.0, 85.0	55.0, 90.0	55.0, 90.0
Min, Max	15, 100	30, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_DESCRIBE_male

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About My Health and Activities

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	18 (100)	35 (90)
Mean (SD)	82.2 (23.04)	85.9 (15.62)	84.1 (19.37)
Median	90.6	93.8	90.6
Q1,Q3	71.9, 96.9	75.0, 100.0	71.9, 96.9
Min, Max	9, 100	56, 100	9, 100
Week 24			
n (%)	19 (90)	17 (94)	36 (92)
Mean (SD)	85.0 (17.73)	85.8 (19.46)	85.4 (18.30)
Median	87.5	93.8	90.6
Q1,Q3	71.9, 100.0	81.3, 100.0	76.6, 100.0
Min, Max	34, 100	25, 100	25, 100
Week 48			
n (%)	18 (86)	14 (78)	32 (82)
Mean (SD)	86.1 (17.06)	91.7 (9.22)	88.6 (14.26)
Median	90.6	93.8	90.6
Q1,Q3	81.3, 100.0	87.5, 100.0	82.8, 100.0
Min, Max	38, 100	69, 100	38, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	19 (90)	11 (61)	30 (77)
Mean (SD)	84.4 (19.09)	89.5 (10.39)	86.3 (16.43)
Median	90.6	93.8	90.6
Q1,Q3	78.1, 100.0	84.4, 96.9	81.3, 96.9
Min, Max	28, 100	69, 100	28, 100
Week 96			
n (%)	16 (76)	10 (56)	26 (67)
Mean (SD)	85.9 (14.07)	85.0 (22.86)	85.6 (17.52)
Median	89.1	96.9	90.6
Q1,Q3	84.4, 95.3	78.1, 100.0	78.1, 100.0
Min, Max	47, 100	28, 100	28, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About My Feelings

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	18 (100)	35 (90)
Mean (SD)	69.7 (27.30)	81.1 (16.94)	75.6 (22.97)
Median	70.0	85.0	85.0
Q1,Q3	50.0, 95.0	60.0, 95.0	55.0, 95.0
Min, Max	15, 100	55, 100	15, 100
Week 24			
n (%)	19 (90)	17 (94)	36 (92)
Mean (SD)	78.9 (17.37)	75.0 (20.69)	77.1 (18.84)
Median	80.0	75.0	77.5
Q1,Q3	65.0, 100.0	55.0, 90.0	62.5, 95.0
Min, Max	50, 100	35, 100	35, 100
Week 48			
n (%)	18 (86)	14 (78)	32 (82)
Mean (SD)	79.4 (20.21)	83.2 (18.46)	81.1 (19.25)
Median	82.5	90.0	85.0
Q1,Q3	65.0, 100.0	65.0, 100.0	65.0, 100.0
Min, Max	40, 100	45, 100	40, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	19 (90)	11 (61)	30 (77)
Mean (SD)	74.5 (23.39)	78.6 (19.12)	76.0 (21.67)
Median	80.0	80.0	80.0
Q1,Q3	60.0, 90.0	60.0, 100.0	60.0, 95.0
Min, Max	25, 100	50, 100	25, 100
Week 96			
n (%)	16 (76)	10 (56)	26 (67)
Mean (SD)	66.6 (23.99)	80.0 (24.15)	71.7 (24.49)
Median	70.0	90.0	72.5
Q1,Q3	55.0, 82.5	70.0, 95.0	60.0, 95.0
Min, Max	25, 100	25, 100	25, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. How I get Along With Others

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	18 (100)	35 (90)
Mean (SD)	86.5 (18.35)	92.5 (11.28)	89.6 (15.21)
Median	95.0	100.0	100.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	35, 100	70, 100	35, 100
Week 24			
n (%)	19 (90)	17 (94)	36 (92)
Mean (SD)	86.1 (16.21)	91.8 (11.45)	88.8 (14.26)
Median	90.0	95.0	95.0
Q1,Q3	75.0, 100.0	85.0, 100.0	80.0, 100.0
Min, Max	45, 100	60, 100	45, 100
Week 48			
n (%)	18 (86)	14 (78)	32 (82)
Mean (SD)	83.6 (22.28)	95.7 (9.38)	88.9 (18.61)
Median	95.0	100.0	97.5
Q1,Q3	80.0, 100.0	95.0, 100.0	85.0, 100.0
Min, Max	30, 100	65, 100	30, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	19 (90)	11 (61)	30 (77)
Mean (SD)	84.7 (19.33)	96.4 (5.52)	89.0 (16.58)
Median	90.0	100.0	95.0
Q1,Q3	80.0, 100.0	90.0, 100.0	85.0, 100.0
Min, Max	30, 100	85, 100	30, 100
Week 96			
n (%)	16 (76)	10 (56)	26 (67)
Mean (SD)	82.5 (18.17)	91.5 (13.34)	86.0 (16.79)
Median	87.5	100.0	90.0
Q1,Q3	72.5, 97.5	85.0, 100.0	80.0, 100.0
Min, Max	35, 100	60, 100	35, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About Work or School

	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Baseline			
n (%)	17 (81)	18 (100)	35 (90)
Mean (SD)	67.6 (24.05)	73.9 (14.81)	70.9 (19.80)
Median	70.0	75.0	75.0
Q1,Q3	55.0, 85.0	65.0, 90.0	60.0, 90.0
Min, Max	15, 95	45, 90	15, 95
Week 24			
n (%)	19 (90)	17 (94)	36 (92)
Mean (SD)	71.6 (25.17)	69.7 (21.97)	70.7 (23.40)
Median	65.0	75.0	75.0
Q1,Q3	50.0, 95.0	60.0, 85.0	55.0, 90.0
Min, Max	25, 100	10, 100	10, 100
Week 48			
n (%)	18 (86)	14 (78)	32 (82)
Mean (SD)	74.4 (22.74)	75.0 (20.29)	74.7 (21.36)
Median	75.0	80.0	80.0
Q1,Q3	60.0, 95.0	60.0, 90.0	60.0, 92.5
Min, Max	15, 100	40, 100	15, 100

	DMF (N= 21)	**IFN B-1a (N= 18)**	**Total (N= 39)**
Week 72			
n (%)	19 (90)	11 (61)	30 (77)
Mean (SD)	65.7 (22.43)	79.5 (12.93)	70.8 (20.39)
Median	68.8	80.0	72.5
Q1,Q3	50.0, 80.0	65.0, 90.0	60.0, 85.0
Min, Max	15, 100	65, 100	15, 100
Week 96			
n (%)	16 (76)	10 (56)	26 (67)
Mean (SD)	70.0 (21.21)	73.5 (25.61)	71.3 (22.56)
Median	67.5	72.5	70.0
Q1,Q3	50.0, 87.5	65.0, 95.0	60.0, 95.0
Min, Max	40, 100	15, 100	15, 100

Note: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_DESCRIBE_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_HEDGESCI_age13to14

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	-0.252	-1.074	0.569
	48	-0.136	-1.061	0.789
	72	-0.455	-1.435	0.524
	96	-0.741	-1.790	0.307
GET ALONG WITH OTHERS	24	-0.277	-1.099	0.546
	48	-0.235	-1.163	0.692
	72	-0.557	-1.543	0.430
	96	-1.023	-2.103	0.058
HEALTH AND ACTIVITIES	24	-0.201	-1.022	0.619
	48	-0.155	-1.081	0.770
	72	-0.431	-1.409	0.547
	96	-0.317	-1.336	0.702
SCHOOL	24	-0.235	-1.057	0.586
	48	-0.382	-1.315	0.552
	72	-0.466	-1.446	0.514
	96	-0.012	-1.025	1.000

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_HEDGESCI_age15to17

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	0.396	-0.057	0.850
	48	0.528	0.026	1.031
	72	0.072	-0.489	0.633
	96	-0.692	-1.432	0.048
GET ALONG WITH OTHERS	24	0	-0.449	0.449
	48	-0.028	-0.522	0.466
	72	0.045	-0.516	0.606
	96	-0.621	-1.356	0.115
HEALTH AND ACTIVITIES	24	0.323	-0.128	0.775
	48	0.078	-0.416	0.572
	72	0.092	-0.469	0.653
	96	-0.818	-1.567	-0.069
SCHOOL	24	0.507	0.051	0.963
	48	0.498	-0.004	1.000
	72	0.046	-0.515	0.607
	96	-0.025	-0.742	0.692

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_HEDGESCI_female

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	0.088	-0.388	0.565
	48	0.427	-0.108	0.962
	72	0.073	-0.506	0.651
	96	-0.442	-1.144	0.260
GET ALONG WITH OTHERS	24	-0.017	-0.493	0.459
	48	-0.086	-0.615	0.443
	72	-0.122	-0.701	0.457
	96	-0.697	-1.412	0.018
HEALTH AND ACTIVITIES	24	0.117	-0.360	0.593
	48	0.012	-0.517	0.541
	72	-0.01	-0.588	0.569
	96	-0.743	-1.461	-0.025
SCHOOL	24	0.203	-0.274	0.681
	48	0.184	-0.346	0.714
	72	0.092	-0.487	0.671
	96	-0.057	-0.750	0.636

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_HEDGESCI_male

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX

Trial	TIME POINTS	EFFECT SIZE	LOWER LIMIT	UPPER LIMIT
FEELINGS	24	0.69	-0.026	1.406
	48	0.312	-0.462	1.086
	72	-0.317	-1.217	0.584
	96	-1.268	-2.442	-0.094
GET ALONG WITH OTHERS	24	-0.04	-0.734	0.655
	48	-0.04	-0.809	0.729
	72	0.104	-0.792	0.999
	96	-0.799	-1.905	0.306
HEALTH AND ACTIVITIES	24	0.495	-0.211	1.200
	48	0.051	-0.718	0.820
	72	-0.014	-0.908	0.881
	96	-0.553	-1.635	0.528
SCHOOL	24	0.65	-0.064	1.363
	48	0.636	-0.154	1.425
	72	-0.565	-1.478	0.349
	96	-0.083	-1.142	0.976

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: The effect size is calculated as a Hedges' g using the change in scores between baseline and each follow-up timepoint.
Note3: Hedges' g calculation reference: Hedges, L.V. (1981, June). Distribution Theory for Glass's Estimator of Effect size and Related Estimators. Journal of Educational Statistics, 6(2), 107-128. https://doi.org/10.3102/10769986006002107.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_HEDGESCI_SubGr.sas date: 09MAR2022

109MS306_table45_47_CHG_LSMEANS_age13to14

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Health and Activities

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	12 (67)	11 (79)
Lsmean (SE)	1.78 (2.671)	2.60 (2.791)
Lsmean_95 % CI	(-3.791, 7.353)	(-3.218, 8.424)
Diffrence (95% CI)	-0.822 (-8.903, 7.259)	
SE_Difference	3.8740	
p-value	0.8341	
Week 48		
n (%)	9 (50)	9 (64)
Lsmean (SE)	-2.99 (4.785)	-0.48 (4.785)
Lsmean_95 % CI	(-13.189, 7.209)	(-10.681, 9.717)
Diffrence (95% CI)	-2.508 (-17.438, 12.423)	
SE_Difference	7.0048	
p-value	0.7253	

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	7 (50)
Lsmean (SE)	3.10 (2.642)	1.82 (3.201)
Lsmean_95 % CI	(-2.564, 8.769)	(-5.048, 8.683)
Diffrence (95% CI)	1.286 (-7.942, 10.514)	
SE_Difference	4.3024	
p-value	0.7695	
Week 96		
n (%)	10 (56)	6 (43)
Lsmean (SE)	-0.78 (4.095)	-0.79 (5.348)
Lsmean_95 % CI	(-9.622, 8.071)	(-12.345, 10.763)
Diffrence (95% CI)	0.016 (-14.848, 14.880)	
SE_Difference	6.8801	
p-value	0.9982	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About My Feelings

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	12 (67)	11 (79)
Lsmean (SE)	2.43 (3.174)	5.30 (3.316)
Lsmean_95 % CI	(-4.192, 9.052)	(-1.613, 12.220)
Diffrence (95% CI)	-2.874 (-12.456, 6.709)	
SE_Difference	4.5937	
p-value	0.5387	
Week 48		
n (%)	9 (50)	9 (64)
Lsmean (SE)	-1.81 (6.323)	0.98 (6.323)
Lsmean_95 % CI	(-15.288, 11.666)	(-12.499, 14.454)
Diffrence (95% CI)	-2.789 (-21.901, 16.324)	
SE_Difference	8.9669	
p-value	0.7601	

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	7 (50)
Lsmean (SE)	0.61 (5.530)	8.06 (6.613)
Lsmean_95 % CI	(-11.254, 12.465)	(-6.121, 22.247)
Diffrence (95% CI)	-7.457 (-25.978, 11.063)	
SE_Difference	8.6350	
p-value	0.4024	
Week 96		
n (%)	10 (56)	6 (43)
Lsmean (SE)	-1.25 (6.684)	13.33 (8.641)
Lsmean_95 % CI	(-15.689, 13.189)	(-5.334, 32.002)
Diffrence (95% CI)	-14.584 (-38.249, 9.081)	
SE_Difference	0.9540	
p-value	0.2059	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. How I get Along With Others

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	12 (67)	11 (79)
Lsmean (SE)	3.49 (1.493)	3.35 (1.561)
Lsmean_95 % CI	(0.380, 6.607)	(0.092, 6.603)
Diffrence (95% CI)	0.146 (-4.413, 4.705)	
SE_Difference	2.1855	
p-value	0.9474	
Week 48		
n (%)	9 (50)	9 (64)
Lsmean (SE)	-3.67 (3.206)	0.33 (3.206)
Lsmean_95 % CI	(-10.502, 3.166)	(-6.499, 7.168)
Diffrence (95% CI)	-4.003 (-13.937, 5.932)	
SE_Difference	4.6610	
p-value	0.4040	

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	7 (50)
Lsmean (SE)	1.77 (1.520)	2.47 (1.832)
Lsmean_95 % CI	(-1.488, 5.032)	(-1.462, 6.398)
Diffrence (95% CI)	-0.696 (-5.921, 4.529)	
SE_Difference	2.4362	
p-value	0.7793	
Week 96		
n (%)	10 (56)	6 (43)
Lsmean (SE)	-4.17 (3.308)	4.45 (4.319)
Lsmean_95 % CI	(-11.317, 2.976)	(-4.879, 13.781)
Diffrence (95% CI)	-8.621 (-20.617, 3.374)	
SE_Difference	5.5525	
p-value	0.1445	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 13 TO 14. About Work or School

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 24		
n (%)	12 (67)	11 (79)
Lsmean (SE)	-0.87 (3.595)	2.31 (3.755)
Lsmean_95 % CI	(-8.370, 6.631)	(-5.521, 10.146)
Diffrence (95% CI)	-3.182 (-14.027, 7.664)	
SE_Difference	5.1991	
p-value	0.5475	
Week 48		
n (%)	9 (50)	9 (64)
Lsmean (SE)	-6.50 (4.551)	0.39 (4.551)
Lsmean_95 % CI	(-16.205, 3.195)	(-9.306, 10.094)
Diffrence (95% CI)	-6.899 (-21.037, 7.239)	
SE_Difference	6.6329	
p-value	0.3148	

	DMF (N= 18)	**IFN B-1a (N= 14)**
Week 72		
n (%)	10 (56)	7 (50)
Lsmean (SE)	-0.65 (4.289)	4.51 (5.174)
Lsmean_95 % CI	(-9.853, 8.546)	(-6.592, 15.603)
Diffrence (95% CI)	-5.159 (-19.934, 9.616)	
SE_Difference	6.8886	
p-value	0.4663	
Week 96		
n (%)	10 (56)	6 (43)
Lsmean (SE)	-3.98 (8.090)	-5.04 (10.45)
Lsmean_95 % CI	(-21.452, 13.501)	(-27.617, 17.534)
Diffrence (95% CI)	1.066 (-27.517, 29.649)	
SE_Difference	3.2303	
p-value	0.9370	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table45_47_CHG_LSMEANS_age15to17

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Health and Activities

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	35 (66)	42 (84)
Lsmean (SE)	2.77 (2.083)	-1.19 (1.902)
Lsmean_95 % CI	(-1.385, 6.918)	(-4.979, 2.600)
Diffrence (95% CI)	3.956 (-1.666, 9.578)	
SE_Difference	2.8216	
p-value	0.1651	
Week 48		
n (%)	31 (58)	32 (64)
Lsmean (SE)	0.65 (2.109)	1.13 (2.076)
Lsmean_95 % CI	(-3.567, 4.871)	(-3.026, 5.278)
Diffrence (95% CI)	-0.474 (-6.416, 5.469)	
SE_Difference	2.9708	
p-value	0.8739	

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	26 (49)	23 (46)
Lsmean (SE)	-3.23 (2.841)	-2.19 (3.023)
Lsmean_95 % CI	(-8.947, 2.489)	(-8.277, 3.892)
Diffrence (95% CI)	-1.037 (-9.444, 7.370)	
SE_Difference	4.1766	
p-value	0.8051	
Week 96		
n (%)	14 (26)	16 (32)
Lsmean (SE)	-9.85 (4.407)	3.54 (4.121)
Lsmean_95 % CI	(-18.891, -0.807)	(-4.917, 11.996)
Diffrence (95% CI)	-13.389 (-25.790, -0.987)	
SE_Difference	6.0439	
p-value	0.0354	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About My Feelings

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	35 (66)	42 (84)
Lsmean (SE)	1.58 (3.015)	-1.55 (2.745)
Lsmean_95 % CI	(-4.430, 7.585)	(-7.021, 3.916)
Diffrence (95% CI)	3.130 (-5.119, 11.379)	
SE_Difference	4.1400	
p-value	0.4520	
Week 48		
n (%)	31 (58)	32 (64)
Lsmean (SE)	6.57 (3.287)	0.36 (3.234)
Lsmean_95 % CI	(-0.010, 13.141)	(-6.111, 6.827)
Diffrence (95% CI)	6.207 (-3.144, 15.559)	
SE_Difference	4.6749	
p-value	0.1893	

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	26 (49)	23 (46)
Lsmean (SE)	1.16 (3.212)	4.34 (3.422)
Lsmean_95 % CI	(-5.305, 7.627)	(-2.548, 11.228)
Diffrence (95% CI)	-3.179 (-12.778, 6.420)	
SE_Difference	4.7688	
p-value	0.5083	
Week 96		
n (%)	14 (26)	16 (32)
Lsmean (SE)	-9.65 (4.251)	7.82 (3.969)
Lsmean_95 % CI	(-18.370, -0.927)	(-0.326, 15.960)
Diffrence (95% CI)	-17.465 (-29.560, -5.370)	
SE_Difference	5.8947	
p-value	0.0063	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. How I get Along With Others

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	35 (66)	42 (84)
Lsmean (SE)	-1.07 (1.763)	-0.42 (1.609)
Lsmean_95 % CI	(-4.580, 2.447)	(-3.628, 2.786)
Diffrence (95% CI)	-0.645 (-5.407, 4.117)	
SE_Difference	2.3898	
p-value	0.7879	
Week 48		
n (%)	31 (58)	32 (64)
Lsmean (SE)	0.047 (1.838)	0.89 (1.809)
Lsmean_95 % CI	(-3.630, 3.724)	(-2.727, 4.511)
Diffrence (95% CI)	-0.846 (-6.011, 4.320)	
SE_Difference	2.5823	
p-value	0.7445	

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	26 (49)	23 (46)
Lsmean (SE)	0.49 (1.883)	1.40 (2.003)
Lsmean_95 % CI	(-3.303, 4.279)	(-2.628, 5.437)
Diffrence (95% CI)	-0.916 (-6.471, 4.638)	
SE_Difference	2.7595	
p-value	0.7414	
Week 96		
n (%)	14 (26)	16 (32)
Lsmean (SE)	-3.95 (3.780)	5.33 (3.535)
Lsmean_95 % CI	(-11.709, 3.803)	(-1.921, 12.588)
Diffrence (95% CI)	-9.286 (-19.919, 1.346)	
SE_Difference	5.1817	
p-value	0.0843	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for AGES 15 TO 17. About Work or School

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 24		
n (%)	35 (66)	42 (84)
Lsmean (SE)	3.82 (2.545)	-1.99 (2.319)
Lsmean_95 % CI	(-1.253, 8.887)	(-6.610, 2.630)
Diffrence (95% CI)	5.807 (-1.121, 12.736)	
SE_Difference	3.4772	
p-value	0.0991	
Week 48		
n (%)	31 (58)	32 (64)
Lsmean (SE)	6.58 (2.942)	1.91 (2.894)
Lsmean_95 % CI	(0.693, 12.463)	(-3.880, 7.698)
Diffrence (95% CI)	4.669 (-3.730, 13.068)	
SE_Difference	4.1989	
p-value	0.2706	

	DMF (N= 53)	**IFN B-1a (N= 50)**
Week 72		
n (%)	26 (49)	23 (46)
Lsmean (SE)	-1.56 (3.031)	2.63 (3.232)
Lsmean_95 % CI	(-7.661, 4.541)	(-3.874, 9.139)
Diffrence (95% CI)	-4.192 (-13.331, 4.946)	
SE_Difference	4.5398	
p-value	0.3606	
Week 96		
n (%)	14 (26)	16 (32)
Lsmean (SE)	-2.47 (5.754)	3.42 (5.370)
Lsmean_95 % CI	(-14.280, 9.331)	(-7.604, 14.434)
Diffrence (95% CI)	-5.890 (-22.300, 10.521)	
SE_Difference	7.9979	
p-value	0.4678	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table45_47_CHG_LSMEANS_female

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Health and Activities

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	32 (64)	36 (78)
Lsmean (SE)	2.12 (2.403)	-0.24 (2.281)
Lsmean_95 % CI	(-2.681, 6.921)	(-4.793, 4.322)
Diffrence (95% CI)	2.356 (-3.625, 8.337)	
SE_Difference	2.9940	
p-value	0.4343	
Week 48		
n (%)	27 (54)	28 (61)
Lsmean (SE)	-2.29 (3.036)	-2.35 (2.931)
Lsmean_95 % CI	(-8.390, 3.802)	(-8.230, 3.539)
Diffrence (95% CI)	0.051 (-7.428, 7.530)	
SE_Difference	3.7254	
p-value	0.9891	

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	24 (48)	22 (48)
Lsmean (SE)	-0.77 (3.281)	1.31 (3.403)
Lsmean_95 % CI	(-7.391, 5.850)	(-5.562, 8.175)
Diffrence (95% CI)	-2.077 (-10.652, 6.499)	
SE_Difference	4.2493	
p-value	0.6276	
Week 96		
n (%)	16 (32)	16 (35)
Lsmean (SE)	-9.80 (4.085)	1.81 (4.195)
Lsmean_95 % CI	(-18.172, -1.437)	(-6.780, 10.408)
Diffrence (95% CI)	-11.618 (-22.978, -0.259)	
SE_Difference	5.5455	
p-value	0.0453	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About My Feelings

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	32 (64)	36 (78)
Lsmean (SE)	0.69 (3.198)	1.27 (3.057)
Lsmean_95 % CI	(-5.704, 7.075)	(-4.836, 7.379)
Diffrence (95% CI)	-0.586 (-8.660, 7.488)	
SE_Difference	4.0415	
p-value	0.8851	
Week 48		
n (%)	27 (54)	28 (61)
Lsmean (SE)	0.87 (3.970)	-4.96 (3.876)
Lsmean_95 % CI	(-7.099, 8.842)	(-12.741, 2.823)
Diffrence (95% CI)	5.831 (-4.106, 15.767)	
SE_Difference	4.9495	
p-value	0.2443	

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	24 (48)	22 (48)
Lsmean (SE)	1.28 (3.838)	3.55 (4.047)
Lsmean_95 % CI	(-6.462, 9.028)	(-4.621, 11.714)
Diffrence (95% CI)	-2.264 (-12.544, 8.016)	
SE_Difference	5.0940	
p-value	0.6590	
Week 96		
n (%)	16 (32)	16 (35)
Lsmean (SE)	-5.74 (4.869)	6.47 (5.117)
Lsmean_95 % CI	(-15.711, 4.238)	(-4.016, 16.948)
Diffrence (95% CI)	-12.203 (-26.121, 1.716)	
SE_Difference	6.7946	
p-value	0.0833	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. How I get Along With Others

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	32 (64)	36 (78)
Lsmean (SE)	2.10 (1.947)	1.29 (1.854)
Lsmean_95 % CI	(-1.787, 5.994)	(-2.410, 4.998)
Diffrence (95% CI)	0.810 (-4.053, 5.672)	
SE_Difference	2.4340	
p-value	0.7405	
Week 48		
n (%)	27 (54)	28 (61)
Lsmean (SE)	-1.90 (2.378)	-1.67 (2.284)
Lsmean_95 % CI	(-6.679, 2.870)	(-6.253, 2.919)
Diffrence (95% CI)	-0.238 (-6.126, 5.651)	
SE_Difference	2.9332	
p-value	0.9357	

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	24 (48)	22 (48)
Lsmean (SE)	0.98 (2.224)	1.81 (2.263)
Lsmean_95 % CI	(-3.512, 5.463)	(-2.761, 6.375)
Diffrence (95% CI)	-0.831 (-6.581, 4.918)	
SE_Difference	2.8491	
p-value	0.7719	
Week 96		
n (%)	16 (32)	16 (35)
Lsmean (SE)	-3.69 (3.796)	5.06 (3.861)
Lsmean_95 % CI	(-11.462, 4.091)	(-2.851, 12.968)
Diffrence (95% CI)	-8.744 (-19.288, 1.799)	
SE_Difference	5.1471	
p-value	0.1004	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for FEMALE SEX. About Work or School

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 24		
n (%)	32 (64)	36 (78)
Lsmean (SE)	2.52 (2.613)	1.36 (2.507)
Lsmean_95 % CI	(-2.695, 7.744)	(-3.646, 6.372)
Diffrence (95% CI)	1.162 (-5.398, 7.721)	
SE_Difference	3.2836	
p-value	0.7247	
Week 48		
n (%)	27 (54)	28 (61)
Lsmean (SE)	0.91 (3.349)	0.24 (3.299)
Lsmean_95 % CI	(-5.815, 7.631)	(-6.384, 6.861)
Diffrence (95% CI)	0.670 (-7.674, 9.014)	
SE_Difference	4.1562	
p-value	0.8726	

	DMF (N= 50)	**IFN B-1a (N= 46)**
Week 72		
n (%)	24 (48)	22 (48)
Lsmean (SE)	2.95 (3.559)	4.94 (3.799)
Lsmean_95 % CI	(-4.234, 10.130)	(-2.725, 12.607)
Diffrence (95% CI)	-1.993 (-11.443, 7.456)	
SE_Difference	4.6824	
p-value	0.6725	
Week 96		
n (%)	16 (32)	16 (35)
Lsmean (SE)	-5.67 (6.284)	-0.46 (6.677)
Lsmean_95 % CI	(-18.547, 7.198)	(-14.141, 13.214)
Diffrence (95% CI)	-5.211 (-23.002, 12.580)	
SE_Difference	8.6851	
p-value	0.5533	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

109MS306_table45_47_CHG_LSMEANS_male

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About My Health and Activities

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	17 (94)
Lsmean (SE)	5.13 (2.729)	1.11 (2.854)
Lsmean_95 % CI	(-0.463, 10.717)	(-4.733, 6.961)
Diffrence (95% CI)	4.013 (-3.573, 11.599)	
SE_Difference	3.7032	
p-value	0.2878	
Week 48		
n (%)	13 (62)	13 (72)
Lsmean (SE)	4.07 (1.519)	4.70 (1.592)
Lsmean_95 % CI	(0.923, 7.224)	(1.393, 7.998)
Diffrence (95% CI)	-0.622 (-4.913, 3.669)	
SE_Difference	2.0690	
p-value	0.7665	

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	8 (44)
Lsmean (SE)	2.20 (2.094)	3.35 (2.685)
Lsmean_95 % CI	(-2.243, 6.637)	(-2.338, 9.045)
Diffrence (95% CI)	-1.157 (-8.221, 5.906)	
SE_Difference	3.3318	
p-value	0.7329	
Week 96		
n (%)	8 (38)	6 (33)
Lsmean (SE)	3.44 (4.573)	4.79 (5.367)
Lsmean_95 % CI	(-6.749, 13.629)	(-7.170, 16.746)
Diffrence (95% CI)	-1.348 (-17.910, 15.214)	
SE_Difference	7.4331	
p-value	0.8597	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About My Feelings

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	17 (94)
Lsmean (SE)	7.77 (4.249)	1.38 (4.487)
Lsmean_95 % CI	(-0.930, 16.476)	(-7.813, 10.568)
Diffrence (95% CI)	6.395 (-5.616, 18.406)	
SE_Difference	5.8635	
p-value	0.2847	
Week 48		
n (%)	13 (62)	13 (72)
Lsmean (SE)	10.64 (4.802)	8.56 (5.069)
Lsmean_95 % CI	(0.684, 20.602)	(-1.948, 19.077)
Diffrence (95% CI)	2.079 (-11.574, 15.731)	
SE_Difference	6.5831	
p-value	0.7552	

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	8 (44)
Lsmean (SE)	0.49 (3.927)	10.23 (5.041)
Lsmean_95 % CI	(-7.830, 8.819)	(-0.457, 20.917)
Diffrence (95% CI)	-9.735 (-22.990, 3.519)	
SE_Difference	6.2523	
p-value	0.1390	
Week 96		
n (%)	8 (38)	6 (33)
Lsmean (SE)	-8.08 (3.891)	19.11 (4.537)
Lsmean_95 % CI	(-16.753, 0.585)	(9.003, 29.221)
Diffrence (95% CI)	-27.196 (-40.954, -13.437)	
SE_Difference	6.1748	
p-value	0.0013	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. How I get Along With Others

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	17 (94)
Lsmean (SE)	-0.68 (2.306)	2.23 (2.417)
Lsmean_95 % CI	(-5.405, 4.043)	(-2.718, 7.184)
Diffrence (95% CI)	-2.914 (-9.404, 3.576)	
SE_Difference	3.1681	
p-value	0.3656	
Week 48		
n (%)	13 (62)	13 (72)
Lsmean (SE)	0.81 (2.827)	2.83 (2.983)
Lsmean_95 % CI	(-5.055, 6.670)	(-3.357, 9.015)
Diffrence (95% CI)	-2.022 (-10.210, 6.167)	
SE_Difference	3.9482	
p-value	0.6137	

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	8 (44)
Lsmean (SE)	2.72 (1.733)	4.36 (2.245)
Lsmean_95 % CI	(-0.948, 6.397)	(-0.402, 9.115)
Diffrence (95% CI)	-1.632 (-7.568, 4.303)	
SE_Difference	2.7999	
p-value	0.5680	
Week 96		
n (%)	8 (38)	6 (33)
Lsmean (SE)	-3.77 (3.680)	5.03 (4.279)
Lsmean_95 % CI	(-11.968, 4.429)	(-4.509, 14.561)
Diffrence (95% CI)	-8.795 (-21.675, 4.085)	
SE_Difference	5.7805	
p-value	0.1591	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source: W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

Table 45: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment - mITT Population, Aged 13 years and older (n=135). Subgroup analysis for MALE SEX. About Work or School

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 24		
n (%)	15 (71)	17 (94)
Lsmean (SE)	4.82 (4.355)	-5.96 (4.622)
Lsmean_95 % CI	(-4.102, 13.739)	(-15.425, 3.512)
Diffrence (95% CI)	10.775 (-1.504, 23.054)	
SE_Difference	5.9943	
p-value	0.0830	
Week 48		
n (%)	13 (62)	13 (72)
Lsmean (SE)	8.08 (5.071)	-1.24 (5.474)
Lsmean_95 % CI	(-2.432, 18.601)	(-12.594, 10.110)
Diffrence (95% CI)	9.327 (-5.276, 23.930)	
SE_Difference	7.0412	
p-value	0.1989	

	DMF (N= 21)	**IFN B-1a (N= 18)**
Week 72		
n (%)	12 (57)	8 (44)
Lsmean (SE)	-3.42 (3.361)	3.73 (4.411)
Lsmean_95 % CI	(-10.549, 3.700)	(-5.625, 13.078)
Diffrence (95% CI)	-7.151 (-18.732, 4.430)	
SE_Difference	5.4631	
p-value	0.2090	
Week 96		
n (%)	8 (38)	6 (33)
Lsmean (SE)	-0.11 (5.548)	4.32 (6.449)
Lsmean_95 % CI	(-12.474, 12.250)	(-10.054, 18.685)
Diffrence (95% CI)	-4.427 (-23.809, 14.955)	
SE_Difference	8.6986	
p-value	0.6218	

Note1: Only results for subgroups that fulfill the criterium of >=10 patients in every arm and subgroup are presented
Note2: LS Means were calculated based on multiple linear regression, which is the same as ANCOVA model. Change from baseline to follow up (follow-up minus baseline)was the outcome (dependent variable)and treatment group, age group and baseline score were as covariates.
NOTE3: Change from baseline to follow up (follow-up minus baseline) was the outcome (dependent variable)
NOTE4: Treatment group, age group and baseline score were covariates.
NOTE5: For age subgroup analyses, we did NOT include AGE as a covariate.
Source:
W:\Biogen\109MS306\TFLs\SubGroup\T45_47/109MS306_table45_47_CHG_LSMEANS_SubGr.sas date: 18APR2022

MCID 4,4

109MS306_Table45_47_MCID_4.4_EFFECTMEASURES_age13to14

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.600	0.692	-0.103
	95% CI	(0.103, 3.495)	(0.193, 2.477)	(-0.454, 0.249)
	p-value	0.5699	0.5718	0.5675
Feelings scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.255	0.369	-0.263
	95% CI	(0.038, 1.692)	(0.087, 1.558)	(-0.604, 0.078)
	p-value	0.1568	0.1750	0.1309
Feelings scale Week 72 >=4.4 point decrease from baseline	Effect measure	2.222	1.846	0.141
	95% CI	(0.325, 15.180)	(0.410, 8.317)	(-0.187, 0.469)
	p-value	0.4153	0.4247	0.3990
Feelings scale Week 96 >=4.4 point decrease from baseline	Effect measure	3.125	2.308	0.218
	95% CI	(0.474, 20.583)	(0.547, 9.739)	(-0.120, 0.556)
	p-value	0.2361	0.2550	0.2066

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
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NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.909	0.923	-0.013
	95% CI	(0.107, 7.718)	(0.153, 5.562)	(-0.301, 0.275)
	p-value	0.9304	0.9304	0.9305
Get along scale Week 48 >=4.4 point decrease from baseline	Effect measure	2.222	1.846	0.141
	95% CI	(0.325, 15.180)	(0.410, 8.317)	(-0.187, 0.469)
	p-value	0.4153	0.4247	0.3990
Get along scale Week 72 >=4.4 point decrease from baseline	Effect measure	2.000	1.846	0.071
	95% CI	(0.157, 25.404)	(0.191, 17.845)	(-0.180, 0.321)
	p-value	0.5930	0.5963	0.5817
Get along scale Week 96 >=4.4 point decrease from baseline	Effect measure	3.300	2.769	0.147
	95% CI	(0.294, 37.103)	(0.331, 23.136)	(-0.130, 0.425)
	p-value	0.3335	0.3470	0.2974

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point decrease from baseline	Effect measure	3.125	2.308	0.218
	95% CI	(0.474, 20.583)	(0.547, 9.739)	(-0.120, 0.556)
	p-value	0.2361	0.2550	0.2066
Health scale Week 72 >=4.4 point decrease from baseline	Effect measure	3.300	2.769	0.147
	95% CI	(0.294, 37.103)	(0.331, 23.136)	(-0.130, 0.425)
	p-value	0.3335	0.3470	0.2974
Health scale Week 96 >=4.4 point decrease from baseline	Effect measure	4.889	3.692	0.224
	95% CI	(0.461, 51.869)	(0.477, 28.568)	(-0.071, 0.520)
	p-value	0.1878	0.2108	0.1369

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point decrease from baseline	Effect measure	1.875	1.538	0.135
	95% CI	(0.336, 10.463)	(0.465, 5.093)	(-0.226, 0.495)
	p-value	0.4736	0.4806	0.4642
School scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.333	1.231	0.058
	95% CI	(0.230, 7.743)	(0.344, 4.404)	(-0.293, 0.408)
	p-value	0.7486	0.7496	0.7471
School scale Week 72 >=4.4 point decrease from baseline	Effect measure	4.286	2.769	0.295
	95% CI	(0.661, 27.785)	(0.686, 11.171)	(-0.048, 0.638)
	p-value	0.1270	0.1523	0.0923
School scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.875	1.538	0.135
	95% CI	(0.336, 10.463)	(0.465, 5.093)	(-0.226, 0.495)
	p-value	0.4736	0.4806	0.4642

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point increase from baseline	Effect measure	2.240	1.477	0.199
	95% CI	(0.451, 11.114)	(0.667, 3.272)	(-0.186, 0.583)
	p-value	0.3237	0.3367	0.3109
Feelings scale Week 48 >=4.4 point increase from baseline	Effect measure	0.889	0.923	-0.026
	95% CI	(0.165, 4.777)	(0.295, 2.893)	(-0.392, 0.341)
	p-value	0.8908	0.8908	0.8908
Feelings scale Week 72 >=4.4 point increase from baseline	Effect measure	1.250	1.154	0.051
	95% CI	(0.243, 6.443)	(0.402, 3.314)	(-0.324, 0.427)
	p-value	0.7897	0.7904	0.7890
Feelings scale Week 96 >=4.4 point increase from baseline	Effect measure	1.250	1.154	0.051
	95% CI	(0.243, 6.443)	(0.402, 3.314)	(-0.324, 0.427)
	p-value	0.7897	0.7904	0.7890

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point increase from baseline	Effect measure	0.317	0.527	-0.276
	95% CI	(0.061, 1.644)	(0.205, 1.357)	(-0.651, 0.100)
	p-value	0.1714	0.1847	0.1499
Get along scale Week 48 >=4.4 point increase from baseline	Effect measure	0.167	0.231	-0.256
	95% CI	(0.016, 1.777)	(0.030, 1.785)	(-0.560, 0.047)
	p-value	0.1379	0.1601	0.0978
Get along scale Week 72 >=4.4 point increase from baseline	Effect measure	0.117	0.185	-0.340
	95% CI	(0.011, 1.212)	(0.025, 1.362)	(-0.654, -0.025)
	p-value	0.0720	0.0975	0.0341
Get along scale Week 96 >=4.4 point increase from baseline	Effect measure	0.070	0.103	-0.333
	95% CI	(0.003, 1.470)	(0.006, 1.724)	(-0.680, 0.014)
	p-value	0.0869	0.1138	0.0628

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point increase from baseline	Effect measure	0.875	0.923	-0.032
	95% CI	(0.176, 4.341)	(0.354, 2.410)	(-0.416, 0.352)
	p-value	0.8702	0.8701	0.8702
Health scale Week 48 >=4.4 point increase from baseline	Effect measure	0.167	0.231	-0.256
	95% CI	(0.016, 1.777)	(0.030, 1.785)	(-0.560, 0.047)
	p-value	0.1379	0.1601	0.0978
Health scale Week 72 >=4.4 point increase from baseline	Effect measure	0.900	0.923	-0.019
	95% CI	(0.143, 5.646)	(0.229, 3.724)	(-0.355, 0.316)
	p-value	0.9105	0.9104	0.9105
Health scale Week 96 >=4.4 point increase from baseline	Effect measure	1.333	1.231	0.058
	95% CI	(0.230, 7.743)	(0.344, 4.404)	(-0.293, 0.408)
	p-value	0.7486	0.7496	0.7471

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
School scale Week 24 >=4.4 point increase from baseline	Effect measure	0.444	0.615	-0.192
	95% CI	(0.087, 2.276)	(0.228, 1.660)	(-0.570, 0.186)
	p-value	0.3305	0.3377	0.3189
School scale Week 48 >=4.4 point increase from baseline	Effect measure	0.622	0.738	-0.109
	95% CI	(0.120, 3.222)	(0.257, 2.121)	(-0.484, 0.266)
	p-value	0.5717	0.5733	0.5692
School scale Week 72 >=4.4 point increase from baseline	Effect measure	0.889	0.923	-0.026
	95% CI	(0.165, 4.777)	(0.295, 2.893)	(-0.392, 0.341)
	p-value	0.8908	0.8908	0.8908
School scale Week 96 >=4.4 point increase from baseline	Effect measure	1.875	1.538	0.135
	95% CI	(0.336, 10.463)	(0.465, 5.093)	(-0.226, 0.495)
	p-value	0.4736	0.4806	0.4642

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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109MS306_Table45_47_MCID_4.4_EFFECTMEASURES_age15to17

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.864	0.921	-0.036
	95% CI	(0.370, 2.018)	(0.571, 1.486)	(-0.244, 0.172)
	p-value	0.7355	0.7358	0.7352
Feelings scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.688	0.782	-0.084
	95% CI	(0.283, 1.676)	(0.435, 1.408)	(-0.283, 0.115)
	p-value	0.4105	0.4130	0.4075
Feelings scale Week 72 >=4.4 point decrease from baseline	Effect measure	0.929	0.950	-0.016
	95% CI	(0.374, 2.304)	(0.508, 1.779)	(-0.210, 0.179)
	p-value	0.8730	0.8731	0.8730
Feelings scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.151	1.102	0.030
	95% CI	(0.464, 2.857)	(0.589, 2.063)	(-0.164, 0.225)
	p-value	0.7614	0.7615	0.7613

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.737	0.804	-0.062
	95% CI	(0.290, 1.874)	(0.412, 1.569)	(-0.252, 0.127)
	p-value	0.5210	0.5224	0.5191
Get along scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.178	1.137	0.028
	95% CI	(0.426, 3.263)	(0.513, 2.521)	(-0.146, 0.202)
	p-value	0.7520	0.7521	0.7519
Get along scale Week 72 >=4.4 point decrease from baseline	Effect measure	2.452	2.047	0.143
	95% CI	(0.825, 7.283)	(0.844, 4.960)	(-0.025, 0.311)
	p-value	0.1065	0.1129	0.0961
Get along scale Week 96 >=4.4 point decrease from baseline	Effect measure	3.019	2.456	0.165
	95% CI	(0.961, 9.487)	(0.945, 6.381)	(0.002, 0.329)
	p-value	0.0585	0.0652	0.0475

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	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.649	0.731	-0.086
	95% CI	(0.251, 1.679)	(0.365, 1.463)	(-0.272, 0.101)
	p-value	0.3731	0.3761	0.3689
Health scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.287	1.194	0.053
	95% CI	(0.513, 3.231)	(0.625, 2.279)	(-0.139, 0.245)
	p-value	0.5906	0.5912	0.5899
Health scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.505	1.364	0.075
	95% CI	(0.559, 4.052)	(0.641, 2.903)	(-0.105, 0.254)
	p-value	0.4182	0.4201	0.4155

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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.608	0.748	-0.120
	95% CI	(0.256, 1.445)	(0.449, 1.246)	(-0.327, 0.087)
	p-value	0.2603	0.2653	0.2550
School scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.857	0.898	-0.032
	95% CI	(0.341, 2.156)	(0.471, 1.711)	(-0.226, 0.161)
	p-value	0.7432	0.7435	0.7428
School scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.333	1.222	0.061
	95% CI	(0.530, 3.355)	(0.641, 2.329)	(-0.133, 0.255)
	p-value	0.5412	0.5419	0.5404
School scale Week 96 >=4.4 point decrease from baseline	Effect measure	0.946	0.960	-0.011
	95% CI	(0.364, 2.461)	(0.477, 1.935)	(-0.198, 0.176)
	p-value	0.9098	0.9098	0.9097

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	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point increase from baseline	Effect measure	1.144	1.087	0.032
	95% CI	(0.481, 2.722)	(0.635, 1.862)	(-0.172, 0.236)
	p-value	0.7606	0.7607	0.7604
Feelings scale Week 48 >=4.4 point increase from baseline	Effect measure	2.498	1.732	0.216
	95% CI	(1.035, 6.032)	(1.007, 2.977)	(0.015, 0.417)
	p-value	0.0418	0.0470	0.0353
Feelings scale Week 72 >=4.4 point increase from baseline	Effect measure	2.545	1.791	0.216
	95% CI	(1.042, 6.218)	(1.011, 3.171)	(0.017, 0.415)
	p-value	0.0403	0.0456	0.0338
Feelings scale Week 96 >=4.4 point increase from baseline	Effect measure	1.429	1.279	0.076
	95% CI	(0.573, 3.559)	(0.680, 2.407)	(-0.118, 0.270)
	p-value	0.4438	0.4454	0.4418

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	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point increase from baseline	Effect measure	1.580	1.364	0.099
	95% CI	(0.638, 3.914)	(0.734, 2.535)	(-0.096, 0.295)
	p-value	0.3227	0.3255	0.3190
Get along scale Week 48 >=4.4 point increase from baseline	Effect measure	1.821	1.535	0.122
	95% CI	(0.709, 4.680)	(0.777, 3.032)	(-0.067, 0.310)
	p-value	0.2130	0.2175	0.2068
Get along scale Week 72 >=4.4 point increase from baseline	Effect measure	0.929	0.950	-0.016
	95% CI	(0.374, 2.304)	(0.508, 1.779)	(-0.210, 0.179)
	p-value	0.8730	0.8731	0.8730
Get along scale Week 96 >=4.4 point increase from baseline	Effect measure	0.631	0.708	-0.086
	95% CI	(0.237, 1.681)	(0.338, 1.483)	(-0.268, 0.095)
	p-value	0.3572	0.3604	0.3523

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point increase from baseline	Effect measure	2.667	2.047	0.190
	95% CI	(0.996, 7.137)	(0.979, 4.278)	(0.006, 0.374)
	p-value	0.0509	0.0570	0.0427
Health scale Week 48 >=4.4 point increase from baseline	Effect measure	1.607	1.395	0.099
	95% CI	(0.636, 4.060)	(0.725, 2.686)	(-0.093, 0.290)
	p-value	0.3157	0.3186	0.3117
Health scale Week 72 >=4.4 point increase from baseline	Effect measure	3.456	2.485	0.236
	95% CI	(1.255, 9.518)	(1.147, 5.385)	(0.055, 0.418)
	p-value	0.0164	0.0211	0.0108
Health scale Week 96 >=4.4 point increase from baseline	Effect measure	1.742	1.535	0.097
	95% CI	(0.631, 4.808)	(0.697, 3.381)	(-0.079, 0.273)
	p-value	0.2840	0.2876	0.2787

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	Result	OR	RR	ARR
School scale Week 24 >=4.4 point increase from baseline	Effect measure	1.315	1.187	0.064
	95% CI	(0.547, 3.158)	(0.685, 2.059)	(-0.140, 0.268)
	p-value	0.5407	0.5412	0.5397
School scale Week 48 >=4.4 point increase from baseline	Effect measure	2.124	1.455	0.186
	95% CI	(0.898, 5.023)	(0.943, 2.246)	(-0.022, 0.394)
	p-value	0.0862	0.0903	0.0790
School scale Week 72 >=4.4 point increase from baseline	Effect measure	1.813	1.484	0.132
	95% CI	(0.733, 4.484)	(0.810, 2.721)	(-0.066, 0.330)
	p-value	0.1976	0.2017	0.1921
School scale Week 96 >=4.4 point increase from baseline	Effect measure	2.424	1.746	0.203
	95% CI	(0.987, 5.952)	(0.980, 3.110)	(0.003, 0.404)
	p-value	0.0533	0.0585	0.0465

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109MS306_Table45_47_MCID_4.4_EFFECTMEASURES_female

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point decrease from baseline	Effect measure	1.629	1.322	0.119
	95% CI	(0.655, 4.047)	(0.781, 2.238)	(-0.101, 0.338)
	p-value	0.2937	0.2981	0.2887
Feelings scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.383	0.541	-0.217
	95% CI	(0.147, 1.001)	(0.288, 1.017)	(-0.427, -0.008)
	p-value	0.0502	0.0565	0.0423
Feelings scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.091	1.063	0.018
	95% CI	(0.411, 2.897)	(0.536, 2.109)	(-0.186, 0.223)
	p-value	0.8614	0.8614	0.8613
Feelings scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.227	1.152	0.044
	95% CI	(0.467, 3.227)	(0.591, 2.244)	(-0.163, 0.250)
	p-value	0.6780	0.6785	0.6773

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	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.723	0.779	-0.058
	95% CI	(0.250, 2.087)	(0.345, 1.762)	(-0.247, 0.131)
	p-value	0.5483	0.5493	0.5470
Get along scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.266	1.191	0.045
	95% CI	(0.455, 3.520)	(0.557, 2.545)	(-0.150, 0.241)
	p-value	0.6514	0.6520	0.6504

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	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.962	0.974	-0.009
	95% CI	(0.374, 2.473)	(0.521, 1.821)	(-0.220, 0.203)
	p-value	0.9351	0.9351	0.9351
Health scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.527	1.392	0.072
	95% CI	(0.513, 4.545)	(0.591, 3.277)	(-0.112, 0.257)
	p-value	0.4467	0.4491	0.4426
Health scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.750	1.462	0.121
	95% CI	(0.665, 4.608)	(0.753, 2.839)	(-0.086, 0.329)
	p-value	0.2573	0.2625	0.2505
Health scale Week 96 >=4.4 point decrease from baseline	Effect measure	2.214	1.810	0.149
	95% CI	(0.770, 6.368)	(0.811, 4.039)	(-0.043, 0.342)
	p-value	0.1402	0.1477	0.1291

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	Result	OR	RR	ARR
School scale Week 24 >=4.4 point decrease from baseline	Effect measure	1.000	1.000	0.000
	95% CI	(0.402, 2.486)	(0.590, 1.694)	(-0.222, 0.222)
	p-value	>0.99	>0.99	>0.99
School scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.133	1.091	0.026
	95% CI	(0.425, 3.017)	(0.551, 2.161)	(-0.180, 0.233)
	p-value	0.8029	0.8030	0.8027
School scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.276	1.182	0.053
	95% CI	(0.484, 3.367)	(0.608, 2.299)	(-0.156, 0.261)
	p-value	0.6219	0.6226	0.6211
School scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.133	1.091	0.026
	95% CI	(0.425, 3.017)	(0.551, 2.161)	(-0.180, 0.233)
	p-value	0.8029	0.8030	0.8027

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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point increase from baseline	Effect measure	0.958	0.974	-0.010
	95% CI	(0.383, 2.395)	(0.557, 1.704)	(-0.228, 0.208)
	p-value	0.9274	0.9274	0.9274
Feelings scale Week 48 >=4.4 point increase from baseline	Effect measure	2.400	1.754	0.198
	95% CI	(0.921, 6.255)	(0.933, 3.296)	(-0.012, 0.408)
	p-value	0.0733	0.0809	0.0640
Feelings scale Week 72 >=4.4 point increase from baseline	Effect measure	1.674	1.380	0.120
	95% CI	(0.659, 4.251)	(0.766, 2.487)	(-0.095, 0.335)
	p-value	0.2784	0.2832	0.2727
Feelings scale Week 96 >=4.4 point increase from baseline	Effect measure	1.227	1.152	0.044
	95% CI	(0.467, 3.227)	(0.591, 2.244)	(-0.163, 0.250)
	p-value	0.6780	0.6785	0.6773

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
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NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point increase from baseline	Effect measure	1.071	1.044	0.016
	95% CI	(0.426, 2.695)	(0.587, 1.856)	(-0.200, 0.233)
	p-value	0.8834	0.8835	0.8834
Get along scale Week 48 >=4.4 point increase from baseline	Effect measure	1.400	1.267	0.070
	95% CI	(0.524, 3.738)	(0.634, 2.533)	(-0.134, 0.274)
	p-value	0.5019	0.5037	0.4995
Get along scale Week 72 >=4.4 point increase from baseline	Effect measure	0.460	0.585	-0.164
	95% CI	(0.171, 1.237)	(0.292, 1.172)	(-0.368, 0.040)
	p-value	0.1238	0.1302	0.1153
Get along scale Week 96 >=4.4 point increase from baseline	Effect measure	0.396	0.520	-0.190
	95% CI	(0.144, 1.090)	(0.250, 1.081)	(-0.390, 0.011)
	p-value	0.0730	0.0799	0.0639

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point increase from baseline	Effect measure	1.948	1.559	0.147
	95% CI	(0.743, 5.105)	(0.813, 2.991)	(-0.061, 0.356)
	p-value	0.1750	0.1817	0.1665
Health scale Week 48 >=4.4 point increase from baseline	Effect measure	0.846	0.886	-0.033
	95% CI	(0.310, 2.310)	(0.427, 1.839)	(-0.232, 0.166)
	p-value	0.7448	0.7449	0.7446
Health scale Week 72 >=4.4 point increase from baseline	Effect measure	2.214	1.810	0.149
	95% CI	(0.770, 6.368)	(0.811, 4.039)	(-0.043, 0.342)
	p-value	0.1402	0.1477	0.1291

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point increase from baseline	Effect measure	0.802	0.875	-0.053
	95% CI	(0.319, 2.016)	(0.500, 1.530)	(-0.272, 0.167)
	p-value	0.6390	0.6396	0.6383
School scale Week 48 >=4.4 point increase from baseline	Effect measure	1.238	1.125	0.053
	95% CI	(0.500, 3.061)	(0.681, 1.857)	(-0.171, 0.276)
	p-value	0.6447	0.6452	0.6441
School scale Week 72 >=4.4 point increase from baseline	Effect measure	2.343	1.778	0.184
	95% CI	(0.873, 6.287)	(0.899, 3.515)	(-0.023, 0.391)
	p-value	0.0908	0.0981	0.0814
School scale Week 96 >=4.4 point increase from baseline	Effect measure	2.343	1.778	0.184
	95% CI	(0.873, 6.287)	(0.899, 3.515)	(-0.023, 0.391)
	p-value	0.0908	0.0981	0.0814

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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109MS306_Table45_47_MCID_4.4_EFFECTMEASURES_male

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.107	0.212	-0.438
	95% CI	(0.019, 0.610)	(0.054, 0.830)	(-0.714, -0.162)
	p-value	0.0119	0.0259	0.0019
Feelings scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.458	1.324	0.072
	95% CI	(0.318, 6.696)	(0.425, 4.120)	(-0.218, 0.361)
	p-value	0.6276	0.6285	0.6264
Feelings scale Week 72 >=4.4 point decrease from baseline	Effect measure	1.083	1.059	0.016
	95% CI	(0.250, 4.698)	(0.371, 3.018)	(-0.283, 0.316)
	p-value	0.9148	0.9148	0.9149
Feelings scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.909	1.588	0.131
	95% CI	(0.430, 8.483)	(0.541, 4.666)	(-0.167, 0.428)
	p-value	0.3954	0.4001	0.3891

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.833	0.882	-0.039
	95% CI	(0.199, 3.487)	(0.330, 2.361)	(-0.346, 0.268)
	p-value	0.8029	0.8032	0.8024
Get along scale Week 48 >=4.4 point decrease from baseline	Effect measure	1.714	1.588	0.065
	95% CI	(0.249, 11.782)	(0.301, 8.369)	(-0.167, 0.298)
	p-value	0.5837	0.5853	0.5812

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.667	0.706	-0.049
	95% CI	(0.097, 4.579)	(0.134, 3.719)	(-0.279, 0.181)
	p-value	0.6800	0.6812	0.6767
Health scale Week 48 >=4.4 point decrease from baseline	Effect measure	2.267	2.118	0.062
	95% CI	(0.186, 27.582)	(0.211, 21.273)	(-0.124, 0.248)
	p-value	0.5210	0.5239	0.5133
Health scale Week 72 >=4.4 point decrease from baseline	Effect measure	0.667	0.706	-0.049
	95% CI	(0.097, 4.579)	(0.134, 3.719)	(-0.279, 0.181)
	p-value	0.6800	0.6812	0.6767
Health scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.071	1.059	0.010
	95% CI	(0.185, 6.217)	(0.247, 4.544)	(-0.240, 0.260)
	p-value	0.9387	0.9387	0.9387

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
School scale Week 24 >=4.4 point decrease from baseline	Effect measure	0.385	0.529	-0.209
	95% CI	(0.090, 1.650)	(0.195, 1.440)	(-0.515, 0.096)
	p-value	0.1984	0.2128	0.1797
School scale Week 48 >=4.4 point decrease from baseline	Effect measure	0.615	0.706	-0.098
	95% CI	(0.139, 2.727)	(0.240, 2.074)	(-0.395, 0.199)
	p-value	0.5227	0.5264	0.5173
School scale Week 72 >=4.4 point decrease from baseline	Effect measure	3.500	2.471	0.245
	95% CI	(0.727, 16.848)	(0.760, 8.032)	(-0.045, 0.536)
	p-value	0.1182	0.1327	0.0982
School scale Week 96 >=4.4 point decrease from baseline	Effect measure	1.077	1.059	0.013
	95% CI	(0.222, 5.219)	(0.314, 3.576)	(-0.265, 0.292)
	p-value	0.9267	0.9267	0.9267

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Feelings scale Week 24 >=4.4 point increase from baseline	Effect measure	2.857	1.765	0.255
	95% CI	(0.722, 11.311)	(0.821, 3.792)	(-0.065, 0.575)
	p-value	0.1348	0.1455	0.1180
Feelings scale Week 48 >=4.4 point increase from baseline	Effect measure	1.397	1.210	0.082
	95% CI	(0.364, 5.353)	(0.561, 2.608)	(-0.245, 0.409)
	p-value	0.6259	0.6264	0.6245
Feelings scale Week 72 >=4.4 point increase from baseline	Effect measure	3.938	2.382	0.307
	95% CI	(0.911, 17.014)	(0.900, 6.307)	(0.002, 0.612)
	p-value	0.0664	0.0805	0.0486
Feelings scale Week 96 >=4.4 point increase from baseline	Effect measure	1.820	1.482	0.134
	95% CI	(0.443, 7.477)	(0.581, 3.783)	(-0.178, 0.446)
	p-value	0.4062	0.4102	0.4004

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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	Result	OR	RR	ARR
Get along scale Week 24 >=4.4 point increase from baseline	Effect measure	1.083	1.059	0.016
	95% CI	(0.250, 4.698)	(0.371, 3.018)	(-0.283, 0.316)
	p-value	0.9148	0.9148	0.9149
Get along scale Week 48 >=4.4 point increase from baseline	Effect measure	0.750	0.794	-0.046
	95% CI	(0.141, 3.985)	(0.207, 3.039)	(-0.310, 0.218)
	p-value	0.7357	0.7364	0.7342
Get along scale Week 72 >=4.4 point increase from baseline	Effect measure	1.458	1.324	0.072
	95% CI	(0.318, 6.696)	(0.425, 4.120)	(-0.218, 0.361)
	p-value	0.6276	0.6285	0.6264
Get along scale Week 96 >=4.4 point increase from baseline	Effect measure	0.500	0.529	-0.052
	95% CI	(0.041, 6.082)	(0.053, 5.318)	(-0.236, 0.131)
	p-value	0.5866	0.5890	0.5760

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
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NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
Health scale Week 24 >=4.4 point increase from baseline	Effect measure	2.083	1.765	0.127
	95% CI	(0.412, 10.529)	(0.496, 6.275)	(-0.149, 0.404)
	p-value	0.3746	0.3802	0.3666
Health scale Week 48 >=4.4 point increase from baseline	Effect measure	1.909	1.588	0.131
	95% CI	(0.430, 8.483)	(0.541, 4.666)	(-0.167, 0.428)
	p-value	0.3954	0.4001	0.3891
Health scale Week 72 >=4.4 point increase from baseline	Effect measure	3.500	2.471	0.245
	95% CI	(0.727, 16.848)	(0.760, 8.032)	(-0.045, 0.536)
	p-value	0.1182	0.1327	0.0982

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING A MCID OF 4.4 OF THE TOTAL SCORE WHEN COMPARING EACH TIMEPOINT TO BASELINE SCORE BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
School scale Week 24 >=4.4 point increase from baseline	Effect measure	1.820	1.482	0.134
	95% CI	(0.443, 7.477)	(0.581, 3.783)	(-0.178, 0.446)
	p-value	0.4062	0.4102	0.4004
School scale Week 48 >=4.4 point increase from baseline	Effect measure	2.881	1.664	0.258
	95% CI	(0.729, 11.381)	(0.845, 3.275)	(-0.062, 0.578)
	p-value	0.1312	0.1406	0.1137
School scale Week 72 >=4.4 point increase from baseline	Effect measure	0.655	0.756	-0.095
	95% CI	(0.160, 2.680)	(0.296, 1.930)	(-0.407, 0.218)
	p-value	0.5559	0.5590	0.5522
School scale Week 96 >=4.4 point increase from baseline	Effect measure	2.250	1.588	0.196
	95% CI	(0.574, 8.824)	(0.719, 3.507)	(-0.126, 0.518)
	p-value	0.2448	0.2524	0.2328

NOTE1: TO CREATE YES/NO EVENT VARIABLES, WE CALCULATED TIMEPOINT SCORE MINUS BASELINE AND ASSESSED IF THAT CHANGE WAS >=4.4 (CODED AS YES). SCALES ARE 0 TO 100
NOTE2: IF BASELINE SCORE IS MISSING, WE DO not INCLUDE THEM IN ANALYSES. IF TIMEPOINT SCORE IS MISSING, EVENT VARIABLE=0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE5: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE6: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE7: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE8: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

109MS306_Table45_47_MCID_4.4_NPERCENT_EVENT_age13to14

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Feelings scale Week 24 >=4.4 point decrease from baseline				
	Yes	3 (17)	4 (29)	7 (22)
	No	10 (56)	8 (57)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 48 >=4.4 point decrease from baseline				
	Yes	2 (11)	5 (36)	7 (22)
	No	11 (61)	7 (50)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 72 >=4.4 point decrease from baseline				
	Yes	4 (22)	2 (14)	6 (19)
	No	9 (50)	10 (71)	19 (59)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 96 >=4.4 point decrease from baseline				
	Yes	5 (28)	2 (14)	7 (22)
	No	8 (44)	10 (71)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Get along scale Week 24 >=4.4 point decrease from baseline				
	Yes	2 (11)	2 (14)	4 (13)
	No	11 (61)	10 (71)	21 (66)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 48 >=4.4 point decrease from baseline				
	Yes	4 (22)	2 (14)	6 (19)
	No	9 (50)	10 (71)	19 (59)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 72 >=4.4 point decrease from baseline				
	Yes	2 (11)	1 (7)	3 (9)
	No	11 (61)	11 (79)	22 (69)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 96 >=4.4 point decrease from baseline				
	Yes	3 (17)	1 (7)	4 (13)
	No	10 (56)	11 (79)	21 (66)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Health scale Week 24 >=4.4 point decrease from baseline				
	Yes	5 (28)	2 (14)	7 (22)
	No	8 (44)	10 (71)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)
Health scale Week 72 >=4.4 point decrease from baseline				
	Yes	3 (17)	1 (7)	4 (13)
	No	10 (56)	11 (79)	21 (66)
	Missing	5 (28)	2 (14)	7 (22)
Health scale Week 96 >=4.4 point decrease from baseline				
	Yes	4 (22)	1 (7)	5 (16)
	No	9 (50)	11 (79)	20 (63)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
School scale Week 24 >=4.4 point decrease from baseline				
	Yes	5 (28)	3 (21)	8 (25)
	No	8 (44)	9 (64)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 48 >=4.4 point decrease from baseline				
	Yes	4 (22)	3 (21)	7 (22)
	No	9 (50)	9 (64)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 72 >=4.4 point decrease from baseline				
	Yes	6 (33)	2 (14)	8 (25)
	No	7 (39)	10 (71)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 96 >=4.4 point decrease from baseline				
	Yes	5 (28)	3 (21)	8 (25)
	No	8 (44)	9 (64)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Feelings scale Week 24 >=4.4 point increase from baseline				
	Yes	8 (44)	5 (36)	13 (41)
	No	5 (28)	7 (50)	12 (38)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 48 >=4.4 point increase from baseline				
	Yes	4 (22)	4 (29)	8 (25)
	No	9 (50)	8 (57)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 72 >=4.4 point increase from baseline				
	Yes	5 (28)	4 (29)	9 (28)
	No	8 (44)	8 (57)	16 (50)
	Missing	5 (28)	2 (14)	7 (22)
Feelings scale Week 96 >=4.4 point increase from baseline				
	Yes	5 (28)	4 (29)	9 (28)
	No	8 (44)	8 (57)	16 (50)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Get along scale Week 24 >=4.4 point increase from baseline				
	Yes	4 (22)	7 (50)	11 (34)
	No	9 (50)	5 (36)	14 (44)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 48 >=4.4 point increase from baseline				
	Yes	1 (6)	4 (29)	5 (16)
	No	12 (67)	8 (57)	20 (63)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 72 >=4.4 point increase from baseline				
	Yes	1 (6)	5 (36)	6 (19)
	No	12 (67)	7 (50)	19 (59)
	Missing	5 (28)	2 (14)	7 (22)
Get along scale Week 96 >=4.4 point increase from baseline				
	Yes	0 (0)	4 (29)	4 (13)
	No	13 (72)	8 (57)	21 (66)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Health scale Week 24 >=4.4 point increase from baseline				
	Yes	5 (28)	5 (36)	10 (31)
	No	8 (44)	7 (50)	15 (47)
	Missing	5 (28)	2 (14)	7 (22)
Health scale Week 48 >=4.4 point increase from baseline				
	Yes	1 (6)	4 (29)	5 (16)
	No	12 (67)	8 (57)	20 (63)
	Missing	5 (28)	2 (14)	7 (22)
Health scale Week 72 >=4.4 point increase from baseline				
	Yes	3 (17)	3 (21)	6 (19)
	No	10 (56)	9 (64)	19 (59)
	Missing	5 (28)	2 (14)	7 (22)
Health scale Week 96 >=4.4 point increase from baseline				
	Yes	4 (22)	3 (21)	7 (22)
	No	9 (50)	9 (64)	18 (56)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event (n (%))	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
School scale Week 24 >=4.4 point increase from baseline				
	Yes	4 (22)	6 (43)	10 (31)
	No	9 (50)	6 (43)	15 (47)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 48 >=4.4 point increase from baseline				
	Yes	4 (22)	5 (36)	9 (28)
	No	9 (50)	7 (50)	16 (50)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 72 >=4.4 point increase from baseline				
	Yes	4 (22)	4 (29)	8 (25)
	No	9 (50)	8 (57)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)
School scale Week 96 >=4.4 point increase from baseline				
	Yes	5 (28)	3 (21)	8 (25)
	No	8 (44)	9 (64)	17 (53)
	Missing	5 (28)	2 (14)	7 (22)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

109MS306_Table45_47_MCID_4.4_NPERCENT_EVENT_age15to17

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Feelings scale Week 24 >=4.4 point decrease from baseline				
	Yes	18 (34)	20 (40)	38 (37)
	No	25 (47)	24 (48)	49 (48)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 48 >=4.4 point decrease from baseline				
	Yes	13 (25)	17 (34)	30 (29)
	No	30 (57)	27 (54)	57 (55)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 72 >=4.4 point decrease from baseline				
	Yes	13 (25)	14 (28)	27 (26)
	No	30 (57)	30 (60)	60 (58)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 96 >=4.4 point decrease from baseline				
	Yes	14 (26)	13 (26)	27 (26)
	No	29 (55)	31 (62)	60 (58)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Get along scale Week 24 >=4.4 point decrease from baseline				
	Yes	11 (21)	14 (28)	25 (24)
	No	32 (60)	30 (60)	62 (60)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 48 >=4.4 point decrease from baseline				
	Yes	10 (19)	9 (18)	19 (18)
	No	33 (62)	35 (70)	68 (66)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 72 >=4.4 point decrease from baseline				
	Yes	12 (23)	6 (12)	18 (17)
	No	31 (58)	38 (76)	69 (67)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 96 >=4.4 point decrease from baseline				
	Yes	12 (23)	5 (10)	17 (17)
	No	31 (58)	39 (78)	70 (68)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Health scale Week 24 >=4.4 point decrease from baseline				
	Yes	10 (19)	14 (28)	24 (23)
	No	33 (62)	30 (60)	63 (61)
	Missing	10 (19)	6 (12)	16 (16)
Health scale Week 72 >=4.4 point decrease from baseline				
	Yes	14 (26)	12 (24)	26 (25)
	No	29 (55)	32 (64)	61 (59)
	Missing	10 (19)	6 (12)	16 (16)
Health scale Week 96 >=4.4 point decrease from baseline				
	Yes	12 (23)	9 (18)	21 (20)
	No	31 (58)	35 (70)	66 (64)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
School scale Week 24 >=4.4 point decrease from baseline				
	Yes	15 (28)	21 (42)	36 (35)
	No	27 (51)	23 (46)	50 (49)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 48 >=4.4 point decrease from baseline				
	Yes	12 (23)	14 (28)	26 (25)
	No	30 (57)	30 (60)	60 (58)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 72 >=4.4 point decrease from baseline				
	Yes	14 (26)	12 (24)	26 (25)
	No	28 (53)	32 (64)	60 (58)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 96 >=4.4 point decrease from baseline				
	Yes	11 (21)	12 (24)	23 (22)
	No	31 (58)	32 (64)	63 (61)
	Missing	11 (21)	6 (12)	17 (17)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Feelings scale Week 24 >=4.4 point increase from baseline				
	Yes	17 (32)	16 (32)	33 (32)
	No	26 (49)	28 (56)	54 (52)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 48 >=4.4 point increase from baseline				
	Yes	22 (42)	13 (26)	35 (34)
	No	21 (40)	31 (62)	52 (50)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 72 >=4.4 point increase from baseline				
	Yes	21 (40)	12 (24)	33 (32)
	No	22 (42)	32 (64)	54 (52)
	Missing	10 (19)	6 (12)	16 (16)
Feelings scale Week 96 >=4.4 point increase from baseline				
	Yes	15 (28)	12 (24)	27 (26)
	No	28 (53)	32 (64)	60 (58)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Get along scale Week 24 >=4.4 point increase from baseline				
	Yes	16 (30)	12 (24)	28 (27)
	No	27 (51)	32 (64)	59 (57)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 48 >=4.4 point increase from baseline				
	Yes	15 (28)	10 (20)	25 (24)
	No	28 (53)	34 (68)	62 (60)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 72 >=4.4 point increase from baseline				
	Yes	13 (25)	14 (28)	27 (26)
	No	30 (57)	30 (60)	60 (58)
	Missing	10 (19)	6 (12)	16 (16)
Get along scale Week 96 >=4.4 point increase from baseline				
	Yes	9 (17)	13 (26)	22 (21)
	No	34 (64)	31 (62)	65 (63)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Health scale Week 24 >=4.4 point increase from baseline				
	Yes	16 (30)	8 (16)	24 (23)
	No	27 (51)	36 (72)	63 (61)
	Missing	10 (19)	6 (12)	16 (16)
Health scale Week 48 >=4.4 point increase from baseline				
	Yes	15 (28)	11 (22)	26 (25)
	No	28 (53)	33 (66)	61 (59)
	Missing	10 (19)	6 (12)	16 (16)
Health scale Week 72 >=4.4 point increase from baseline				
	Yes	17 (32)	7 (14)	24 (23)
	No	26 (49)	37 (74)	63 (61)
	Missing	10 (19)	6 (12)	16 (16)
Health scale Week 96 >=4.4 point increase from baseline				
	Yes	12 (23)	8 (16)	20 (19)
	No	31 (58)	36 (72)	67 (65)
	Missing	10 (19)	6 (12)	16 (16)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event (n (%))	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
School scale Week 24 >=4.4 point increase from baseline				
	Yes	17 (32)	15 (30)	32 (31)
	No	25 (47)	29 (58)	54 (52)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 48 >=4.4 point increase from baseline				
	Yes	25 (47)	18 (36)	43 (42)
	No	17 (32)	26 (52)	43 (42)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 72 >=4.4 point increase from baseline				
	Yes	17 (32)	12 (24)	29 (28)
	No	25 (47)	32 (64)	57 (55)
	Missing	11 (21)	6 (12)	17 (17)
School scale Week 96 >=4.4 point increase from baseline				
	Yes	20 (38)	12 (24)	32 (31)
	No	22 (42)	32 (64)	54 (52)
	Missing	11 (21)	6 (12)	17 (17)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

109MS306_Table45_47_MCID_4.4_NPERCENT_EVENT_female

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Feelings scale Week 24 >=4.4 point decrease from baseline				
	Yes	19 (38)	14 (30)	33 (34)
	No	20 (40)	24 (52)	44 (46)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 48 >=4.4 point decrease from baseline				
	Yes	10 (20)	18 (39)	28 (29)
	No	29 (58)	20 (43)	49 (51)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 72 >=4.4 point decrease from baseline				
	Yes	12 (24)	11 (24)	23 (24)
	No	27 (54)	27 (59)	54 (56)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 96 >=4.4 point decrease from baseline				
	Yes	13 (26)	11 (24)	24 (25)
	No	26 (52)	27 (59)	53 (55)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Get along scale Week 24 >=4.4 point decrease from baseline				
	Yes	8 (16)	10 (22)	18 (19)
	No	31 (62)	28 (61)	59 (61)
	Missing	11 (22)	8 (17)	19 (20)
Get along scale Week 48 >=4.4 point decrease from baseline				
	Yes	11 (22)	9 (20)	20 (21)
	No	28 (56)	29 (63)	57 (59)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Health scale Week 24 >=4.4 point decrease from baseline				
	Yes	13 (26)	13 (28)	26 (27)
	No	26 (52)	25 (54)	51 (53)
	Missing	11 (22)	8 (17)	19 (20)
Health scale Week 48 >=4.4 point decrease from baseline				
	Yes	10 (20)	7 (15)	17 (18)
	No	29 (58)	31 (67)	60 (63)
	Missing	11 (22)	8 (17)	19 (20)
Health scale Week 72 >=4.4 point decrease from baseline				
	Yes	15 (30)	10 (22)	25 (26)
	No	24 (48)	28 (61)	52 (54)
	Missing	11 (22)	8 (17)	19 (20)
Health scale Week 96 >=4.4 point decrease from baseline				
	Yes	13 (26)	7 (15)	20 (21)
	No	26 (52)	31 (67)	57 (59)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
School scale Week 24 >=4.4 point decrease from baseline				
	Yes	16 (32)	16 (35)	32 (33)
	No	22 (44)	22 (48)	44 (46)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 48 >=4.4 point decrease from baseline				
	Yes	12 (24)	11 (24)	23 (24)
	No	26 (52)	27 (59)	53 (55)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 72 >=4.4 point decrease from baseline				
	Yes	13 (26)	11 (24)	24 (25)
	No	25 (50)	27 (59)	52 (54)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 96 >=4.4 point decrease from baseline				
	Yes	12 (24)	11 (24)	23 (24)
	No	26 (52)	27 (59)	53 (55)
	Missing	12 (24)	8 (17)	20 (21)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Feelings scale Week 24 >=4.4 point increase from baseline				
	Yes	15 (30)	15 (33)	30 (31)
	No	24 (48)	23 (50)	47 (49)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 48 >=4.4 point increase from baseline				
	Yes	18 (36)	10 (22)	28 (29)
	No	21 (42)	28 (61)	49 (51)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 72 >=4.4 point increase from baseline				
	Yes	17 (34)	12 (26)	29 (30)
	No	22 (44)	26 (57)	48 (50)
	Missing	11 (22)	8 (17)	19 (20)
Feelings scale Week 96 >=4.4 point increase from baseline				
	Yes	13 (26)	11 (24)	24 (25)
	No	26 (52)	27 (59)	53 (55)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Get along scale Week 24 >=4.4 point increase from baseline				
	Yes	15 (30)	14 (30)	29 (30)
	No	24 (48)	24 (52)	48 (50)
	Missing	11 (22)	8 (17)	19 (20)
Get along scale Week 48 >=4.4 point increase from baseline				
	Yes	13 (26)	10 (22)	23 (24)
	No	26 (52)	28 (61)	54 (56)
	Missing	11 (22)	8 (17)	19 (20)
Get along scale Week 72 >=4.4 point increase from baseline				
	Yes	9 (18)	15 (33)	24 (25)
	No	30 (60)	23 (50)	53 (55)
	Missing	11 (22)	8 (17)	19 (20)
Get along scale Week 96 >=4.4 point increase from baseline				
	Yes	8 (16)	15 (33)	23 (24)
	No	31 (62)	23 (50)	54 (56)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Health scale Week 24 >=4.4 point increase from baseline				
	Yes	16 (32)	10 (22)	26 (27)
	No	23 (46)	28 (61)	51 (53)
	Missing	11 (22)	8 (17)	19 (20)
Health scale Week 48 >=4.4 point increase from baseline				
	Yes	10 (20)	11 (24)	21 (22)
	No	29 (58)	27 (59)	56 (58)
	Missing	11 (22)	8 (17)	19 (20)
Health scale Week 72 >=4.4 point increase from baseline				
	Yes	13 (26)	7 (15)	20 (21)
	No	26 (52)	31 (67)	57 (59)
	Missing	11 (22)	8 (17)	19 (20)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Event (n (%))	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
School scale Week 24 >=4.4 point increase from baseline				
	Yes	14 (28)	16 (35)	30 (31)
	No	24 (48)	22 (48)	46 (48)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 48 >=4.4 point increase from baseline				
	Yes	18 (36)	16 (35)	34 (35)
	No	20 (40)	22 (48)	42 (44)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 72 >=4.4 point increase from baseline				
	Yes	16 (32)	9 (20)	25 (26)
	No	22 (44)	29 (63)	51 (53)
	Missing	12 (24)	8 (17)	20 (21)
School scale Week 96 >=4.4 point increase from baseline				
	Yes	16 (32)	9 (20)	25 (26)
	No	22 (44)	29 (63)	51 (53)
	Missing	12 (24)	8 (17)	20 (21)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

109MS306_Table45_47_MCID_4.4_NPERCENT_EVENT_male

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Feelings scale Week 24 >=4.4 point decrease from baseline				
	Yes	2 (10)	10 (56)	12 (31)
	No	15 (71)	8 (44)	23 (59)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 48 >=4.4 point decrease from baseline				
	Yes	5 (24)	4 (22)	9 (23)
	No	12 (57)	14 (78)	26 (67)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 72 >=4.4 point decrease from baseline				
	Yes	5 (24)	5 (28)	10 (26)
	No	12 (57)	13 (72)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 96 >=4.4 point decrease from baseline				
	Yes	6 (29)	4 (22)	10 (26)
	No	11 (52)	14 (78)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Get along scale Week 24 >=4.4 point decrease from baseline				
	Yes	5 (24)	6 (33)	11 (28)
	No	12 (57)	12 (67)	24 (62)
	Missing	4 (19)	0 (0)	4 (10)
Get along scale Week 48 >=4.4 point decrease from baseline				
	Yes	3 (14)	2 (11)	5 (13)
	No	14 (67)	16 (89)	30 (77)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Health scale Week 24 >=4.4 point decrease from baseline				
	Yes	2 (10)	3 (17)	5 (13)
	No	15 (71)	15 (83)	30 (77)
	Missing	4 (19)	0 (0)	4 (10)
Health scale Week 48 >=4.4 point decrease from baseline				
	Yes	2 (10)	1 (6)	3 (8)
	No	15 (71)	17 (94)	32 (82)
	Missing	4 (19)	0 (0)	4 (10)
Health scale Week 72 >=4.4 point decrease from baseline				
	Yes	2 (10)	3 (17)	5 (13)
	No	15 (71)	15 (83)	30 (77)
	Missing	4 (19)	0 (0)	4 (10)
Health scale Week 96 >=4.4 point decrease from baseline				
	Yes	3 (14)	3 (17)	6 (15)
	No	14 (67)	15 (83)	29 (74)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
School scale Week 24 >=4.4 point decrease from baseline				
	Yes	4 (19)	8 (44)	12 (31)
	No	13 (62)	10 (56)	23 (59)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 48 >=4.4 point decrease from baseline				
	Yes	4 (19)	6 (33)	10 (26)
	No	13 (62)	12 (67)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 72 >=4.4 point decrease from baseline				
	Yes	7 (33)	3 (17)	10 (26)
	No	10 (48)	15 (83)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 96 >=4.4 point decrease from baseline				
	Yes	4 (19)	4 (22)	8 (21)
	No	13 (62)	14 (78)	27 (69)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Feelings scale Week 24 >=4.4 point increase from baseline				
	Yes	10 (48)	6 (33)	16 (41)
	No	7 (33)	12 (67)	19 (49)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 48 >=4.4 point increase from baseline				
	Yes	8 (38)	7 (39)	15 (38)
	No	9 (43)	11 (61)	20 (51)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 72 >=4.4 point increase from baseline				
	Yes	9 (43)	4 (22)	13 (33)
	No	8 (38)	14 (78)	22 (56)
	Missing	4 (19)	0 (0)	4 (10)
Feelings scale Week 96 >=4.4 point increase from baseline				
	Yes	7 (33)	5 (28)	12 (31)
	No	10 (48)	13 (72)	23 (59)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Get along scale Week 24 >=4.4 point increase from baseline				
	Yes	5 (24)	5 (28)	10 (26)
	No	12 (57)	13 (72)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)
Get along scale Week 48 >=4.4 point increase from baseline				
	Yes	3 (14)	4 (22)	7 (18)
	No	14 (67)	14 (78)	28 (72)
	Missing	4 (19)	0 (0)	4 (10)
Get along scale Week 72 >=4.4 point increase from baseline				
	Yes	5 (24)	4 (22)	9 (23)
	No	12 (57)	14 (78)	26 (67)
	Missing	4 (19)	0 (0)	4 (10)
Get along scale Week 96 >=4.4 point increase from baseline				
	Yes	1 (5)	2 (11)	3 (8)
	No	16 (76)	16 (89)	32 (82)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Health scale Week 24 >=4.4 point increase from baseline				
	Yes	5 (24)	3 (17)	8 (21)
	No	12 (57)	15 (83)	27 (69)
	Missing	4 (19)	0 (0)	4 (10)
Health scale Week 48 >=4.4 point increase from baseline				
	Yes	6 (29)	4 (22)	10 (26)
	No	11 (52)	14 (78)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)
Health scale Week 72 >=4.4 point increase from baseline				
	Yes	7 (33)	3 (17)	10 (26)
	No	10 (48)	15 (83)	25 (64)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

Tables 45/47: Summary and Analysis of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR EVENTS (>=4.4 MCID) AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Event (n (%))	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
School scale Week 24 >=4.4 point increase from baseline				
	Yes	7 (33)	5 (28)	12 (31)
	No	10 (48)	13 (72)	23 (59)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 48 >=4.4 point increase from baseline				
	Yes	11 (52)	7 (39)	18 (46)
	No	6 (29)	11 (61)	17 (44)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 72 >=4.4 point increase from baseline				
	Yes	5 (24)	7 (39)	12 (31)
	No	12 (57)	11 (61)	23 (59)
	Missing	4 (19)	0 (0)	4 (10)
School scale Week 96 >=4.4 point increase from baseline				
	Yes	9 (43)	6 (33)	15 (38)
	No	8 (38)	12 (67)	20 (51)
	Missing	4 (19)	0 (0)	4 (10)

NOTE1: An event is yes when the MCID is >=4.4 Each scale is 0 to 100
NOTE2: Event is missing when baseline score is missing and thus NOT included in analyses. When timepoint score is missing, event = 0
NOTE3: The only events reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 events in at least one subgroup in at least one arm
NOTE4: Ns in this table refer to patients.
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqos-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban033022.sas date: 30MAR2022

109MS306_Table45_47_MCID_4.4_NPERCENT_RESPONSE_age13to14

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Response (n (%))	DMF (N=18)	IFN-B1a (N=14)	Total (N=32)
Feelings scale Week 0				
	Yes	13 (72)	12 (86)	25 (78)
	No	5 (28)	2 (14)	7 (22)
Feelings scale Week 24				
	Yes	16 (89)	13 (93)	29 (91)
	No	2 (11)	1 (7)	3 (9)
Feelings scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
Feelings scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
Feelings scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Response (n (%))	DMF (N=18)	IFN-B1a (N=14)	Total (N=32)
Get along scale Week 0				
	Yes	13 (72)	12 (86)	25 (78)
	No	5 (28)	2 (14)	7 (22)
Get along scale Week 24				
	Yes	16 (89)	13 (93)	29 (91)
	No	2 (11)	1 (7)	3 (9)
Get along scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
Get along scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
Get along scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Response (n (%))	DMF (N=18)	IFN-B1a (N=14)	Total (N=32)
Health scale Week 0				
	Yes	13 (72)	12 (86)	25 (78)
	No	5 (28)	2 (14)	7 (22)
Health scale Week 24				
	Yes	16 (89)	13 (93)	29 (91)
	No	2 (11)	1 (7)	3 (9)
Health scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
Health scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
Health scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Response (n (%))	DMF (N=18)	IFN-B1a (N=14)	Total (N=32)
School scale Week 0				
	Yes	13 (72)	12 (86)	25 (78)
	No	5 (28)	2 (14)	7 (22)
School scale Week 24				
	Yes	16 (89)	12 (86)	28 (88)
	No	2 (11)	2 (14)	4 (13)
School scale Week 48				
	Yes	13 (72)	10 (71)	23 (72)
	No	5 (28)	4 (29)	9 (28)
School scale Week 72				
	Yes	15 (83)	8 (57)	23 (72)
	No	3 (17)	6 (43)	9 (28)
School scale Week 96				
	Yes	15 (83)	7 (50)	22 (69)
	No	3 (17)	7 (50)	10 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

109MS306_Table45_47_MCID_4.4_NPERCENT_RESPONSE_age15to17

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Response (n (%))	DMF (N=53)	IFN-B1a (N=50)	Total (N=103)
Feelings scale Week 0				
	Yes	43 (81)	44 (88)	87 (84)
	No	10 (19)	6 (12)	16 (16)
Feelings scale Week 24				
	Yes	51 (96)	49 (98)	100 (97)
	No	2 (4)	1 (2)	3 (3)
Feelings scale Week 48				
	Yes	49 (92)	42 (84)	91 (88)
	No	4 (8)	8 (16)	12 (12)
Feelings scale Week 72				
	Yes	44 (83)	33 (66)	77 (75)
	No	9 (17)	17 (34)	26 (25)
Feelings scale Week 96				
	Yes	39 (74)	31 (62)	70 (68)
	No	14 (26)	19 (38)	33 (32)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Response (n (%))	DMF (N=53)	IFN-B1a (N=50)	Total (N=103)
Get along scale Week 0				
	Yes	43 (81)	44 (88)	87 (84)
	No	10 (19)	6 (12)	16 (16)
Get along scale Week 24				
	Yes	51 (96)	49 (98)	100 (97)
	No	2 (4)	1 (2)	3 (3)
Get along scale Week 48				
	Yes	49 (92)	42 (84)	91 (88)
	No	4 (8)	8 (16)	12 (12)
Get along scale Week 72				
	Yes	44 (83)	33 (66)	77 (75)
	No	9 (17)	17 (34)	26 (25)
Get along scale Week 96				
	Yes	39 (74)	31 (62)	70 (68)
	No	14 (26)	19 (38)	33 (32)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Response (n (%))	DMF (N=53)	IFN-B1a (N=50)	Total (N=103)
Health scale Week 0				
	Yes	43 (81)	44 (88)	87 (84)
	No	10 (19)	6 (12)	16 (16)
Health scale Week 24				
	Yes	51 (96)	49 (98)	100 (97)
	No	2 (4)	1 (2)	3 (3)
Health scale Week 48				
	Yes	49 (92)	42 (84)	91 (88)
	No	4 (8)	8 (16)	12 (12)
Health scale Week 72				
	Yes	44 (83)	33 (66)	77 (75)
	No	9 (17)	17 (34)	26 (25)
Health scale Week 96				
	Yes	39 (74)	31 (62)	70 (68)
	No	14 (26)	19 (38)	33 (32)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Response (n (%))	DMF (N=53)	IFN-B1a (N=50)	Total (N=103)
School scale Week 0				
	Yes	42 (79)	44 (88)	86 (83)
	No	11 (21)	6 (12)	17 (17)
School scale Week 24				
	Yes	50 (94)	49 (98)	99 (96)
	No	3 (6)	1 (2)	4 (4)
School scale Week 48				
	Yes	48 (91)	42 (84)	90 (87)
	No	5 (9)	8 (16)	13 (13)
School scale Week 72				
	Yes	44 (83)	33 (66)	77 (75)
	No	9 (17)	17 (34)	26 (25)
School scale Week 96				
	Yes	39 (74)	31 (62)	70 (68)
	No	14 (26)	19 (38)	33 (32)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

109MS306_Table45_47_MCID_4.4_NPERCENT_RESPONSE_female

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Response (n (%))	DMF (N=50)	IFN-B1a (N=46)	Total (N=96)
Feelings scale Week 0				
	Yes	39 (78)	38 (83)	77 (80)
	No	11 (22)	8 (17)	19 (20)
Feelings scale Week 24				
	Yes	48 (96)	45 (98)	93 (97)
	No	2 (4)	1 (2)	3 (3)
Feelings scale Week 48				
	Yes	44 (88)	38 (83)	82 (85)
	No	6 (12)	8 (17)	14 (15)
Feelings scale Week 72				
	Yes	40 (80)	30 (65)	70 (73)
	No	10 (20)	16 (35)	26 (27)
Feelings scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Response (n (%))	DMF (N=50)	IFN-B1a (N=46)	Total (N=96)
Get along scale Week 0				
	Yes	39 (78)	38 (83)	77 (80)
	No	11 (22)	8 (17)	19 (20)
Get along scale Week 24				
	Yes	48 (96)	45 (98)	93 (97)
	No	2 (4)	1 (2)	3 (3)
Get along scale Week 48				
	Yes	44 (88)	38 (83)	82 (85)
	No	6 (12)	8 (17)	14 (15)
Get along scale Week 72				
	Yes	40 (80)	30 (65)	70 (73)
	No	10 (20)	16 (35)	26 (27)
Get along scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Response (n (%))	DMF (N=50)	IFN-B1a (N=46)	Total (N=96)
Health scale Week 0				
	Yes	39 (78)	38 (83)	77 (80)
	No	11 (22)	8 (17)	19 (20)
Health scale Week 24				
	Yes	48 (96)	45 (98)	93 (97)
	No	2 (4)	1 (2)	3 (3)
Health scale Week 48				
	Yes	44 (88)	38 (83)	82 (85)
	No	6 (12)	8 (17)	14 (15)
Health scale Week 72				
	Yes	40 (80)	30 (65)	70 (73)
	No	10 (20)	16 (35)	26 (27)
Health scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Female sex

	Response (n (%))	DMF (N=50)	IFN-B1a (N=46)	Total (N=96)
School scale Week 0				
	Yes	38 (76)	38 (83)	76 (79)
	No	12 (24)	8 (17)	20 (21)
School scale Week 24				
	Yes	47 (94)	44 (96)	91 (95)
	No	3 (6)	2 (4)	5 (5)
School scale Week 48				
	Yes	43 (86)	38 (83)	81 (84)
	No	7 (14)	8 (17)	15 (16)
School scale Week 72				
	Yes	40 (80)	30 (65)	70 (73)
	No	10 (20)	16 (35)	26 (27)
School scale Week 96				
	Yes	38 (76)	28 (61)	66 (69)
	No	12 (24)	18 (39)	30 (31)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

109MS306_Table45_47_MCID_4.4_NPERCENT_RESPONSE_male

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Response (n (%))	DMF (N=21)	IFN-B1a (N=18)	Total (N=39)
Feelings scale Week 0				
	Yes	17 (81)	18 (100)	35 (90)
	No	4 (19)	0 (0)	4 (10)
Feelings scale Week 24				
	Yes	19 (90)	17 (94)	36 (92)
	No	2 (10)	1 (6)	3 (8)
Feelings scale Week 48				
	Yes	18 (86)	14 (78)	32 (82)
	No	3 (14)	4 (22)	7 (18)
Feelings scale Week 72				
	Yes	19 (90)	11 (61)	30 (77)
	No	2 (10)	7 (39)	9 (23)
Feelings scale Week 96				
	Yes	16 (76)	10 (56)	26 (67)
	No	5 (24)	8 (44)	13 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Response (n (%))	DMF (N=21)	IFN-B1a (N=18)	Total (N=39)
Get along scale Week 0				
	Yes	17 (81)	18 (100)	35 (90)
	No	4 (19)	0 (0)	4 (10)
Get along scale Week 24				
	Yes	19 (90)	17 (94)	36 (92)
	No	2 (10)	1 (6)	3 (8)
Get along scale Week 48				
	Yes	18 (86)	14 (78)	32 (82)
	No	3 (14)	4 (22)	7 (18)
Get along scale Week 72				
	Yes	19 (90)	11 (61)	30 (77)
	No	2 (10)	7 (39)	9 (23)
Get along scale Week 96				
	Yes	16 (76)	10 (56)	26 (67)
	No	5 (24)	8 (44)	13 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Response (n (%))	DMF (N=21)	IFN-B1a (N=18)	Total (N=39)
Health scale Week 0				
	Yes	17 (81)	18 (100)	35 (90)
	No	4 (19)	0 (0)	4 (10)
Health scale Week 24				
	Yes	19 (90)	17 (94)	36 (92)
	No	2 (10)	1 (6)	3 (8)
Health scale Week 48				
	Yes	18 (86)	14 (78)	32 (82)
	No	3 (14)	4 (22)	7 (18)
Health scale Week 72				
	Yes	19 (90)	11 (61)	30 (77)
	No	2 (10)	7 (39)	9 (23)
Health scale Week 96				
	Yes	16 (76)	10 (56)	26 (67)
	No	5 (24)	8 (44)	13 (33)

NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsql-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

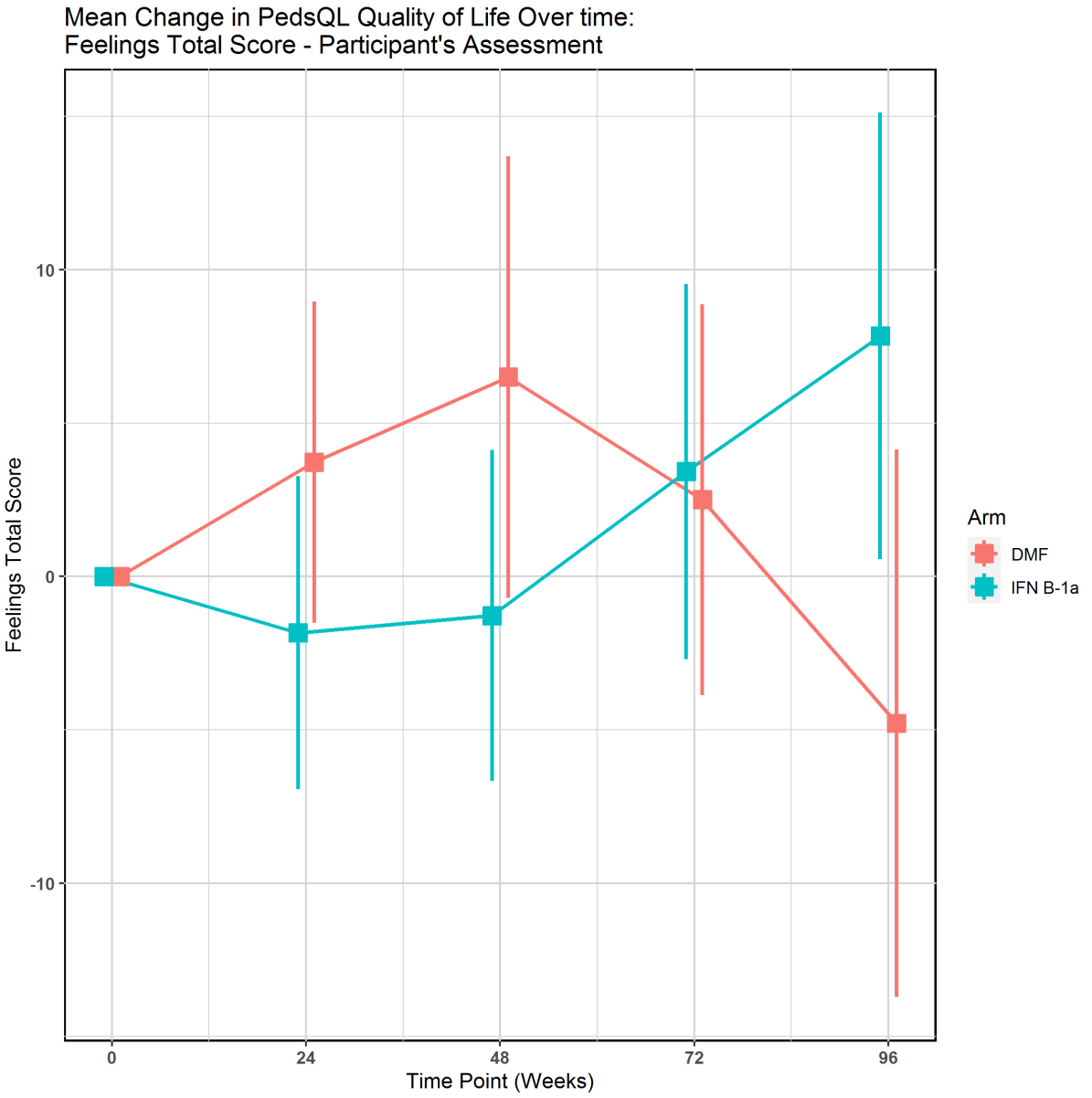
Tables 45/47: Summary of PedsQL Quality of Life Scale Scores, Participant's Assessment- ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING NON-MISSING RESPONSES AT EACH TIMEPOINT BY STUDY ARM. Subgroup analysis for Male sex

	Response (n (%))	DMF (N=21)	IFN-B1a (N=18)	Total (N=39)
School scale Week 0				
	Yes	17 (81)	18 (100)	35 (90)
	No	4 (19)	0 (0)	4 (10)
School scale Week 24				
	Yes	19 (90)	17 (94)	36 (92)
	No	2 (10)	1 (6)	3 (8)
School scale Week 48				
	Yes	18 (86)	14 (78)	32 (82)
	No	3 (14)	4 (22)	7 (18)
School scale Week 72				
	Yes	19 (90)	11 (61)	30 (77)
	No	2 (10)	7 (39)	9 (23)
School scale Week 96				
	Yes	16 (76)	10 (56)	26 (67)
	No	5 (24)	8 (44)	13 (33)

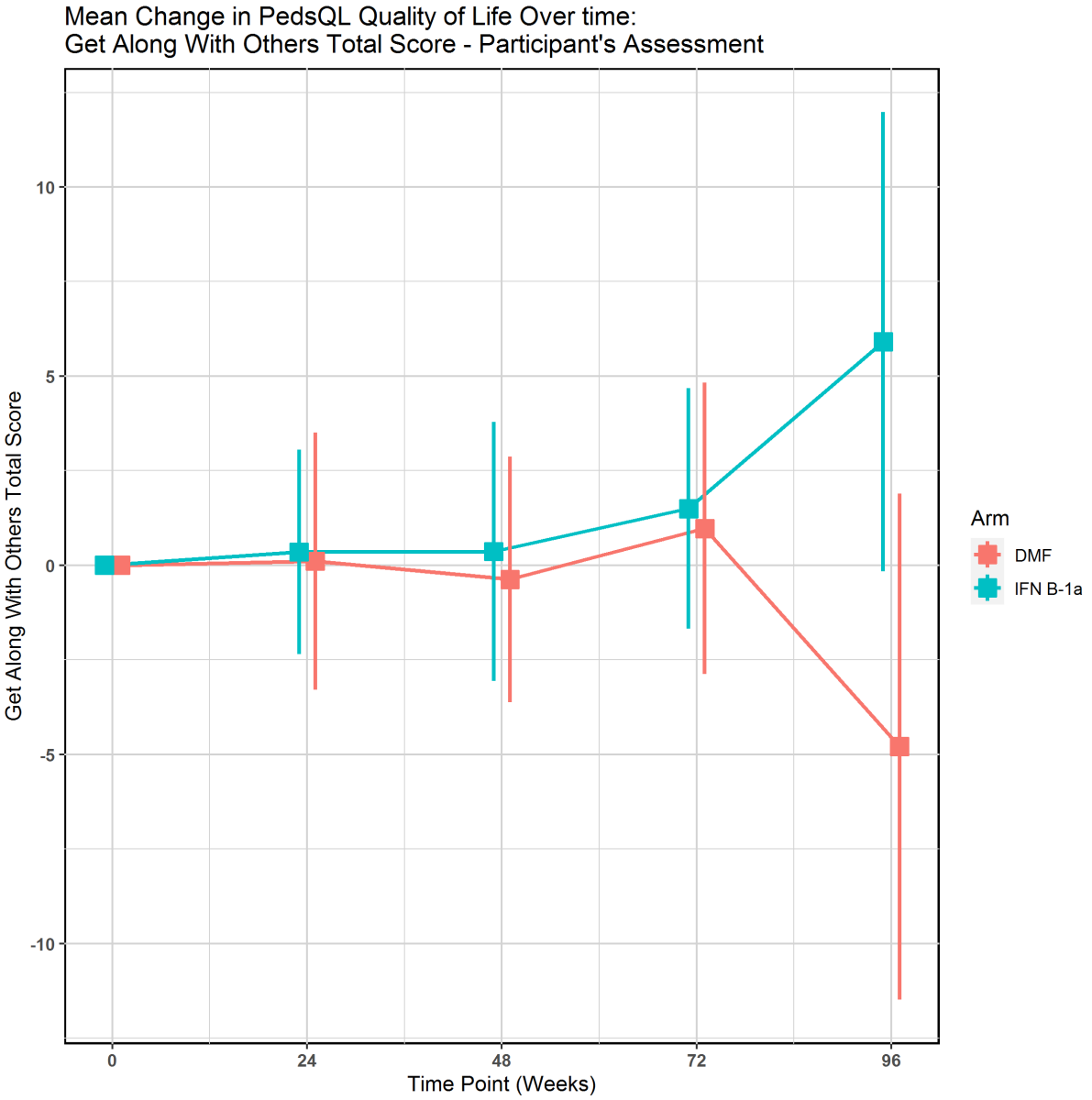
NOTE1: Responder rates are yes when we have non-missing scale data for the given timepoint
NOTE2: Ns in this table refer to patients. Some patients had multiple observations per time point. In those cases, we took the average of their scores
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table45_47_t-ef-ana-pedsqol-subj_MCID4pt4_NewMethod_3pvalues_n=135_subgroups_ban020222.sas date: 02FEB2022

Graphics

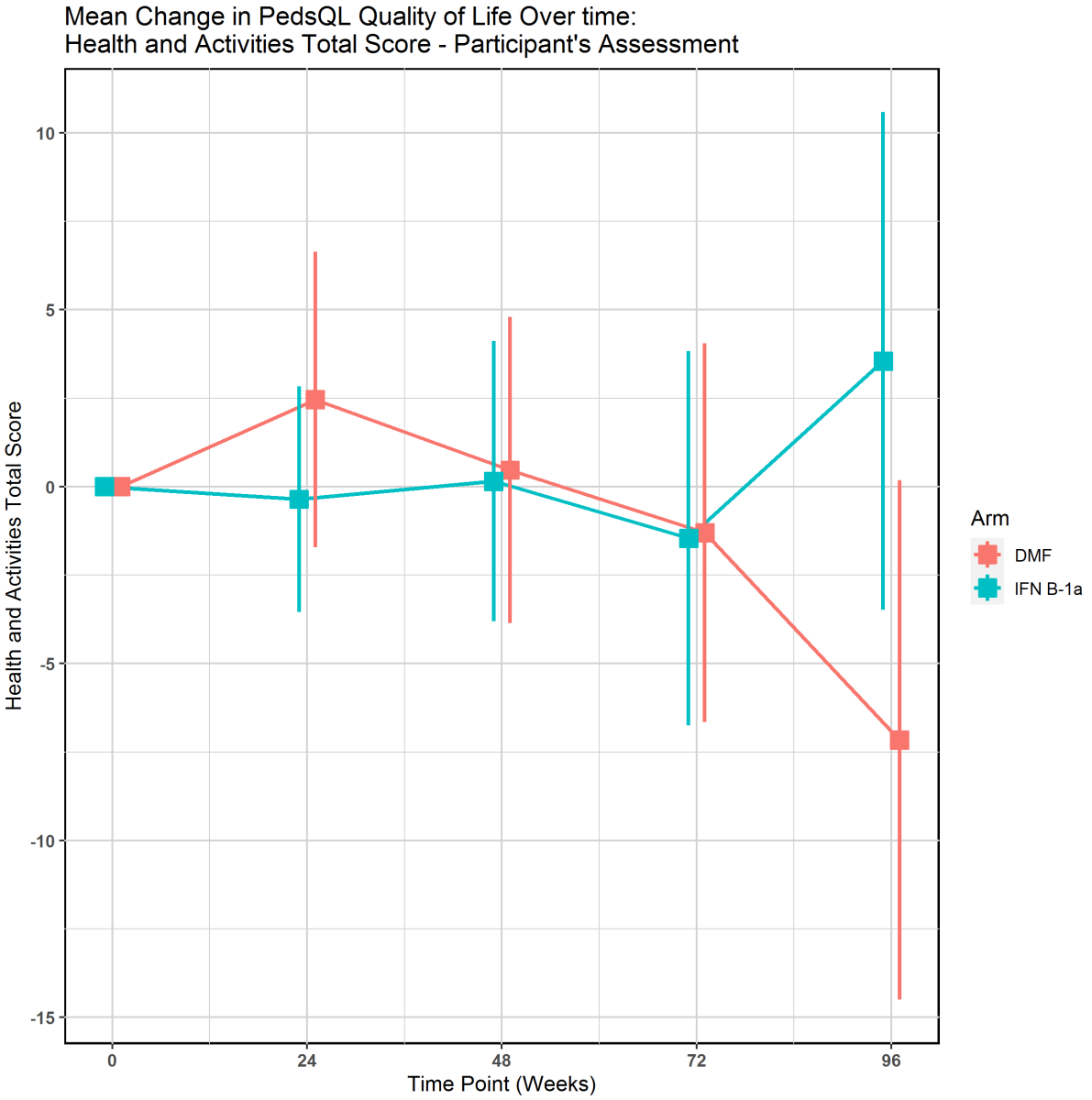
Change from baselineFeelings Total Score Participant's Assessment



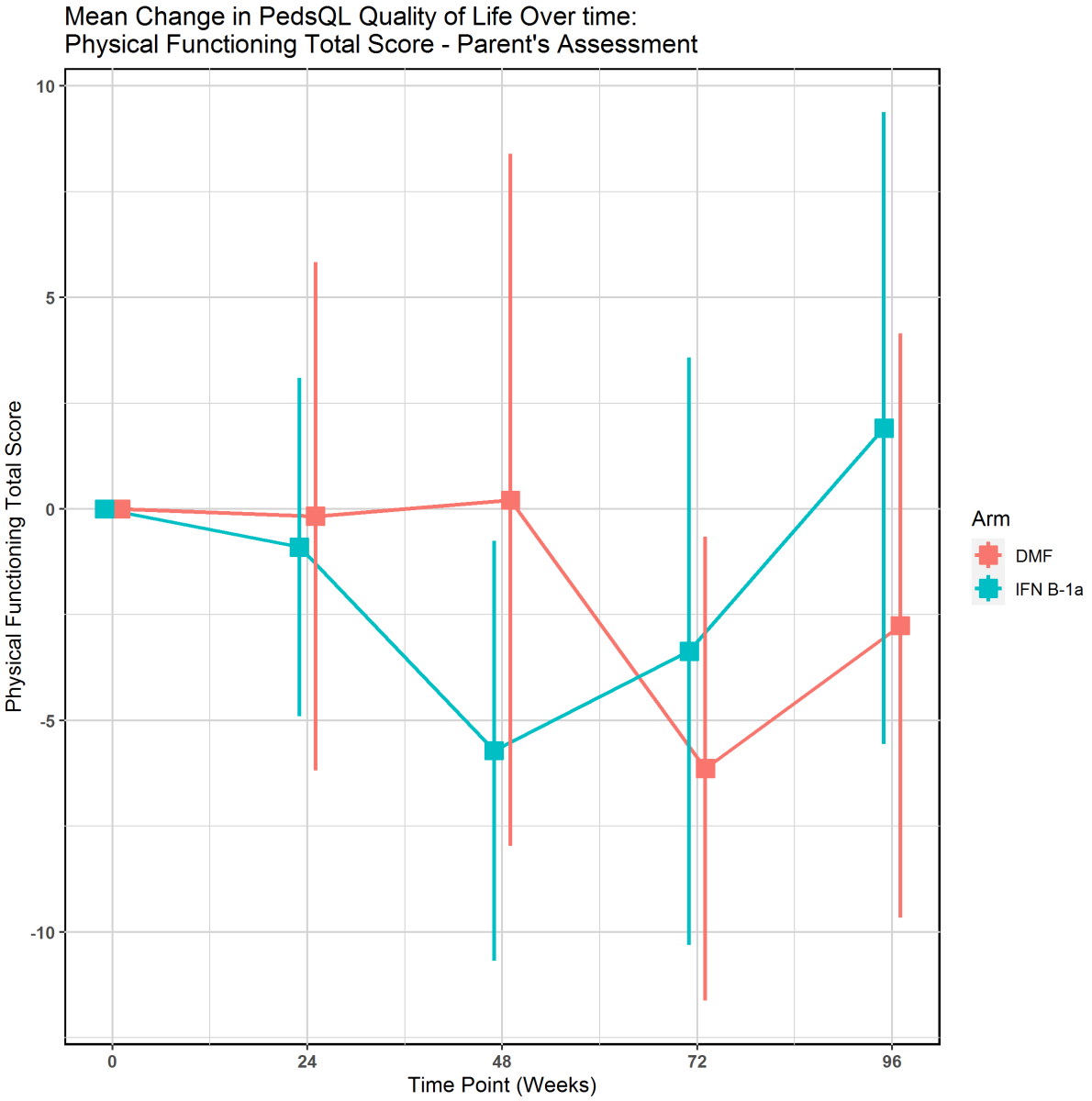
Change from baselineGet Along With Others Total Score Participant's Assessment



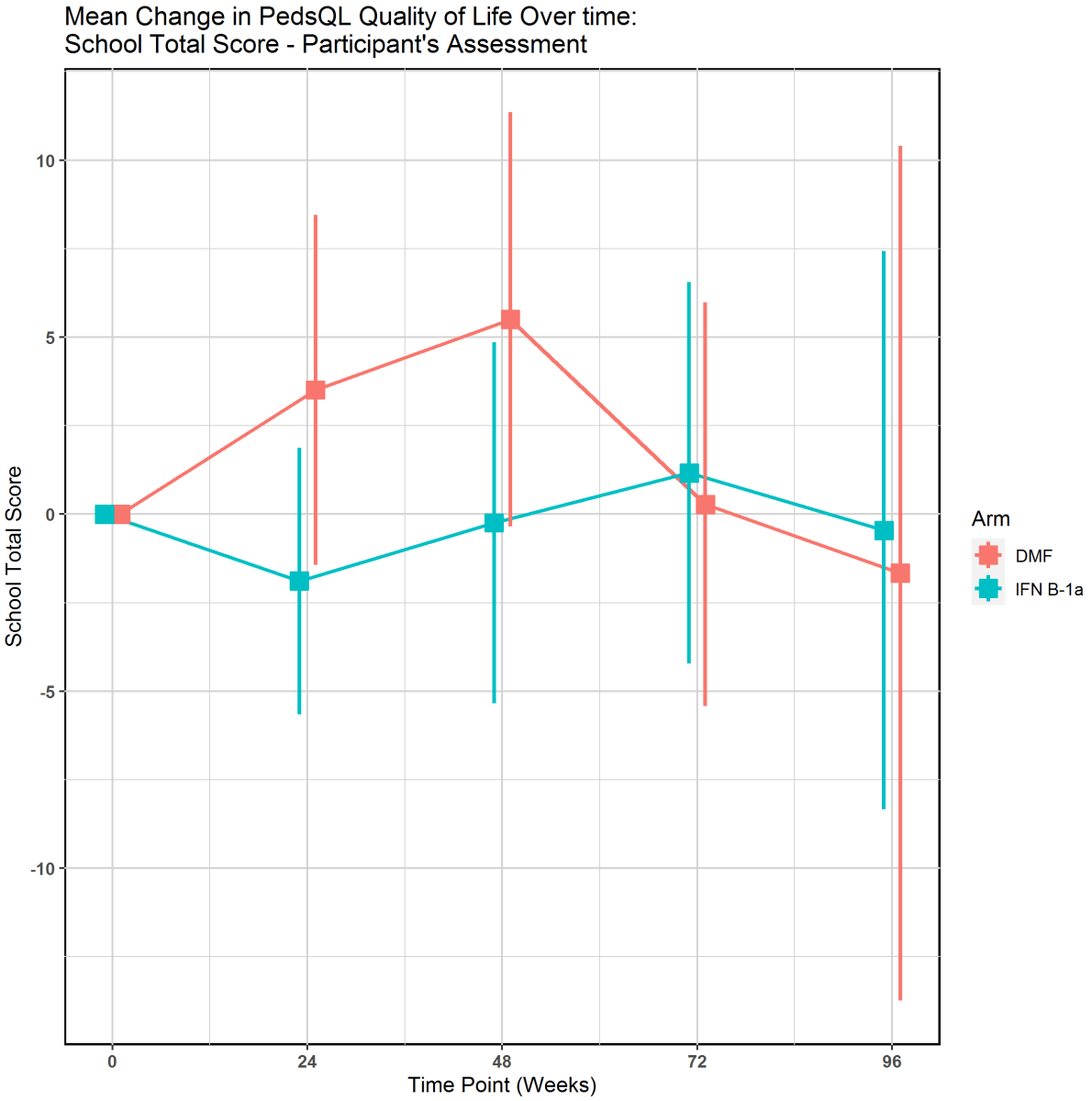
Change from baselineHealth and Activities Total Score Participant's Assessment



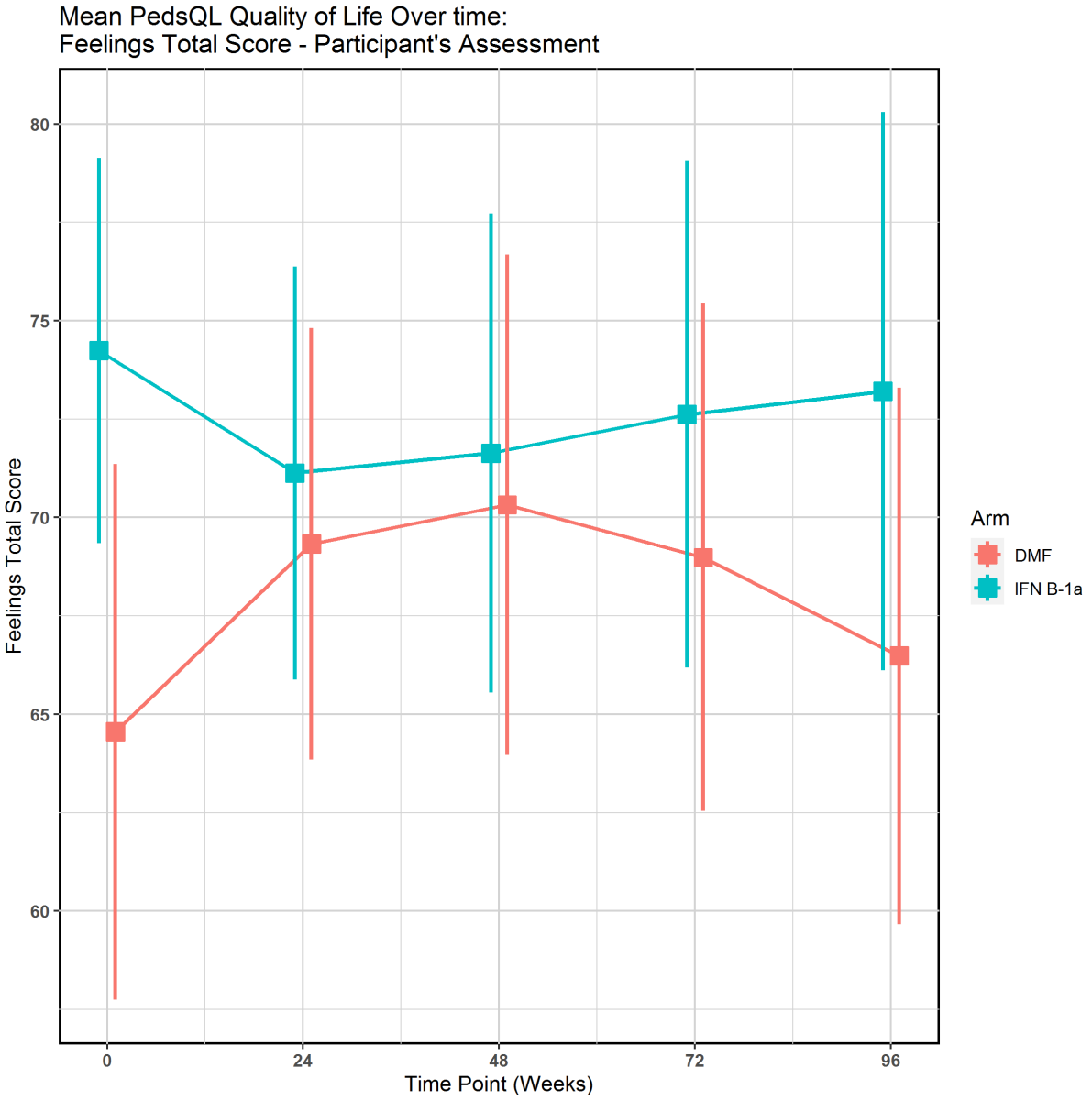
Change from baselinePhysical Functioning Total Score Parent's Assessment



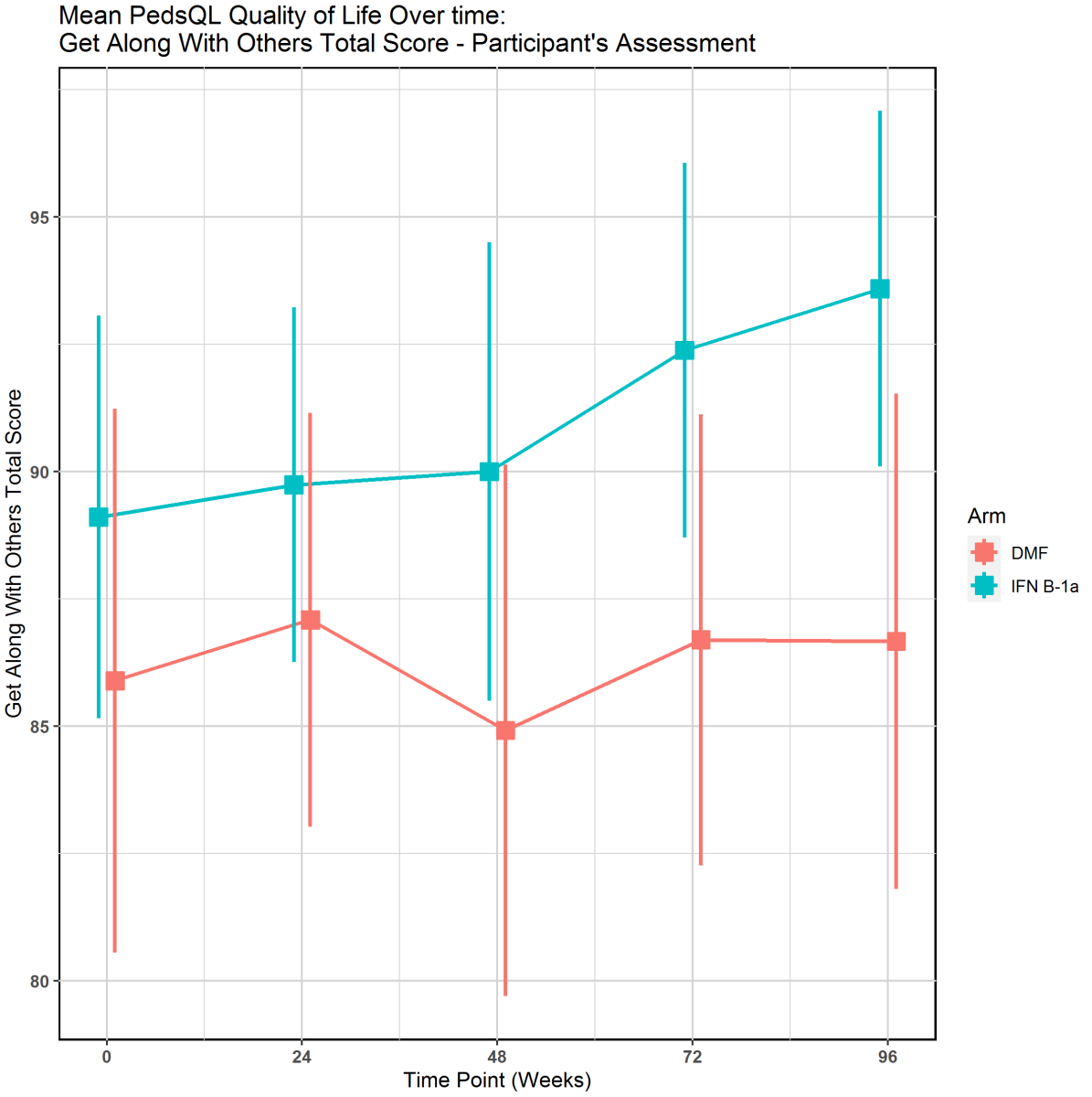
Change from baselineSchool Total Score Participant's Assessment



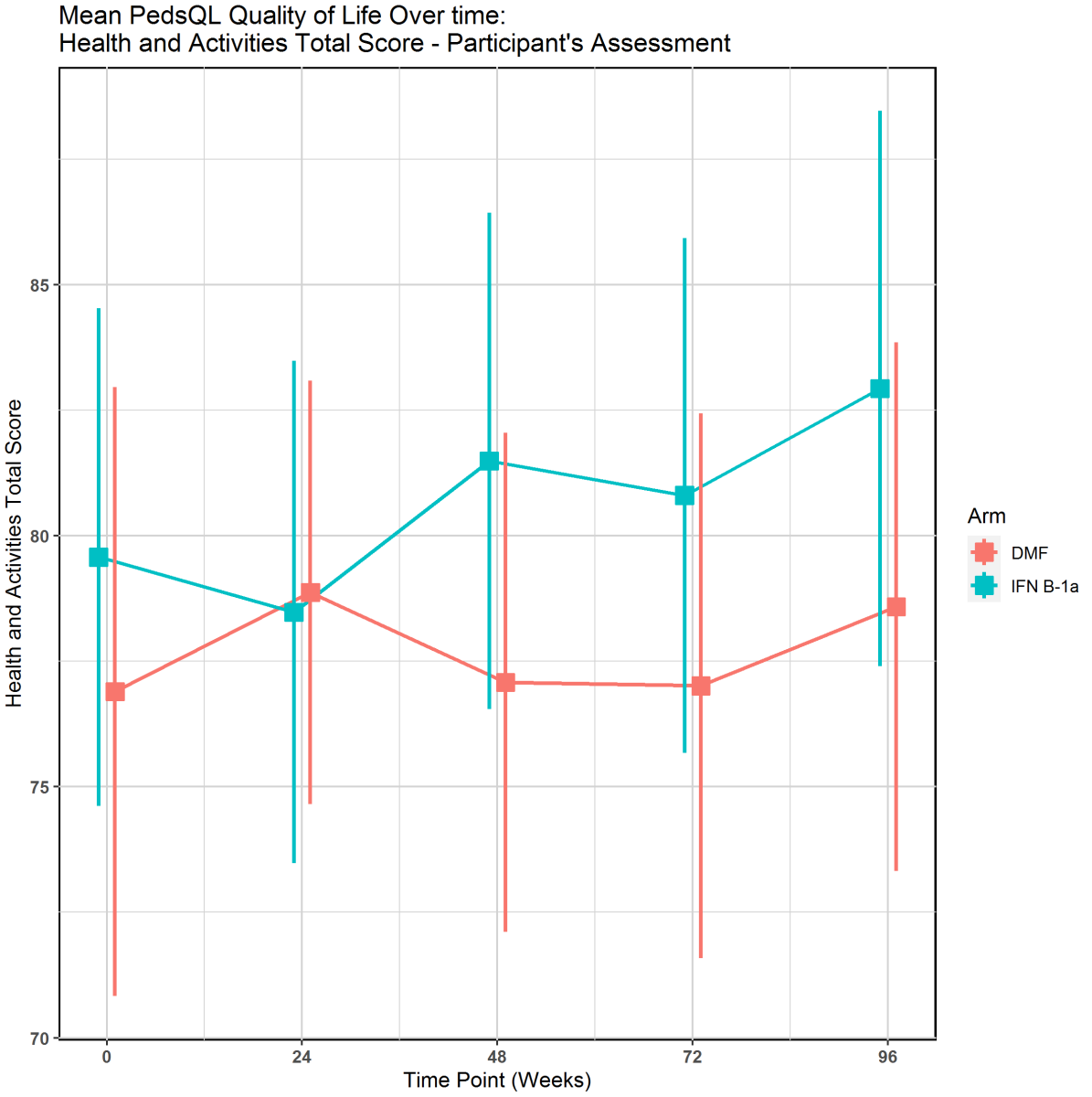
Feelings Total Score Participant's Assessment



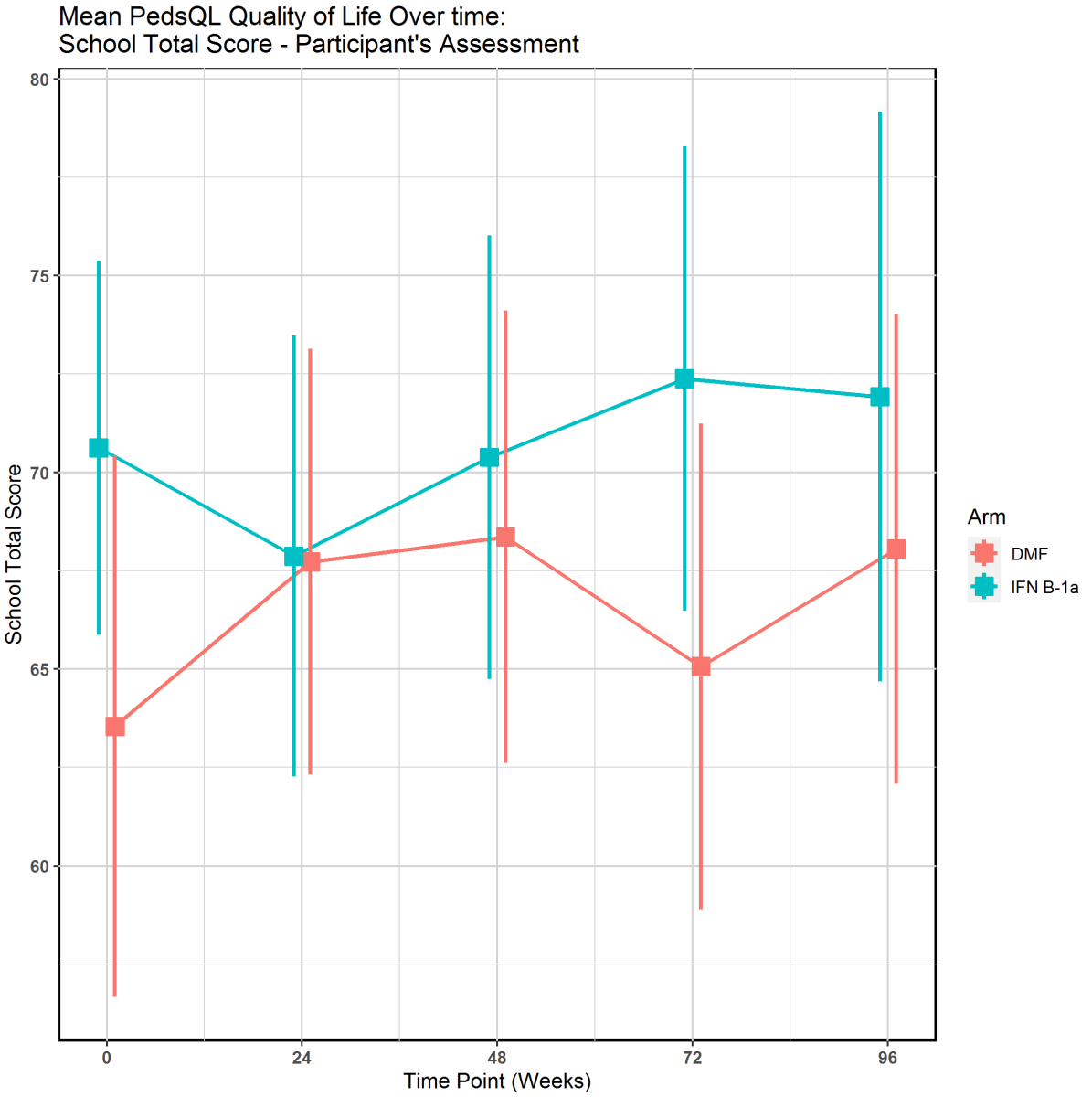
Get Along With Others Total Score Participant's Assessment



Health and Activities Total Score Participant's Assessment



School Total Score Participant's Assessment



Safety

Overall rates

109MS306_Table12_AE_EFFECTMEASURES

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135)

OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM

ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
>=1 any AE	Effect measure	1.115	1.005	0.005
	95% CI	(0.217, 5.731)	(0.934, 1.081)	(-0.065, 0.074)
	p-value	0.8965	0.8968	0.8967
>=1 mild AE	Effect measure	0.957	0.974	-0.010
	95% CI	(0.478, 1.916)	(0.636, 1.491)	(-0.175, 0.154)
	p-value	0.9019	0.9018	0.9019
>=1 moderate AE	Effect measure	1.886	1.387	0.157
	95% CI	(0.951, 3.740)	(0.967, 1.988)	(-0.010, 0.324)
	p-value	0.0694	0.0751	0.0647
>=1 severe AE	Effect measure	0.077	0.090	-0.142
	95% CI	(0.010, 0.621)	(0.012, 0.685)	(-0.235, -0.049)
	p-value	0.0161	0.0200	0.0028
>=1 serious AE	Effect measure	0.540	0.631	-0.115
	95% CI	(0.246, 1.188)	(0.349, 1.142)	(-0.262, 0.031)
	p-value	0.1258	0.1284	0.1229

	Result	OR	RR	ARR
>=1 event leading to drug withdrawal	Effect measure	0.530	0.563	-0.055
	95% CI	(0.164, 1.713)	(0.194, 1.634)	(-0.155, 0.046)
	p-value	0.2891	0.2910	0.2873
>=1 event leading to study discontinuation	Effect measure	0.530	0.563	-0.055
	95% CI	(0.164, 1.713)	(0.194, 1.634)	(-0.155, 0.046)
	p-value	0.2891	0.2910	0.2873

NOTE1: For mild, moderate and severe endpoints, we took the highest severity per patient
NOTE2: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE3: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE4: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE5: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE6: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxpdev/TEC/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_ban12822.sas date: 28JAN2022

109MS306_Table12_AE_NPERCENT_event

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135)
N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM
ANALYSIS NOT USING SUBGROUPS

	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
>=1 any AE				
	Yes	68 (96)	61 (95)	129 (96)
	No	3 (4)	3 (5)	6 (4)
>=1 mild AE				
	Yes	27 (38)	25 (39)	52 (39)
	No	44 (62)	39 (61)	83 (61)
>=1 moderate AE				
	Yes	40 (56)	26 (41)	66 (49)
	No	31 (44)	38 (59)	69 (51)
>=1 severe AE				
	Yes	1 (1)	10 (16)	11 (8)
	No	70 (99)	54 (84)	124 (92)
>=1 serious AE				
	Yes	14 (20)	20 (31)	34 (25)
	No	57 (80)	44 (69)	101 (75)
>=1 event leading to drug withdrawal				
	Yes	5 (7)	8 (13)	13 (10)
	No	66 (93)	56 (88)	122 (90)
>=1 event leading to study discontinuation				
	Yes	5 (7)	8 (13)	13 (10)
	No	66 (93)	56 (88)	122 (90)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_ban012822.sas

Sub groups

109MS306_Table12_AE_EFFECTMEASURES_age13to14

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
>=1 any AE	Effect measure	NA	NA	NA
	95% CI	NA	NA	NA
	p-value	NA	NA	NA
>=1 mild AE	Effect measure	1.333	1.167	0.071
	95% CI	(0.327, 5.434)	(0.545, 2.497)	(-0.276, 0.419)
	p-value	0.6882	0.6914	0.6868
>=1 moderate AE	Effect measure	2.500	1.750	0.214
	95% CI	(0.568, 11.011)	(0.678, 4.518)	(-0.116, 0.545)
	p-value	0.2258	0.2475	0.2041
>=1 serious AE	Effect measure	0.106	0.156	-0.302
	95% CI	(0.011, 1.050)	(0.020, 1.185)	(-0.574, -0.029)
	p-value	0.0551	0.0724	0.0300

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas date: 25MAR2022

109MS306_Table12_AE_EFFECTMEASURES_age15to17

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
>=1 any AE	Effect measure	1.064	1.004	0.003
	95% CI	(0.204, 5.534)	(0.912, 1.105)	(-0.087, 0.094)
	p-value	0.9414	0.9414	0.9414
>=1 mild AE	Effect measure	0.839	0.894	-0.040
	95% CI	(0.375, 1.878)	(0.533, 1.497)	(-0.226, 0.145)
	p-value	0.6696	0.6696	0.6694
>=1 moderate AE	Effect measure	1.793	1.329	0.145
	95% CI	(0.821, 3.917)	(0.903, 1.956)	(-0.046, 0.336)
	p-value	0.1428	0.1486	0.1373
>=1 serious AE	Effect measure	0.758	0.818	-0.055
	95% CI	(0.318, 1.811)	(0.434, 1.542)	(-0.227, 0.117)
	p-value	0.5333	0.5338	0.5327

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas date: 25MAR2022

109MS306_Table12_AE_EFFECTMEASURES_female

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
>=1 any AE	Effect measure	1.674	1.027	0.025
	95% CI	(0.267, 10.500)	(0.934, 1.129)	(-0.064, 0.115)
	p-value	0.5821	0.5829	0.5815
>=1 mild AE	Effect measure	1.137	1.082	0.030
	95% CI	(0.499, 2.592)	(0.651, 1.798)	(-0.164, 0.225)
	p-value	0.7596	0.7600	0.7593
>=1 moderate AE	Effect measure	2.201	1.553	0.192
	95% CI	(0.966, 5.013)	(0.969, 2.487)	(-0.003, 0.387)
	p-value	0.0603	0.0673	0.0534
>=1 severe AE	Effect measure	0.073	0.092	-0.197
	95% CI	(0.009, 0.600)	(0.012, 0.691)	(-0.323, -0.072)
	p-value	0.0148	0.0204	0.0020
>=1 serious AE	Effect measure	0.583	0.675	-0.106
	95% CI	(0.235, 1.448)	(0.346, 1.315)	(-0.284, 0.071)
	p-value	0.2449	0.2476	0.2416

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas date: 25MAR2022

109MS306_Table12_AE_EFFECTMEASURES_male

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
>=1 any AE	Effect measure	0.369	0.953	-0.048
	95% CI	(0.014, 9.639)	(0.869, 1.047)	(-0.190, 0.095)
	p-value	0.5495	0.3174	0.9320
>=1 mild AE	Effect measure	0.625	0.750	-0.111
	95% CI	(0.170, 2.291)	(0.339, 1.661)	(-0.417, 0.194)
	p-value	0.4782	0.4784	0.4760
>=1 moderate AE	Effect measure	1.300	1.114	0.063
	95% CI	(0.361, 4.679)	(0.654, 1.897)	(-0.246, 0.373)
	p-value	0.6880	0.6903	0.6877
>=1 severe AE	Effect measure	NA	NA	NA
	95% CI	NA	NA	NA
	p-value	NA	NA	NA
>=1 serious AE	Effect measure	0.433	0.514	-0.135
	95% CI	(0.088, 2.145)	(0.142, 1.860)	(-0.390, 0.120)
	p-value	0.3054	0.3106	0.3004

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
NOTE2: For mild, moderate and severe endpoints, we took the highest severity per patient
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/IFN B-1a
NOTE4: Absolute risk reductions (ARR) are represented as DMF - IFN B-1a
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
Source: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE_t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas date: 25MAR2022

109MS306_Table12_AE_NPERCENT_event_age13to14

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
>=1 any AE				
	Yes	18 (100)	14 (100)	32 (100)
	No	0 (0)	0 (0)	0 (0)
>=1 mild AE				
	Yes	9 (50)	6 (43)	15 (47)
	No	9 (50)	8 (57)	17 (53)
>=1 moderate AE				
	Yes	9 (50)	4 (29)	13 (41)
	No	9 (50)	10 (71)	19 (59)
>=1 serious AE				
	Yes	1 (6)	5 (36)	6 (19)
	No	17 (94)	9 (64)	26 (81)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas

109MS306_Table12_AE_NPERCENT_event_age15to17

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
>=1 any AE				
	Yes	50 (94)	47 (94)	97 (94)
	No	3 (6)	3 (6)	6 (6)
>=1 mild AE				
	Yes	18 (34)	19 (38)	37 (36)
	No	35 (66)	31 (62)	66 (64)
>=1 moderate AE				
	Yes	31 (58)	22 (44)	53 (51)
	No	22 (42)	28 (56)	50 (49)
>=1 serious AE				
	Yes	13 (25)	15 (30)	28 (27)
	No	40 (75)	35 (70)	75 (73)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas

109MS306_Table12_AE_NPERCENT_event_female

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Female sex

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
>=1 any AE				
	Yes	48 (96)	43 (93)	91 (95)
	No	2 (4)	3 (7)	5 (5)
>=1 mild AE				
	Yes	20 (40)	17 (37)	37 (39)
	No	30 (60)	29 (63)	59 (61)
>=1 moderate AE				
	Yes	27 (54)	16 (35)	43 (45)
	No	23 (46)	30 (65)	53 (55)
>=1 severe AE				
	Yes	1 (2)	10 (22)	11 (11)
	No	49 (98)	36 (78)	85 (89)
>=1 serious AE				
	Yes	11 (22)	15 (33)	26 (27)
	No	39 (78)	31 (67)	70 (73)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas

109MS306_Table12_AE_NPERCENT_event_male

Table 12: Overall summary of treatment emergent adverse events - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Male sex

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
>=1 any AE				
	Yes	20 (95)	18 (100)	38 (97)
	No	1 (5)	0 (0)	1 (3)
>=1 mild AE				
	Yes	7 (33)	8 (44)	15 (38)
	No	14 (67)	10 (56)	24 (62)
>=1 moderate AE				
	Yes	13 (62)	10 (56)	23 (59)
	No	8 (38)	8 (44)	16 (41)
>=1 severe AE				
	Yes	0 (0)	0 (0)	0 (0)
	No	21 (100)	18 (100)	39 (100)
>=1 serious AE				
	Yes	3 (14)	5 (28)	8 (21)
	No	18 (86)	13 (72)	31 (79)

NOTE1: Event rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table12_AE-t-ae-summary_3pvalues_n=135_subgroups_ban032522.sas

AE severity SOC PT

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135)

OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM´. The only AEs reported here are those with >=10% in either arm (>=5% for severe AEs). ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
Adverse event	Effect measure	1.115	1.005	0.005
	95% CI	(0.217, 5.731)	(0.934, 1.081)	(-0.065, 0.074)
	p-value	0.8965	0.8968	0.8967
___Mild	Effect measure	0.957	0.974	-0.010
	95% CI	(0.478, 1.916)	(0.636, 1.491)	(-0.175, 0.154)
	p-value	0.9019	0.9018	0.9019
___Moderate	Effect measure	1.886	1.387	0.157
	95% CI	(0.951, 3.740)	(0.967, 1.988)	(-0.010, 0.324)
	p-value	0.0694	0.0751	0.0647
___Severe	Effect measure	0.077	0.090	-0.142
	95% CI	(0.010, 0.621)	(0.012, 0.685)	(-0.235, -0.049)
	p-value	0.0161	0.0200	0.0028
Gastrointestinal disorders	Effect measure	6.478	2.389	0.434
	95% CI	(3.054, 13.739)	(1.621, 3.521)	(0.282, 0.586)
	p-value	<0.0001	<0.0001	<0.0001

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Gastrointestinal disorders , Mild	Effect measure	4.889	2.479	0.370
	95% CI	(2.329, 10.261)	(1.562, 3.934)	(0.215, 0.525)
	p-value	<0.0001	0.0001	<0.0001
Gastrointestinal disorders , Moderate	Effect measure	2.000	1.803	0.088
	95% CI	(0.752, 5.322)	(0.777, 4.185)	(-0.032, 0.208)
	p-value	0.1651	0.1701	0.1517
___Abdominal pain	Effect measure	7.684	5.048	0.316
	95% CI	(2.744, 21.512)	(2.074, 12.287)	(0.185, 0.448)
	p-value	0.0001	0.0004	<0.0001
___Abdominal pain , Mild	Effect measure	7.660	5.408	0.276
	95% CI	(2.486, 23.599)	(1.983, 14.748)	(0.151, 0.401)
	p-value	0.0004	0.0010	<0.0001
___Vomiting	Effect measure	3.433	2.885	0.147
	95% CI	(1.178, 10.000)	(1.120, 7.426)	(0.030, 0.265)
	p-value	0.0238	0.0281	0.0139

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Vomiting , Mild	Effect measure	6.305	5.408	0.138
	95% CI	(1.353, 29.375)	(1.258, 23.250)	(0.041, 0.235)
	p-value	0.0190	0.0233	0.0054
___Diarrhoea	Effect measure	3.684	3.155	0.135
	95% CI	(1.145, 11.857)	(1.095, 9.094)	(0.025, 0.245)
	p-value	0.0288	0.0334	0.0163
___Diarrhoea , Mild	Effect measure	2.177	2.028	0.064
	95% CI	(0.636, 7.450)	(0.656, 6.268)	(-0.033, 0.162)
	p-value	0.2150	0.2193	0.1964
___Abdominal pain upper	Effect measure	12.814	10.817	0.153
	95% CI	(1.616, 101.61)	(1.447, 80.878)	(0.061, 0.246)
	p-value	0.0158	0.0204	0.0011
___Abdominal pain upper , Mild	Effect measure	10.328	9.014	0.125
	95% CI	(1.283, 83.130)	(1.187, 68.475)	(0.039, 0.212)
	p-value	0.0282	0.0336	0.0045

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Nausea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708, 6.607)	(0.728, 5.400)	(-0.030, 0.184)
	p-value	0.1756	0.1804	0.1587
___Nausea , Mild	Effect measure	2.459	2.254	0.078
	95% CI	(0.731, 8.272)	(0.743, 6.833)	(-0.022, 0.179)
	p-value	0.1460	0.1511	0.1259
Infections and infestations	Effect measure	1.531	1.202	0.104
	95% CI	(0.771, 3.038)	(0.891, 1.621)	(-0.062, 0.271)
	p-value	0.2234	0.2285	0.2206
Infections and infestations , Mild	Effect measure	1.322	1.159	0.070
	95% CI	(0.671, 2.606)	(0.808, 1.662)	(-0.099, 0.238)
	p-value	0.4195	0.4222	0.4178
Infections and infestations , Moderate	Effect measure	1.569	1.465	0.058
	95% CI	(0.604, 4.074)	(0.649, 3.304)	(-0.063, 0.179)
	p-value	0.3549	0.3577	0.3469

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Nasopharyngitis	Effect measure	1.778	1.603	0.085
	95% CI	(0.724, 4.364)	(0.762, 3.371)	(-0.044, 0.214)
	p-value	0.2092	0.2138	0.1988
___Nasopharyngitis , Mild	Effect measure	2.369	2.060	0.116
	95% CI	(0.905, 6.201)	(0.906, 4.685)	(-0.008, 0.240)
	p-value	0.0790	0.0846	0.0660
___Gastroenteritis	Effect measure	1.713	1.623	0.049
	95% CI	(0.542, 5.409)	(0.574, 4.589)	(-0.053, 0.150)
	p-value	0.3589	0.3616	0.3479
___Upper respiratory tract infection	Effect measure	2.952	2.704	0.080
	95% CI	(0.762, 11.427)	(0.765, 9.555)	(-0.013, 0.173)
	p-value	0.1171	0.1224	0.0927
Nervous system disorders	Effect measure	0.555	0.825	-0.129
	95% CI	(0.267, 1.154)	(0.650, 1.047)	(-0.286, 0.028)
	p-value	0.1149	0.1134	0.1079

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Nervous system disorders , Mild	Effect measure	0.576	0.738	-0.135
	95% CI	(0.290, 1.144)	(0.504, 1.079)	(-0.302, 0.031)
	p-value	0.1152	0.1165	0.1112
Nervous system disorders , Moderate	Effect measure	0.800	0.862	-0.050
	95% CI	(0.391, 1.639)	(0.535, 1.389)	(-0.209, 0.110)
	p-value	0.5425	0.5424	0.5425
Nervous system disorders , Severe	Effect measure	0.138	0.150	-0.080
	95% CI	(0.016, 1.180)	(0.019, 1.214)	(-0.156, -0.003)
	p-value	0.0705	0.0754	0.0412
___Multiple sclerosis relapse	Effect measure	0.449	0.620	-0.190
	95% CI	(0.222, 0.906)	(0.405, 0.948)	(-0.353, -0.027)
	p-value	0.0254	0.0273	0.0223
___Multiple sclerosis relapse , Mild	Effect measure	0.400	0.451	-0.103
	95% CI	(0.141, 1.138)	(0.180, 1.131)	(-0.218, 0.012)
	p-value	0.0859	0.0895	0.0804

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Multiple sclerosis relapse , Moderate	Effect measure	0.741	0.795	-0.054
	95% CI	(0.334, 1.640)	(0.434, 1.459)	(-0.198, 0.090)
	p-value	0.4591	0.4594	0.4593
___Headache	Effect measure	0.570	0.685	-0.123
	95% CI	(0.276, 1.179)	(0.419, 1.120)	(-0.281, 0.035)
	p-value	0.1295	0.1316	0.1265
___Headache , Mild	Effect measure	0.741	0.795	-0.054
	95% CI	(0.334, 1.640)	(0.434, 1.459)	(-0.198, 0.090)
	p-value	0.4591	0.4594	0.4593
Vascular disorders	Effect measure	8.883	5.108	0.385
	95% CI	(3.398, 23.220)	(2.296, 11.362)	(0.249, 0.522)
	p-value	<0.0001	0.0001	<0.0001
Vascular disorders , Mild	Effect measure	6.818	4.687	0.288
	95% CI	(2.427, 19.149)	(1.914, 11.477)	(0.158, 0.418)
	p-value	0.0003	0.0007	<0.0001

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Vascular disorders , Moderate	Effect measure	8.000	7.211	0.097
	95% CI	(0.972, 65.853)	(0.927, 56.085)	(0.017, 0.177)
	p-value	0.0532	0.0591	0.0168
___Flushing	Effect measure	41.023	25.239	0.379
	95% CI	(5.377, 312.98)	(3.534, 180.23)	(0.261, 0.496)
	p-value	0.0003	0.0013	<0.0001
___Flushing , Mild	Effect measure	51.350	36.986	0.282
	95% CI	(3.033, 869.46)	(2.283, 599.25)	(0.162, 0.401)
	p-value	0.0064	0.0111	<0.0001
___Flushing , Moderate	Effect measure	8.000	7.211	0.097
	95% CI	(0.972, 65.853)	(0.927, 56.085)	(0.017, 0.177)
	p-value	0.0532	0.0591	0.0168
Respiratory thoracic and mediastinal disorders	Effect measure	3.354	2.592	0.199
	95% CI	(1.375, 8.185)	(1.249, 5.378)	(0.063, 0.335)
	p-value	0.0078	0.0106	0.0041

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Respiratory thoracic and mediastinal disorders , Mild	Effect measure	2.745	2.254	0.157
	95% CI	(1.112, 6.775)	(1.068, 4.757)	(0.024, 0.289)
	p-value	0.0285	0.0330	0.0203
___Oropharyngeal pain	Effect measure	3.051	2.704	0.107
	95% CI	(0.931, 10.001)	(0.918, 7.963)	(0.001, 0.212)
	p-value	0.0656	0.0710	0.0477
___Oropharyngeal pain , Mild	Effect measure	2.750	2.479	0.092
	95% CI	(0.829, 9.121)	(0.831, 7.398)	(-0.011, 0.195)
	p-value	0.0982	0.1037	0.0785
___Cough	Effect measure	5.082	4.507	0.110
	95% CI	(1.069, 24.155)	(1.026, 19.802)	(0.018, 0.201)
	p-value	0.0409	0.0462	0.0188
___Cough , Mild	Effect measure	4.500	4.056	0.096
	95% CI	(0.934, 21.675)	(0.910, 18.079)	(0.007, 0.184)
	p-value	0.0608	0.0663	0.0341

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Skin and subcutaneous tissue disorders	Effect measure	9.129	6.610	0.263
	95% CI	(2.580, 32.298)	(2.076, 21.044)	(0.144, 0.382)
	p-value	0.0006	0.0014	<0.0001
Skin and subcutaneous tissue disorders , Mild	Effect measure	7.974	6.009	0.235
	95% CI	(2.241, 28.371)	(1.873, 19.276)	(0.118, 0.352)
	p-value	0.0013	0.0026	0.0001
___Rash	Effect measure	9.145	8.113	0.111
	95% CI	(1.125, 74.347)	(1.057, 62.278)	(0.028, 0.194)
	p-value	0.0384	0.0441	0.0088
___Rash , Mild	Effect measure	9.145	8.113	0.111
	95% CI	(1.125, 74.347)	(1.057, 62.278)	(0.028, 0.194)
	p-value	0.0384	0.0441	0.0088
General disorders and administration site conditions	Effect measure	0.096	0.313	-0.526
	95% CI	(0.044, 0.213)	(0.202, 0.484)	(-0.670, -0.383)
	p-value	<0.0001	<0.0001	<0.0001

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
General disorders and administration site conditions , Mild	Effect measure	0.138	0.308	-0.443
	95% CI	(0.063, 0.299)	(0.186, 0.509)	(-0.593, -0.294)
	p-value	<0.0001	<0.0001	<0.0001
General disorders and administration site conditions , Moderate	Effect measure	0.191	0.225	-0.145
	95% CI	(0.051, 0.713)	(0.067, 0.763)	(-0.252, -0.039)
	p-value	0.0137	0.0166	0.0075
___Pyrexia	Effect measure	0.213	0.258	-0.162
	95% CI	(0.066, 0.687)	(0.089, 0.742)	(-0.277, -0.048)
	p-value	0.0096	0.0120	0.0055
___Pyrexia , Mild	Effect measure	0.140	0.164	-0.144
	95% CI	(0.030, 0.657)	(0.038, 0.712)	(-0.244, -0.044)
	p-value	0.0127	0.0158	0.0049
___Influenza like illness	Effect measure	0.027	0.055	-0.487
	95% CI	(0.006, 0.121)	(0.014, 0.219)	(-0.616, -0.359)
	p-value	<0.0001	<0.0001	<0.0001

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Influenza like illness , Mild	Effect measure	0.052	0.078	-0.331
	95% CI	(0.012, 0.231)	(0.019, 0.319)	(-0.455, -0.208)
	p-value	0.0001	0.0004	<0.0001
___Influenza like illness , Moderate	Effect measure	0.046	0.053	-0.125
	95% CI	(0.003, 0.823)	(0.003, 0.901)	(-0.221, -0.029)
	p-value	0.0363	0.0422	0.0077
___Fatigue	Effect measure	0.116	0.129	-0.095
	95% CI	(0.014, 0.973)	(0.016, 1.018)	(-0.177, -0.014)
	p-value	0.0471	0.0520	0.0215
Musculoskeletal and connective tissue disorders	Effect measure	0.561	0.666	-0.120
	95% CI	(0.266, 1.184)	(0.393, 1.130)	(-0.274, 0.034)
	p-value	0.1295	0.1318	0.1265
Musculoskeletal and connective tissue disorders , Mild	Effect measure	0.589	0.676	-0.101
	95% CI	(0.271, 1.282)	(0.379, 1.205)	(-0.249, 0.047)
	p-value	0.1823	0.1843	0.1801

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Pain in extremity	Effect measure	0.359	0.386	-0.067
	95% CI	(0.089, 1.453)	(0.104, 1.431)	(-0.157, 0.023)
	p-value	0.1511	0.1546	0.1422
___Pain in extremity , Mild	Effect measure	0.359	0.386	-0.067
	95% CI	(0.089, 1.453)	(0.104, 1.431)	(-0.157, 0.023)
	p-value	0.1511	0.1546	0.1422
___Myalgia	Effect measure	0.100	0.113	-0.111
	95% CI	(0.012, 0.823)	(0.014, 0.876)	(-0.196, -0.025)
	p-value	0.0323	0.0370	0.0110
___Myalgia , Mild	Effect measure	0.116	0.129	-0.095
	95% CI	(0.014, 0.973)	(0.016, 1.018)	(-0.177, -0.014)
	p-value	0.0471	0.0520	0.0215
Injury poisoning and procedural complications	Effect measure	4.364	3.606	0.163
	95% CI	(1.375, 13.852)	(1.272, 10.224)	(0.049, 0.277)
	p-value	0.0124	0.0159	0.0051

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
Injury poisoning and procedural complications , Mild	Effect measure	3.728	3.305	0.108
	95% CI	(0.990, 14.030)	(0.965, 11.320)	(0.009, 0.207)
	p-value	0.0517	0.0570	0.0321
Eye disorders	Effect measure	1.243	1.202	0.028
	95% CI	(0.486, 3.179)	(0.542, 2.663)	(-0.093, 0.150)
	p-value	0.6499	0.6505	0.6480
Eye disorders , Mild	Effect measure	1.120	1.102	0.014
	95% CI	(0.432, 2.908)	(0.488, 2.485)	(-0.105, 0.134)
	p-value	0.8153	0.8155	0.8149
Reproductive system and breast disorders	Effect measure	1.656	1.545	0.060
	95% CI	(0.609, 4.505)	(0.648, 3.684)	(-0.056, 0.176)
	p-value	0.3231	0.3262	0.3134
Reproductive system and breast disorders , Mild	Effect measure	3.728	3.305	0.108
	95% CI	(0.990, 14.030)	(0.965, 11.320)	(0.009, 0.207)
	p-value	0.0517	0.0570	0.0321

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

	Result	OR	RR	ARR
___Dysmenorrhoea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708, 6.607)	(0.728, 5.400)	(-0.030, 0.184)
	p-value	0.1756	0.1804	0.1587
___Dysmenorrhoea , Mild	Effect measure	10.328	9.014	0.125
	95% CI	(1.283, 83.130)	(1.187, 68.475)	(0.039, 0.212)
	p-value	0.0282	0.0336	0.0045
Psychiatric disorders	Effect measure	1.002	1.002	0.000
	95% CI	(0.379, 2.647)	(0.435, 2.308)	(-0.117, 0.118)
	p-value	0.9971	0.9971	0.9971
Psychiatric disorders , Mild	Effect measure	1.498	1.442	0.035
	95% CI	(0.464, 4.840)	(0.497, 4.184)	(-0.064, 0.133)
	p-value	0.4990	0.5004	0.4924

NOTE1: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_ah_ban021522.sas

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135)

N(%) FOR HAVING AT LEAST 1 OF EACH TYPE (of maximum severity when applicable) OF ADVERSE EVENT BY STUDY ARM
The only AEs reported here are those with >=10% in either study arm (>=5% for severe AEs)
ANALYSIS NOT USING SUBGROUPS

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N = 135)
Adverse event				
	No	3 (4)	3 (5)	6 (4)
	Yes	68 (96)	61 (95)	129 (96)
___Mild				
	No	44 (62)	39 (61)	83 (61)
	Yes	27 (38)	25 (39)	52 (39)
___Moderate				
	No	31 (44)	38 (59)	69 (51)
	Yes	40 (56)	26 (41)	66 (49)
___Severe				
	No	70 (99)	54 (84)	124 (92)
	Yes	1 (1)	10 (16)	11 (8)
Gastrointestinal disorders				
	No	18 (25)	44 (69)	62 (46)
	Yes	53 (75)	20 (31)	73 (54)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N = 135)
Gastrointestinal disorders , Mild				
	No	27 (38)	48 (75)	75 (56)
	Yes	44 (62)	16 (25)	60 (44)
Gastrointestinal disorders , Moderate				
	No	57 (80)	57 (89)	114 (84)
	Yes	14 (20)	7 (11)	21 (16)
___Abdominal pain				
	No	43 (61)	59 (92)	102 (76)
	Yes	28 (39)	5 (8)	33 (24)
___Abdominal pain , Mild				
	No	47 (66)	60 (94)	107 (79)
	Yes	24 (34)	4 (6)	28 (21)
___Vomiting				
	No	55 (77)	59 (92)	114 (84)
	Yes	16 (23)	5 (8)	21 (16)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Vomiting , Mild				
	No	59 (83)	62 (97)	121 (90)
	Yes	12 (17)	2 (3)	14 (10)
___Diarrhoea				
	No	57 (80)	60 (94)	117 (87)
	Yes	14 (20)	4 (6)	18 (13)
___Diarrhoea , Mild				
	No	62 (87)	60 (94)	122 (90)
	Yes	9 (13)	4 (6)	13 (10)
___Abdominal pain upper				
	No	59 (83)	63 (98)	122 (90)
	Yes	12 (17)	1 (2)	13 (10)
___Abdominal pain upper , Mild				
	No	61 (86)	63 (98)	124 (92)
	Yes	10 (14)	1 (2)	11 (8)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Nausea				
	No	60 (85)	59 (92)	119 (88)
	Yes	11 (15)	5 (8)	16 (12)
___Nausea , Mild				
	No	61 (86)	60 (94)	121 (90)
	Yes	10 (14)	4 (6)	14 (10)
Infections and infestations				
	No	27 (38)	31 (48)	58 (43)
	Yes	44 (62)	33 (52)	77 (57)
Infections and infestations , Mild				
	No	35 (49)	36 (56)	71 (53)
	Yes	36 (51)	28 (44)	64 (47)
Infections and infestations , Moderate				
	No	58 (82)	56 (88)	114 (84)
	Yes	13 (18)	8 (13)	21 (16)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Nasopharyngitis				
	No	55 (77)	55 (86)	110 (81)
	Yes	16 (23)	9 (14)	25 (19)
___Nasopharyngitis , Mild				
	No	55 (77)	57 (89)	112 (83)
	Yes	16 (23)	7 (11)	23 (17)
___Gastroenteritis				
	No	62 (87)	59 (92)	121 (90)
	Yes	9 (13)	5 (8)	14 (10)
___Upper respiratory tract infection				
	No	62 (87)	61 (95)	123 (91)
	Yes	9 (13)	3 (5)	12 (9)
Nervous system disorders				
	No	28 (39)	17 (27)	45 (33)
	Yes	43 (61)	47 (73)	90 (67)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Nervous system disorders , Mild				
	No	44 (62)	31 (48)	75 (56)
	Yes	27 (38)	33 (52)	60 (44)
Nervous system disorders , Moderate				
	No	49 (69)	41 (64)	90 (67)
	Yes	22 (31)	23 (36)	45 (33)
Nervous system disorders , Severe				
	No	70 (99)	58 (91)	128 (95)
	Yes	1 (1)	6 (9)	7 (5)
___Multiple sclerosis relapse				
	No	49 (69)	32 (50)	81 (60)
	Yes	22 (31)	32 (50)	54 (40)
___Multiple sclerosis relapse , Mild				
	No	65 (92)	52 (81)	117 (87)
	Yes	6 (8)	12 (19)	18 (13)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Multiple sclerosis relapse , Moderate				
	No	56 (79)	47 (73)	103 (76)
	Yes	15 (21)	17 (27)	32 (24)
___Headache				
	No	52 (73)	39 (61)	91 (67)
	Yes	19 (27)	25 (39)	44 (33)
___Headache , Mild				
	No	56 (79)	47 (73)	103 (76)
	Yes	15 (21)	17 (27)	32 (24)
Vascular disorders				
	No	37 (52)	58 (91)	95 (70)
	Yes	34 (48)	6 (9)	40 (30)
Vascular disorders , Mild				
	No	45 (63)	59 (92)	104 (77)
	Yes	26 (37)	5 (8)	31 (23)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Vascular disorders , Moderate				
	No	63 (89)	63 (98)	126 (93)
	Yes	8 (11)	1 (2)	9 (7)
___Flushing				
	No	43 (61)	63 (98)	106 (79)
	Yes	28 (39)	1 (2)	29 (21)
___Flushing , Mild				
	No	51 (72)	64 (100)	115 (85)
	Yes	20 (28)	0 (0)	20 (15)
___Flushing , Moderate				
	No	63 (89)	63 (98)	126 (93)
	Yes	8 (11)	1 (2)	9 (7)
Respiratory thoracic and mediastinal disorders				
	No	48 (68)	56 (88)	104 (77)
	Yes	23 (32)	8 (13)	31 (23)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Respiratory thoracic and mediastinal disorders , Mild				
	No	51 (72)	56 (88)	107 (79)
	Yes	20 (28)	8 (13)	28 (21)
___Oropharyngeal pain				
	No	59 (83)	60 (94)	119 (88)
	Yes	12 (17)	4 (6)	16 (12)
___Oropharyngeal pain , Mild				
	No	60 (85)	60 (94)	120 (89)
	Yes	11 (15)	4 (6)	15 (11)
___Cough				
	No	61 (86)	62 (97)	123 (91)
	Yes	10 (14)	2 (3)	12 (9)
___Cough , Mild				
	No	62 (87)	62 (97)	124 (92)
	Yes	9 (13)	2 (3)	11 (8)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Skin and subcutaneous tissue disorders				
	No	49 (69)	61 (95)	110 (81)
	Yes	22 (31)	3 (5)	25 (19)
Skin and subcutaneous tissue disorders , Mild				
	No	51 (72)	61 (95)	112 (83)
	Yes	20 (28)	3 (5)	23 (17)
___Rash				
	No	62 (87)	63 (98)	125 (93)
	Yes	9 (13)	1 (2)	10 (7)
___Rash , Mild				
	No	62 (87)	63 (98)	125 (93)
	Yes	9 (13)	1 (2)	10 (7)
General disorders and administration site conditions				
	No	54 (76)	15 (23)	69 (51)
	Yes	17 (24)	49 (77)	66 (49)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
General disorders and administration site conditions , Mild				
	No	57 (80)	23 (36)	80 (59)
	Yes	14 (20)	41 (64)	55 (41)
General disorders and administration site conditions , Moderate				
	No	68 (96)	52 (81)	120 (89)
	Yes	3 (4)	12 (19)	15 (11)
___Pyrexia				
	No	67 (94)	50 (78)	117 (87)
	Yes	4 (6)	14 (22)	18 (13)
___Pyrexia , Mild				
	No	69 (97)	53 (83)	122 (90)
	Yes	2 (3)	11 (17)	13 (10)
___Influenza like illness				
	No	69 (97)	31 (48)	100 (74)
	Yes	2 (3)	33 (52)	35 (26)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Influenza like illness , Mild				
	No	69 (97)	41 (64)	110 (81)
	Yes	2 (3)	23 (36)	25 (19)
___Influenza like illness , Moderate				
	No	71 (100)	56 (88)	127 (94)
	Yes	0 (0)	8 (13)	8 (6)
___Fatigue				
	No	70 (99)	57 (89)	127 (94)
	Yes	1 (1)	7 (11)	8 (6)
Musculoskeletal and connective tissue disorders				
	No	54 (76)	41 (64)	95 (70)
	Yes	17 (24)	23 (36)	40 (30)
Musculoskeletal and connective tissue disorders , Mild				
	No	56 (79)	44 (69)	100 (74)
	Yes	15 (21)	20 (31)	35 (26)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Pain in extremity				
	No	68 (96)	57 (89)	125 (93)
	Yes	3 (4)	7 (11)	10 (7)
___Pain in extremity , Mild				
	No	68 (96)	57 (89)	125 (93)
	Yes	3 (4)	7 (11)	10 (7)
___Myalgia				
	No	70 (99)	56 (88)	126 (93)
	Yes	1 (1)	8 (13)	9 (7)
___Myalgia , Mild				
	No	70 (99)	57 (89)	127 (94)
	Yes	1 (1)	7 (11)	8 (6)
Injury poisoning and procedural complications				
	No	55 (77)	60 (94)	115 (85)
	Yes	16 (23)	4 (6)	20 (15)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Injury poisoning and procedural complications , Mild				
	No	60 (85)	61 (95)	121 (90)
	Yes	11 (15)	3 (5)	14 (10)
Eye disorders				
	No	59 (83)	55 (86)	114 (84)
	Yes	12 (17)	9 (14)	21 (16)
Eye disorders , Mild				
	No	60 (85)	55 (86)	115 (85)
	Yes	11 (15)	9 (14)	20 (15)
Reproductive system and breast disorders				
	No	59 (83)	57 (89)	116 (86)
	Yes	12 (17)	7 (11)	19 (14)
Reproductive system and breast disorders , Mild				
	No	60 (85)	61 (95)	121 (90)
	Yes	11 (15)	3 (5)	14 (10)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

ENDPOINT_SETUP	Event	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Dysmenorrhoea				
	No	60 (85)	59 (92)	119 (88)
	Yes	11 (15)	5 (8)	16 (12)
___Dysmenorrhoea , Mild				
	No	61 (86)	63 (98)	124 (92)
	Yes	10 (14)	1 (2)	11 (8)
Psychiatric disorders				
	No	61 (86)	55 (86)	116 (86)
	Yes	10 (14)	9 (14)	19 (14)
Psychiatric disorders , Mild				
	No	63 (89)	59 (92)	122 (90)
	Yes	8 (11)	5 (8)	13 (10)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: Since we are only including PTs and SOCs >=10% in either arm (>=5% for severe AEs), the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_AH_BN021422.sas

Sub groups

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_age13to14

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
Gastrointestinal Disorders	Effect measure	4.667	1.815	0.349
	95% CI	(1.006, 21.652)	(0.944, 3.488)	(0.027, 0.672)
	p-value	0.0491	0.0738	0.0339
Gastrointestinal Disorders , MILD	Effect measure	5.762	2.852	0.397
	95% CI	(1.175, 28.251)	(0.980, 8.303)	(0.086, 0.708)
	p-value	0.0309	0.0546	0.0125
___Abdominal Pain	Effect measure	6.500	4.667	0.262
	95% CI	(0.680, 62.149)	(0.633, 34.430)	(0.006, 0.518)
	p-value	0.1042	0.1308	0.0451
___Abdominal Pain , MILD	Effect measure	11.815	8.622	0.278
	95% CI	(0.595, 234.58)	(0.518, 143.53)	(0.007, 0.548)
	p-value	0.1053	0.1333	0.0424
Respiratory Thoracic And Mediastinal Disorders	Effect measure	10.400	6.222	0.373
	95% CI	(1.111, 97.335)	(0.878, 44.086)	(0.107, 0.639)
	p-value	0.0401	0.0673	0.0060

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	8.273	5.444	0.317
	95% CI	(0.877, 78.010)	(0.755, 39.254)	(0.055, 0.580)
	p-value	0.0649	0.0927	0.0178
Vascular Disorders	Effect measure	18.913	11.757	0.389
	95% CI	(0.975, 366.99)	(0.730, 189.31)	(0.100, 0.678)
	p-value	0.0520	0.0822	0.0046
Vascular Disorders , MILD	Effect measure	11.815	8.622	0.278
	95% CI	(0.595, 234.58)	(0.518, 143.53)	(0.007, 0.548)
	p-value	0.1053	0.1333	0.0424
___Flushing	Effect measure	15.080	10.189	0.333
	95% CI	(0.770, 295.19)	(0.624, 166.40)	(0.052, 0.615)
	p-value	0.0738	0.1033	0.0152
___Flushing , MILD	Effect measure	9.000	7.054	0.222
	95% CI	(0.443, 182.78)	(0.412, 120.70)	(-0.033, 0.478)
	p-value	0.1526	0.1775	0.1053

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
General Disorders And Administration Site Conditions	Effect measure	0.154	0.389	-0.437
	95% CI	(0.033, 0.726)	(0.172, 0.879)	(-0.751, -0.122)
	p-value	0.0181	0.0232	0.0065
General Disorders And Administration Site Conditions , MILD	Effect measure	0.159	0.346	-0.421
	95% CI	(0.033, 0.754)	(0.134, 0.892)	(-0.737, -0.105)
	p-value	0.0207	0.0281	0.0091
___Pyrexia	Effect measure	0.313	0.389	-0.175
	95% CI	(0.048, 2.032)	(0.083, 1.827)	(-0.452, 0.103)
	p-value	0.2234	0.2315	0.2177
___Influenza Like Illness	Effect measure	0.027	0.052	-0.500
	95% CI	(0.001, 0.535)	(0.003, 0.841)	(-0.825, -0.175)
	p-value	0.0178	0.0374	0.0011
___Influenza Like Illness , MILD	Effect measure	0.047	0.071	-0.357
	95% CI	(0.002, 0.937)	(0.004, 1.186)	(-0.672, -0.043)
	p-value	0.0452	0.0656	0.0218

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Skin And Subcutaneous Tissue Disorders	Effect measure	2.308	1.944	0.135
	95% CI	(0.375, 14.212)	(0.441, 8.573)	(-0.142, 0.411)
	p-value	0.3673	0.3797	0.3388
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	1.200	1.167	0.024
	95% CI	(0.172, 8.380)	(0.225, 6.058)	(-0.228, 0.275)
	p-value	0.8541	0.8545	0.8528
Injury Poisoning And Procedural Complications	Effect measure	9.000	7.054	0.222
	95% CI	(0.443, 182.78)	(0.412, 120.70)	(-0.033, 0.478)
	p-value	0.1526	0.1775	0.1053
___Multiple Sclerosis Relapse	Effect measure	0.016	0.041	-0.643
	95% CI	(0.001, 0.314)	(0.003, 0.651)	(-0.957, -0.328)
	p-value	0.0066	0.0236	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_age15to17

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
Gastrointestinal Disorders	Effect measure	7.163	2.628	0.456
	95% CI	(3.006, 17.069)	(1.638, 4.217)	(0.284, 0.628)
	p-value	<0.0001	0.0001	<0.0001
Gastrointestinal Disorders , MILD	Effect measure	4.696	2.395	0.363
	95% CI	(2.025, 10.892)	(1.435, 3.998)	(0.184, 0.541)
	p-value	0.0003	0.0008	0.0001
___Abdominal Pain	Effect measure	8.161	5.189	0.335
	95% CI	(2.562, 25.998)	(1.923, 14.003)	(0.183, 0.488)
	p-value	0.0004	0.0012	<0.0001
___Abdominal Pain , MILD	Effect measure	6.426	4.481	0.278
	95% CI	(2.003, 20.619)	(1.638, 12.262)	(0.129, 0.428)
	p-value	0.0018	0.0035	0.0003
Vascular Disorders	Effect measure	7.615	4.245	0.389
	95% CI	(2.777, 20.883)	(1.916, 9.408)	(0.227, 0.551)
	p-value	0.0001	0.0004	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Vascular Disorders , MILD	Effect measure	5.906	3.962	0.296
	95% CI	(2.015, 17.313)	(1.618, 9.702)	(0.140, 0.452)
	p-value	0.0012	0.0026	0.0002
___Flushing	Effect measure	34.774	20.755	0.395
	95% CI	(4.459, 271.17)	(2.905, 148.29)	(0.257, 0.533)
	p-value	0.0007	0.0025	<0.0001
___Flushing , MILD	Effect measure	44.440	31.150	0.302
	95% CI	(2.583, 764.47)	(1.919, 505.67)	(0.159, 0.445)
	p-value	0.0090	0.0156	<0.0001
Skin And Subcutaneous Tissue Disorders	Effect measure	23.139	16.038	0.301
	95% CI	(2.943, 181.94)	(2.216, 116.09)	(0.169, 0.432)
	p-value	0.0028	0.0060	<0.0001
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	23.139	16.038	0.301
	95% CI	(2.943, 181.94)	(2.216, 116.09)	(0.169, 0.432)
	p-value	0.0028	0.0060	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA. SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Respiratory Thoracic And Mediastinal Disorders	Effect measure	2.425	2.022	0.143
	95% CI	(0.894, 6.576)	(0.900, 4.543)	(-0.012, 0.298)
	p-value	0.0818	0.0884	0.0701
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	1.996	1.752	0.105
	95% CI	(0.724, 5.507)	(0.761, 4.033)	(-0.045, 0.256)
	p-value	0.1817	0.1874	0.1705
General Disorders And Administration Site Conditions	Effect measure	0.083	0.290	-0.554
	95% CI	(0.033, 0.209)	(0.173, 0.488)	(-0.714, -0.393)
	p-value	<0.0001	<0.0001	<0.0001
General Disorders And Administration Site Conditions , MILD	Effect measure	0.131	0.295	-0.451
	95% CI	(0.053, 0.321)	(0.162, 0.535)	(-0.621, -0.282)
	p-value	<0.0001	0.0001	<0.0001
___Influenza Like Illness	Effect measure	0.036	0.073	-0.482
	95% CI	(0.008, 0.165)	(0.018, 0.290)	(-0.630, -0.335)
	p-value	<0.0001	0.0002	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Influenza Like Illness , MILD	Effect measure	0.070	0.105	-0.322
	95% CI	(0.015, 0.321)	(0.026, 0.429)	(-0.465, -0.180)
	p-value	0.0006	0.0017	<0.0001
___Pyrexia	Effect measure	0.157	0.189	-0.162
	95% CI	(0.033, 0.757)	(0.043, 0.819)	(-0.284, -0.040)
	p-value	0.0210	0.0260	0.0092
Injury Poisoning And Procedural Complications	Effect measure	3.366	2.830	0.146
	95% CI	(1.006, 11.257)	(0.977, 8.198)	(0.011, 0.282)
	p-value	0.0488	0.0552	0.0341
___Multiple Sclerosis Relapse	Effect measure	0.833	0.902	-0.045
	95% CI	(0.382, 1.817)	(0.582, 1.399)	(-0.236, 0.147)
	p-value	0.6462	0.6462	0.6458

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_female

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Female sex

	Result	OR	RR	ARR
___Severe	Effect measure	0.073	0.092	-0.197
	95% CI	(0.009, 0.600)	(0.012, 0.691)	(-0.323, -0.072)
	p-value	0.0148	0.0204	0.0020
Gastrointestinal Disorders	Effect measure	8.104	2.563	0.476
	95% CI	(3.237, 20.288)	(1.616, 4.064)	(0.300, 0.651)
	p-value	<0.0001	0.0001	<0.0001
Gastrointestinal Disorders , MILD	Effect measure	6.176	2.760	0.421
	95% CI	(2.523, 15.119)	(1.588, 4.796)	(0.241, 0.601)
	p-value	0.0001	0.0003	<0.0001
___Abdominal Pain	Effect measure	6.985	4.232	0.351
	95% CI	(2.367, 20.616)	(1.755, 10.206)	(0.186, 0.516)
	p-value	0.0004	0.0013	<0.0001
___Abdominal Pain , MILD	Effect measure	7.603	4.830	0.333
	95% CI	(2.362, 24.481)	(1.792, 13.017)	(0.174, 0.492)
	p-value	0.0007	0.0019	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Vomiting	Effect measure	3.689	2.990	0.173
	95% CI	(1.106, 12.305)	(1.050, 8.516)	(0.027, 0.319)
	p-value	0.0337	0.0403	0.0205
___Vomiting , MILD	Effect measure	6.947	5.520	0.197
	95% CI	(1.462, 33.015)	(1.305, 23.354)	(0.064, 0.329)
	p-value	0.0148	0.0203	0.0036
___Diarrhoea	Effect measure	11.250	9.200	0.178
	95% CI	(1.379, 91.804)	(1.225, 69.093)	(0.060, 0.297)
	p-value	0.0238	0.0310	0.0032
Vascular Disorders	Effect measure	8.200	4.600	0.391
	95% CI	(2.781, 24.179)	(1.922, 11.010)	(0.226, 0.557)
	p-value	0.0001	0.0006	<0.0001
Vascular Disorders , MILD	Effect measure	6.435	4.370	0.293
	95% CI	(1.990, 20.815)	(1.606, 11.892)	(0.136, 0.450)
	p-value	0.0019	0.0039	0.0003

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Flushing	Effect measure	27.581	17.480	0.358
	95% CI	(3.507, 216.89)	(2.436, 125.42)	(0.217, 0.499)
	p-value	0.0016	0.0044	<0.0001
___Flushing , MILD	Effect measure	33.480	24.861	0.260
	95% CI	(1.926, 581.85)	(1.520, 406.56)	(0.118, 0.402)
	p-value	0.0159	0.0242	0.0001
Respiratory Thoracic And Mediastinal Disorders	Effect measure	4.224	3.128	0.231
	95% CI	(1.410, 12.658)	(1.255, 7.796)	(0.072, 0.390)
	p-value	0.0101	0.0144	0.0044
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	3.514	2.760	0.191
	95% CI	(1.160, 10.643)	(1.089, 6.992)	(0.036, 0.347)
	p-value	0.0262	0.0323	0.0160
Skin And Subcutaneous Tissue Disorders	Effect measure	6.745	4.907	0.255
	95% CI	(1.815, 25.063)	(1.529, 15.751)	(0.107, 0.402)
	p-value	0.0044	0.0075	0.0007

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	6.143	4.600	0.235
	95% CI	(1.645, 22.937)	(1.423, 14.868)	(0.089, 0.380)
	p-value	0.0069	0.0108	0.0016
General Disorders And Administration Site Conditions	Effect measure	0.100	0.298	-0.519
	95% CI	(0.039, 0.254)	(0.172, 0.516)	(-0.690, -0.348)
	p-value	<0.0001	<0.0001	<0.0001
General Disorders And Administration Site Conditions , MILD	Effect measure	0.121	0.297	-0.474
	95% CI	(0.048, 0.306)	(0.165, 0.535)	(-0.649, -0.299)
	p-value	<0.0001	0.0001	<0.0001
___Pyrexia	Effect measure	0.133	0.167	-0.199
	95% CI	(0.028, 0.636)	(0.039, 0.715)	(-0.334, -0.064)
	p-value	0.0116	0.0158	0.0038
___Pyrexia , MILD	Effect measure	0.150	0.184	-0.177
	95% CI	(0.031, 0.727)	(0.043, 0.796)	(-0.308, -0.046)
	p-value	0.0185	0.0235	0.0079

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Influenza Like Illness	Effect measure	0.019	0.038	-0.502
	95% CI	(0.002, 0.147)	(0.005, 0.272)	(-0.651, -0.352)
	p-value	0.0002	0.0011	<0.0001
___Influenza Like Illness , MILD	Effect measure	0.035	0.054	-0.350
	95% CI	(0.004, 0.275)	(0.007, 0.391)	(-0.494, -0.205)
	p-value	0.0015	0.0038	<0.0001
Injury Poisoning And Procedural Complications	Effect measure	3.583	3.067	0.135
	95% CI	(0.920, 13.963)	(0.900, 10.455)	(0.003, 0.267)
	p-value	0.0659	0.0733	0.0451
___Multiple Sclerosis Relapse	Effect measure	0.471	0.640	-0.180
	95% CI	(0.205, 1.078)	(0.389, 1.052)	(-0.374, 0.014)
	p-value	0.0747	0.0783	0.0688
___Dysmenorrhoea , MILD	Effect measure	11.250	9.200	0.178
	95% CI	(1.379, 91.804)	(1.225, 69.093)	(0.060, 0.297)
	p-value	0.0238	0.0310	0.0032

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

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NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_EFFECTMEASURES_male

Tables 63, 64, 67, 68: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR FOR HAVING AT LEAST 1 OF EACH TYPE OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Male sex

	Result	OR	RR	ARR
___Severe	Effect measure	NA	NA	NA
	95% CI	NA	NA	NA
	p-value	NA	NA	NA
Gastrointestinal Disorders	Effect measure	4.000	2.000	0.333
	95% CI	(1.052, 15.207)	(0.974, 4.109)	(0.037, 0.630)
	p-value	0.0419	0.0592	0.0277
Gastrointestinal Disorders , MILD	Effect measure	2.860	1.886	0.246
	95% CI	(0.748, 10.929)	(0.807, 4.408)	(-0.051, 0.543)
	p-value	0.1245	0.1432	0.1049
___Abdominal Pain	Effect measure	12.333	9.465	0.238
	95% CI	(0.633, 240.44)	(0.560, 160.00)	(0.004, 0.472)
	p-value	0.0973	0.1192	0.0448
___Abdominal Pain , MILD	Effect measure	7.000	6.023	0.143
	95% CI	(0.337, 145.24)	(0.332, 109.17)	(-0.058, 0.344)
	p-value	0.2085	0.2245	0.2320

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)

NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
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NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Diarrhoea	Effect measure	1.176	1.143	0.024
	95% CI	(0.226, 6.127)	(0.294, 4.444)	(-0.217, 0.264)
	p-value	0.8469	0.8472	0.8462
___Vomiting	Effect measure	2.833	2.571	0.087
	95% CI	(0.268, 29.955)	(0.292, 22.608)	(-0.096, 0.271)
	p-value	0.3867	0.3945	0.3506
Vascular Disorders	Effect measure	12.750	7.714	0.373
	95% CI	(1.421, 114.40)	(1.078, 55.191)	(0.136, 0.610)
	p-value	0.0230	0.0418	0.0020
Vascular Disorders , MILD	Effect measure	8.500	6.000	0.278
	95% CI	(0.931, 77.598)	(0.813, 44.267)	(0.050, 0.505)
	p-value	0.0579	0.0789	0.0168
___Flushing	Effect measure	28.120	16.349	0.429
	95% CI	(1.497, 528.18)	(1.019, 262.23)	(0.165, 0.692)
	p-value	0.0258	0.0484	0.0005

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
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SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Flushing , MILD	Effect measure	19.138	12.907	0.333
	95% CI	(1.008, 363.50)	(0.789, 211.07)	(0.080, 0.587)
	p-value	0.0494	0.0728	0.0062
General Disorders And Administration Site Conditions	Effect measure	0.080	0.343	-0.548
	95% CI	(0.017, 0.381)	(0.169, 0.695)	(-0.806, -0.289)
	p-value	0.0015	0.0030	<0.0001
General Disorders And Administration Site Conditions , MILD	Effect measure	0.188	0.343	-0.365
	95% CI	(0.045, 0.788)	(0.129, 0.908)	(-0.650, -0.081)
	p-value	0.0223	0.0312	0.0119
___Pyrexia	Effect measure	0.526	0.571	-0.071
	95% CI	(0.078, 3.565)	(0.107, 3.050)	(-0.285, 0.142)
	p-value	0.5108	0.5125	0.5112
___Pyrexia , MILD	Effect measure	0.271	0.287	-0.056
	95% CI	(0.010, 7.083)	(0.012, 6.625)	(-0.213, 0.102)
	p-value	0.4332	0.4356	0.9414

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
___Influenza Like Illness	Effect measure	0.050	0.095	-0.452
	95% CI	(0.005, 0.456)	(0.013, 0.681)	(-0.701, -0.204)
	p-value	0.0079	0.0192	0.0004
___Influenza Like Illness , MILD	Effect measure	0.100	0.143	-0.286
	95% CI	(0.011, 0.934)	(0.019, 1.078)	(-0.522, -0.050)
	p-value	0.0434	0.0592	0.0177
Injury Poisoning And Procedural Complications	Effect measure	6.800	5.143	0.230
	95% CI	(0.733, 63.110)	(0.681, 38.816)	(0.010, 0.450)
	p-value	0.0917	0.1123	0.0406
Respiratory Thoracic And Mediastinal Disorders	Effect measure	2.000	1.714	0.119
	95% CI	(0.420, 9.516)	(0.499, 5.892)	(-0.140, 0.378)
	p-value	0.3838	0.3922	0.3673
Respiratory Thoracic And Mediastinal Disorders , MILD	Effect measure	1.563	1.429	0.071
	95% CI	(0.317, 7.703)	(0.395, 5.166)	(-0.179, 0.322)
	p-value	0.5835	0.5866	0.5765

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
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NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.

NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

	Result	OR	RR	ARR
Skin And Subcutaneous Tissue Disorders	Effect measure	15.516	11.186	0.286
	95% CI	(0.808, 297.80)	(0.674, 185.52)	(0.041, 0.531)
	p-value	0.0689	0.0920	0.0176
Skin And Subcutaneous Tissue Disorders , MILD	Effect measure	12.333	9.465	0.238
	95% CI	(0.633, 240.44)	(0.560, 160.00)	(0.004, 0.472)
	p-value	0.0973	0.1192	0.0448
___Multiple Sclerosis Relapse	Effect measure	0.400	0.571	-0.214
	95% CI	(0.107, 1.502)	(0.252, 1.296)	(-0.515, 0.087)
	p-value	0.1746	0.1805	0.1631

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_n=135_subgroups_ah_ban032822.sasdate: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_age13to14

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE (of maximum severity when applicable) OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 13 to 14

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Gastrointestinal Disorders				
	Yes	14 (78)	6 (43)	20 (63)
	No	4 (22)	8 (57)	12 (38)
Gastrointestinal Disorders , MILD				
	Yes	11 (61)	3 (21)	14 (44)
	No	7 (39)	11 (79)	18 (56)
___Abdominal Pain				
	Yes	6 (33)	1 (7)	7 (22)
	No	12 (67)	13 (93)	25 (78)
___Abdominal Pain , MILD				
	Yes	5 (28)	0 (0)	5 (16)
	No	13 (72)	14 (100)	27 (84)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	8 (44)	1 (7)	9 (28)
	No	10 (56)	13 (93)	23 (72)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	7 (39)	1 (7)	8 (25)
	No	11 (61)	13 (93)	24 (75)
Vascular Disorders				
	Yes	7 (39)	0 (0)	7 (22)
	No	11 (61)	14 (100)	25 (78)
Vascular Disorders , MILD				
	Yes	5 (28)	0 (0)	5 (16)
	No	13 (72)	14 (100)	27 (84)
___Flushing				
	Yes	6 (33)	0 (0)	6 (19)
	No	12 (67)	14 (100)	26 (81)
___Flushing , MILD				
	Yes	4 (22)	0 (0)	4 (13)
	No	14 (78)	14 (100)	28 (88)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
General Disorders And Administration Site Conditions				
	Yes	5 (28)	10 (71)	15 (47)
	No	13 (72)	4 (29)	17 (53)
General Disorders And Administration Site Conditions , MILD				
	Yes	4 (22)	9 (64)	13 (41)
	No	14 (78)	5 (36)	19 (59)
___Pyrexia				
	Yes	2 (11)	4 (29)	6 (19)
	No	16 (89)	10 (71)	26 (81)
___Influenza Like Illness				
	Yes	0 (0)	7 (50)	7 (22)
	No	18 (100)	7 (50)	25 (78)
___Influenza Like Illness , MILD				
	Yes	0 (0)	5 (36)	5 (16)
	No	18 (100)	9 (64)	27 (84)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Skin And Subcutaneous Tissue Disorders				
	Yes	5 (28)	2 (14)	7 (22)
	No	13 (72)	12 (86)	25 (78)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	3 (17)	2 (14)	5 (16)
	No	15 (83)	12 (86)	27 (84)
Injury Poisoning And Procedural Complications				
	Yes	4 (22)	0 (0)	4 (13)
	No	14 (78)	14 (100)	28 (88)
___Multiple Sclerosis Relapse				
	Yes	0 (0)	9 (64)	9 (28)
	No	18 (100)	5 (36)	23 (72)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_age15to17

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE (of maximum severity when applicable) OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Ages 15 to 17

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Gastrointestinal Disorders				
	Yes	39 (74)	14 (28)	53 (51)
	No	14 (26)	36 (72)	50 (49)
Gastrointestinal Disorders , MILD				
	Yes	33 (62)	13 (26)	46 (45)
	No	20 (38)	37 (74)	57 (55)
___Abdominal Pain				
	Yes	22 (42)	4 (8)	26 (25)
	No	31 (58)	46 (92)	77 (75)
___Abdominal Pain , MILD				
	Yes	19 (36)	4 (8)	23 (22)
	No	34 (64)	46 (92)	80 (78)
Vascular Disorders				
	Yes	27 (51)	6 (12)	33 (32)
	No	26 (49)	44 (88)	70 (68)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Vascular Disorders , MILD				
	Yes	21 (40)	5 (10)	26 (25)
	No	32 (60)	45 (90)	77 (75)
___Flushing				
	Yes	22 (42)	1 (2)	23 (22)
	No	31 (58)	49 (98)	80 (78)
___Flushing , MILD				
	Yes	16 (30)	0 (0)	16 (16)
	No	37 (70)	50 (100)	87 (84)
Skin And Subcutaneous Tissue Disorders				
	Yes	17 (32)	1 (2)	18 (17)
	No	36 (68)	49 (98)	85 (83)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	17 (32)	1 (2)	18 (17)
	No	36 (68)	49 (98)	85 (83)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	15 (28)	7 (14)	22 (21)
	No	38 (72)	43 (86)	81 (79)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	13 (25)	7 (14)	20 (19)
	No	40 (75)	43 (86)	83 (81)
General Disorders And Administration Site Conditions				
	Yes	12 (23)	39 (78)	51 (50)
	No	41 (77)	11 (22)	52 (50)
General Disorders And Administration Site Conditions , MILD				
	Yes	10 (19)	32 (64)	42 (41)
	No	43 (81)	18 (36)	61 (59)
___Influenza Like Illness				
	Yes	2 (4)	26 (52)	28 (27)
	No	51 (96)	24 (48)	75 (73)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
___Influenza Like Illness , MILD				
	Yes	2 (4)	18 (36)	20 (19)
	No	51 (96)	32 (64)	83 (81)
___Pyrexia				
	Yes	2 (4)	10 (20)	12 (12)
	No	51 (96)	40 (80)	91 (88)
Injury Poisoning And Procedural Complications				
	Yes	12 (23)	4 (8)	16 (16)
	No	41 (77)	46 (92)	87 (84)
___Multiple Sclerosis Relapse				
	Yes	22 (42)	23 (46)	45 (44)
	No	31 (58)	27 (54)	58 (56)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_female

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE (of maximum severity when applicable) OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Female sex

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Severe				
	Yes	1 (2)	10 (22)	11 (11)
	No	49 (98)	36 (78)	85 (89)
Gastrointestinal Disorders				
	Yes	39 (78)	14 (30)	53 (55)
	No	11 (22)	32 (70)	43 (45)
Gastrointestinal Disorders , MILD				
	Yes	33 (66)	11 (24)	44 (46)
	No	17 (34)	35 (76)	52 (54)
___Abdominal Pain				
	Yes	23 (46)	5 (11)	28 (29)
	No	27 (54)	41 (89)	68 (71)
___Abdominal Pain , MILD				
	Yes	21 (42)	4 (9)	25 (26)
	No	29 (58)	42 (91)	71 (74)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Vomiting				
	Yes	13 (26)	4 (9)	17 (18)
	No	37 (74)	42 (91)	79 (82)
___Vomiting , MILD				
	Yes	12 (24)	2 (4)	14 (15)
	No	38 (76)	44 (96)	82 (85)
___Diarrhoea				
	Yes	10 (20)	1 (2)	11 (11)
	No	40 (80)	45 (98)	85 (89)
Vascular Disorders				
	Yes	25 (50)	5 (11)	30 (31)
	No	25 (50)	41 (89)	66 (69)
Vascular Disorders , MILD				
	Yes	19 (38)	4 (9)	23 (24)
	No	31 (62)	42 (91)	73 (76)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Flushing				
	Yes	19 (38)	1 (2)	20 (21)
	No	31 (62)	45 (98)	76 (79)
___Flushing , MILD				
	Yes	13 (26)	0 (0)	13 (14)
	No	37 (74)	46 (100)	83 (86)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	17 (34)	5 (11)	22 (23)
	No	33 (66)	41 (89)	74 (77)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	15 (30)	5 (11)	20 (21)
	No	35 (70)	41 (89)	76 (79)
Skin And Subcutaneous Tissue Disorders				
	Yes	16 (32)	3 (7)	19 (20)
	No	34 (68)	43 (93)	77 (80)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	15 (30)	3 (7)	18 (19)
	No	35 (70)	43 (93)	78 (81)
General Disorders And Administration Site Conditions				
	Yes	11 (22)	34 (74)	45 (47)
	No	39 (78)	12 (26)	51 (53)
General Disorders And Administration Site Conditions , MILD				
	Yes	10 (20)	31 (67)	41 (43)
	No	40 (80)	15 (33)	55 (57)
___Pyrexia				
	Yes	2 (4)	11 (24)	13 (14)
	No	48 (96)	35 (76)	83 (86)
___Pyrexia , MILD				
	Yes	2 (4)	10 (22)	12 (13)
	No	48 (96)	36 (78)	84 (88)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Influenza Like Illness				
	Yes	1 (2)	24 (52)	25 (26)
	No	49 (98)	22 (48)	71 (74)
___Influenza Like Illness , MILD				
	Yes	1 (2)	17 (37)	18 (19)
	No	49 (98)	29 (63)	78 (81)
Injury Poisoning And Procedural Complications				
	Yes	10 (20)	3 (7)	13 (14)
	No	40 (80)	43 (93)	83 (86)
___Multiple Sclerosis Relapse				
	Yes	16 (32)	23 (50)	39 (41)
	No	34 (68)	23 (50)	57 (59)
___Dysmenorrhoea , MILD				
	Yes	10 (20)	1 (2)	11 (11)
	No	40 (80)	45 (98)	85 (89)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

109MS306_Table63_64_67_68_AE_SOCPT_NPERCENT_event_male

Tables 63, 64, 67, 68: Treatment emergent AE by Maximum Severity by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) FOR HAVING AT LEAST 1 OF EACH TYPE (of maximum severity when applicable) OF ADVERSE EVENT BY STUDY ARM. Subgroup analysis for Male sex

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
___Severe				
	Yes	0 (0)	0 (0)	0 (0)
	No	21 (100)	18 (100)	39 (100)
Gastrointestinal Disorders				
	Yes	14 (67)	6 (33)	20 (51)
	No	7 (33)	12 (67)	19 (49)
Gastrointestinal Disorders , MILD				
	Yes	11 (52)	5 (28)	16 (41)
	No	10 (48)	13 (72)	23 (59)
___Abdominal Pain				
	Yes	5 (24)	0 (0)	5 (13)
	No	16 (76)	18 (100)	34 (87)
___Abdominal Pain , MILD				
	Yes	3 (14)	0 (0)	3 (8)
	No	18 (86)	18 (100)	36 (92)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
___Diarrhoea				
	Yes	4 (19)	3 (17)	7 (18)
	No	17 (81)	15 (83)	32 (82)
___Vomiting				
	Yes	3 (14)	1 (6)	4 (10)
	No	18 (86)	17 (94)	35 (90)
Vascular Disorders				
	Yes	9 (43)	1 (6)	10 (26)
	No	12 (57)	17 (94)	29 (74)
Vascular Disorders , MILD				
	Yes	7 (33)	1 (6)	8 (21)
	No	14 (67)	17 (94)	31 (79)
___Flushing				
	Yes	9 (43)	0 (0)	9 (23)
	No	12 (57)	18 (100)	30 (77)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
___Flushing , MILD				
	Yes	7 (33)	0 (0)	7 (18)
	No	14 (67)	18 (100)	32 (82)
General Disorders And Administration Site Conditions				
	Yes	6 (29)	15 (83)	21 (54)
	No	15 (71)	3 (17)	18 (46)
General Disorders And Administration Site Conditions , MILD				
	Yes	4 (19)	10 (56)	14 (36)
	No	17 (81)	8 (44)	25 (64)
___Pyrexia				
	Yes	2 (10)	3 (17)	5 (13)
	No	19 (90)	15 (83)	34 (87)
___Pyrexia , MILD				
	Yes	0 (0)	1 (6)	1 (3)
	No	21 (100)	17 (94)	38 (97)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
___Influenza Like Illness				
	Yes	1 (5)	9 (50)	10 (26)
	No	20 (95)	9 (50)	29 (74)
___Influenza Like Illness , MILD				
	Yes	1 (5)	6 (33)	7 (18)
	No	20 (95)	12 (67)	32 (82)
Injury Poisoning And Procedural Complications				
	Yes	6 (29)	1 (6)	7 (18)
	No	15 (71)	17 (94)	32 (82)
Respiratory Thoracic And Mediastinal Disorders				
	Yes	6 (29)	3 (17)	9 (23)
	No	15 (71)	15 (83)	30 (77)
Respiratory Thoracic And Mediastinal Disorders , MILD				
	Yes	5 (24)	3 (17)	8 (21)
	No	16 (76)	15 (83)	31 (79)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Skin And Subcutaneous Tissue Disorders				
	Yes	6 (29)	0 (0)	6 (15)
	No	15 (71)	18 (100)	33 (85)
Skin And Subcutaneous Tissue Disorders , MILD				
	Yes	5 (24)	0 (0)	5 (13)
	No	16 (76)	18 (100)	34 (87)
___Multiple Sclerosis Relapse				
	Yes	6 (29)	9 (50)	15 (38)
	No	15 (71)	9 (50)	24 (62)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest (of maximum severity when applicable)
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs
in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs >=10% in either arm AND significant Risk Ratio p-value (<0.05) from main analyses,
the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table63_64_67_68_AESeverities_by_SOC_PT_3pvalues_n =135_subgroups_AH_BN032822.sas date: 31MAR2022

AE SOC PT

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135)

OR, RR, ARR for having at least 1 of each type of AE by study arm
The only AEs reported here are those with >=10% in either study arm
Analysis NOT using subgroups

	Event (n (%))	OR	RR	ARR
Adverse event	Effect measure	1.115	1.005	0.005
	95% CI	(0.217, 5.731)	(0.934, 1.081)	(-0.065, 0.074)
	p-value	0.8965	0.8968	0.8967
Gastrointestinal Disorders	Effect measure	6.478	2.389	0.434
	95% CI	(3.054, 13.739)	(1.621, 3.521)	(0.282, 0.586)
	p-value	<0.0001	<0.0001	<0.0001
___Abdominal Pain	Effect measure	7.684	5.048	0.316
	95% CI	(2.744, 21.512)	(2.074, 12.287)	(0.185, 0.448)
	p-value	0.0001	0.0004	<0.0001
___Vomiting	Effect measure	3.433	2.885	0.147
	95% CI	(1.178, 10.000)	(1.120, 7.426)	(0.030, 0.265)
	p-value	0.0238	0.0281	0.0139
___Diarrhoea	Effect measure	3.684	3.155	0.135
	95% CI	(1.145, 11.857)	(1.095, 9.094)	(0.025, 0.245)
	p-value	0.0288	0.0334	0.0163

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)

NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
___Abdominal Pain Upper	Effect measure	12.814	10.817	0.153
	95% CI	(1.616, 101.61)	(1.447, 80.878)	(0.061, 0.246)
	p-value	0.0158	0.0204	0.0011
___Nausea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708, 6.607)	(0.728, 5.400)	(-0.030, 0.184)
	p-value	0.1756	0.1804	0.1587
Infections And Infestations	Effect measure	1.531	1.202	0.104
	95% CI	(0.771, 3.038)	(0.891, 1.621)	(-0.062, 0.271)
	p-value	0.2234	0.2285	0.2206
___Nasopharyngitis	Effect measure	1.778	1.603	0.085
	95% CI	(0.724, 4.364)	(0.762, 3.371)	(-0.044, 0.214)
	p-value	0.2092	0.2138	0.1988
___Gastroenteritis	Effect measure	1.934	1.803	0.063
	95% CI	(0.624, 5.998)	(0.651, 4.994)	(-0.042, 0.167)
	p-value	0.2531	0.2570	0.2384

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
___Upper Respiratory Tract Infection	Effect measure	2.952	2.704	0.080
	95% CI	(0.762, 11.427)	(0.765, 9.555)	(-0.013, 0.173)
	p-value	0.1171	0.1224	0.0927
Nervous System Disorders	Effect measure	0.555	0.825	-0.129
	95% CI	(0.267, 1.154)	(0.650, 1.047)	(-0.286, 0.028)
	p-value	0.1149	0.1134	0.1079
___Multiple Sclerosis Relapse	Effect measure	0.449	0.620	-0.190
	95% CI	(0.222, 0.906)	(0.405, 0.948)	(-0.353, -0.027)
	p-value	0.0254	0.0273	0.0223
___Headache	Effect measure	0.570	0.685	-0.123
	95% CI	(0.276, 1.179)	(0.419, 1.120)	(-0.281, 0.035)
	p-value	0.1295	0.1316	0.1265
Vascular Disorders	Effect measure	8.883	5.108	0.385
	95% CI	(3.398, 23.220)	(2.296, 11.362)	(0.249, 0.522)
	p-value	<0.0001	0.0001	<0.0001

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
___Flushing	Effect measure	41.023	25.239	0.379
	95% CI	(5.377, 312.98)	(3.534, 180.23)	(0.261, 0.496)
	p-value	0.0003	0.0013	<0.0001
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	3.354	2.592	0.199
	95% CI	(1.375, 8.185)	(1.249, 5.378)	(0.063, 0.335)
	p-value	0.0078	0.0106	0.0041
___Oropharyngeal Pain	Effect measure	3.051	2.704	0.107
	95% CI	(0.931, 10.001)	(0.918, 7.963)	(0.001, 0.212)
	p-value	0.0656	0.0710	0.0477
___Cough	Effect measure	5.082	4.507	0.110
	95% CI	(1.069, 24.155)	(1.026, 19.802)	(0.018, 0.201)
	p-value	0.0409	0.0462	0.0188
Skin And Subcutaneous Tissue Disorders	Effect measure	9.129	6.610	0.263
	95% CI	(2.580, 32.298)	(2.076, 21.044)	(0.144, 0.382)
	p-value	0.0006	0.0014	<0.0001

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
___Rash	Effect measure	9.145	8.113	0.111
	95% CI	(1.125, 74.347)	(1.057, 62.278)	(0.028, 0.194)
	p-value	0.0384	0.0441	0.0088
General Disorders And Administration Site Conditions	Effect measure	0.096	0.313	-0.526
	95% CI	(0.044, 0.213)	(0.202, 0.484)	(-0.670, -0.383)
	p-value	<0.0001	<0.0001	<0.0001
___Pyrexia	Effect measure	0.271	0.322	-0.148
	95% CI	(0.091, 0.801)	(0.123, 0.844)	(-0.266, -0.031)
	p-value	0.0182	0.0211	0.0133
___Influenza Like Illness	Effect measure	0.027	0.055	-0.487
	95% CI	(0.006, 0.121)	(0.014, 0.219)	(-0.616, -0.359)
	p-value	<0.0001	<0.0001	<0.0001
___Fatigue	Effect measure	0.116	0.129	-0.095
	95% CI	(0.014, 0.973)	(0.016, 1.018)	(-0.177, -0.014)
	p-value	0.0471	0.0520	0.0215

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
Musculoskeletal And Connective Tissue Disorders	Effect measure	0.561	0.666	-0.120
	95% CI	(0.266, 1.184)	(0.393, 1.130)	(-0.274, 0.034)
	p-value	0.1295	0.1318	0.1265
___Pain In Extremity	Effect measure	0.359	0.386	-0.067
	95% CI	(0.089, 1.453)	(0.104, 1.431)	(-0.157, 0.023)
	p-value	0.1511	0.1546	0.1422
___Myalgia	Effect measure	0.100	0.113	-0.111
	95% CI	(0.012, 0.823)	(0.014, 0.876)	(-0.196, -0.025)
	p-value	0.0323	0.0370	0.0110
Injury, Poisoning And Procedural Complications	Effect measure	4.364	3.606	0.163
	95% CI	(1.375, 13.852)	(1.272, 10.224)	(0.049, 0.277)
	p-value	0.0124	0.0159	0.0051
Eye Disorders	Effect measure	1.370	1.302	0.042
	95% CI	(0.542, 3.459)	(0.597, 2.840)	(-0.081, 0.166)
	p-value	0.5057	0.5071	0.5016

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

	Event (n (%))	OR	RR	ARR
Reproductive System And Breast Disorders	Effect measure	1.656	1.545	0.060
	95% CI	(0.609, 4.505)	(0.648, 3.684)	(-0.056, 0.176)
	p-value	0.3231	0.3262	0.3134
___Dysmenorrhoea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708, 6.607)	(0.728, 5.400)	(-0.030, 0.184)
	p-value	0.1756	0.1804	0.1587
Psychiatric Disorders	Effect measure	1.002	1.002	0.000
	95% CI	(0.379, 2.647)	(0.435, 2.308)	(-0.117, 0.118)
	p-value	0.9971	0.9971	0.9971

NOTE1: Odds ratios and Risk ratios are represented as DMF/(IFN B-1a)
NOTE2: Absolute risk reductions are represented as DMF - (IFN B-1a)
NOTE3: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE4: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE5: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135)
N(%) for having at least 1 of each type of AE by study arm
The only AEs reported here are those with >=10% in either study arm
Analysis NOT using subgroups

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Adverse event				
	Yes	68 (96)	61 (95)	129 (96)
	No	3 (4)	3 (5)	6 (4)
Gastrointestinal Disorders				
	Yes	53 (75)	20 (31)	73 (54)
	No	18 (25)	44 (69)	62 (46)
___Abdominal Pain				
	Yes	28 (39)	5 (8)	33 (24)
	No	43 (61)	59 (92)	102 (76)
___Vomiting				
	Yes	16 (23)	5 (8)	21 (16)
	No	55 (77)	59 (92)	114 (84)
___Diarrhoea				
	Yes	14 (20)	4 (6)	18 (13)
	No	57 (80)	60 (94)	117 (87)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Abdominal Pain Upper				
	Yes	12 (17)	1 (2)	13 (10)
	No	59 (83)	63 (98)	122 (90)
___Nausea				
	Yes	11 (15)	5 (8)	16 (12)
	No	60 (85)	59 (92)	119 (88)
Infections And Infestations				
	Yes	44 (62)	33 (52)	77 (57)
	No	27 (38)	31 (48)	58 (43)
___Nasopharyngitis				
	Yes	16 (23)	9 (14)	25 (19)
	No	55 (77)	55 (86)	110 (81)
___Gastroenteritis				
	Yes	10 (14)	5 (8)	15 (11)
	No	61 (86)	59 (92)	120 (89)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Upper Respiratory Tract Infection				
	Yes	9 (13)	3 (5)	12 (9)
	No	62 (87)	61 (95)	123 (91)
Nervous System Disorders				
	Yes	43 (61)	47 (73)	90 (67)
	No	28 (39)	17 (27)	45 (33)
___Multiple Sclerosis Relapse				
	Yes	22 (31)	32 (50)	54 (40)
	No	49 (69)	32 (50)	81 (60)
___Headache				
	Yes	19 (27)	25 (39)	44 (33)
	No	52 (73)	39 (61)	91 (67)
Vascular Disorders				
	Yes	34 (48)	6 (9)	40 (30)
	No	37 (52)	58 (91)	95 (70)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Flushing				
	Yes	28 (39)	1 (2)	29 (21)
	No	43 (61)	63 (98)	106 (79)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	23 (32)	8 (13)	31 (23)
	No	48 (68)	56 (88)	104 (77)
___Oropharyngeal Pain				
	Yes	12 (17)	4 (6)	16 (12)
	No	59 (83)	60 (94)	119 (88)
___Cough				
	Yes	10 (14)	2 (3)	12 (9)
	No	61 (86)	62 (97)	123 (91)
Skin And Subcutaneous Tissue Disorders				
	Yes	22 (31)	3 (5)	25 (19)
	No	49 (69)	61 (95)	110 (81)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
___Rash				
	Yes	9 (13)	1 (2)	10 (7)
	No	62 (87)	63 (98)	125 (93)
General Disorders And Administration Site Conditions				
	Yes	17 (24)	49 (77)	66 (49)
	No	54 (76)	15 (23)	69 (51)
___Pyrexia				
	Yes	5 (7)	14 (22)	19 (14)
	No	66 (93)	50 (78)	116 (86)
___Influenza Like Illness				
	Yes	2 (3)	33 (52)	35 (26)
	No	69 (97)	31 (48)	100 (74)
___Fatigue				
	Yes	1 (1)	7 (11)	8 (6)
	No	70 (99)	57 (89)	127 (94)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Musculoskeletal And Connective Tissue Disorders				
	Yes	17 (24)	23 (36)	40 (30)
	No	54 (76)	41 (64)	95 (70)
___Pain In Extremity				
	Yes	3 (4)	7 (11)	10 (7)
	No	68 (96)	57 (89)	125 (93)
___Myalgia				
	Yes	1 (1)	8 (13)	9 (7)
	No	70 (99)	56 (88)	126 (93)
Injury, Poisoning And Procedural Complications				
	Yes	16 (23)	4 (6)	20 (15)
	No	55 (77)	60 (94)	115 (85)
Eye Disorders				
	Yes	13 (18)	9 (14)	22 (16)
	No	58 (82)	55 (86)	113 (84)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

ENDPOINT_SETUP	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Reproductive System And Breast Disorders				
	Yes	12 (17)	7 (11)	19 (14)
	No	59 (83)	57 (89)	116 (86)
___Dysmenorrhoea				
	Yes	11 (15)	5 (8)	16 (12)
	No	60 (85)	59 (92)	119 (88)
Psychiatric Disorders				
	Yes	10 (14)	9 (14)	19 (14)
	No	61 (86)	55 (86)	116 (86)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Since we are only including PTs and SOCs >=10% in either arm, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_ah_ban012822.sas date: 28JAN2022

Sub groups

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_age13to14

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for Ages 13 to 14

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.016	0.041	-0.643
	95% CI	(0.001, 0.314)	(0.003, 0.651)	(-0.957, -0.328)
	p-value	0.0066	0.0236	<0.0001
Gastrointestinal Disorders	Effect measure	4.667	1.815	0.349
	95% CI	(1.006, 21.652)	(0.944, 3.488)	(0.027, 0.672)
	p-value	0.0491	0.0738	0.0339
___Abdominal Pain	Effect measure	6.500	4.667	0.262
	95% CI	(0.680, 62.149)	(0.633, 34.430)	(0.006, 0.518)
	p-value	0.1042	0.1308	0.0451
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	10.400	6.222	0.373
	95% CI	(1.111, 97.335)	(0.878, 44.086)	(0.107, 0.639)
	p-value	0.0401	0.0673	0.0060
Vascular Disorders	Effect measure	18.913	11.757	0.389
	95% CI	(0.975, 366.99)	(0.730, 189.31)	(0.100, 0.678)
	p-value	0.0520	0.0822	0.0046

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses

NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
___Flushing	Effect measure	15.080	10.189	0.333
	95% CI	(0.770, 295.19)	(0.624, 166.40)	(0.052, 0.615)
	p-value	0.0738	0.1033	0.0152
General Disorders And Administration Site Conditions	Effect measure	0.154	0.389	-0.437
	95% CI	(0.033, 0.726)	(0.172, 0.879)	(-0.751, -0.122)
	p-value	0.0181	0.0232	0.0065
___Pyrexia	Effect measure	0.500	0.583	-0.119
	95% CI	(0.092, 2.730)	(0.155, 2.192)	(-0.412, 0.174)
	p-value	0.4235	0.4249	0.4253
___Influenza Like Illness	Effect measure	0.027	0.052	-0.500
	95% CI	(0.001, 0.535)	(0.003, 0.841)	(-0.825, -0.175)
	p-value	0.0178	0.0374	0.0011
Skin And Subcutaneous Tissue Disorders	Effect measure	2.308	1.944	0.135
	95% CI	(0.375, 14.212)	(0.441, 8.573)	(-0.142, 0.411)
	p-value	0.3673	0.3797	0.3388

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Injury, Poisoning And Procedural Complications	Effect measure	9.000	7.054	0.222
	95% CI	(0.443, 182.78)	(0.412, 120.70)	(-0.033, 0.478)
	p-value	0.1526	0.1775	0.1053

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_age15to17

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for Ages 15 to 17

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.833	0.902	-0.045
	95% CI	(0.382, 1.817)	(0.582, 1.399)	(-0.236, 0.147)
	p-value	0.6462	0.6462	0.6458
Gastrointestinal Disorders	Effect measure	7.163	2.628	0.456
	95% CI	(3.006, 17.069)	(1.638, 4.217)	(0.284, 0.628)
	p-value	<0.0001	0.0001	<0.0001
___Abdominal Pain	Effect measure	8.161	5.189	0.335
	95% CI	(2.562, 25.998)	(1.923, 14.003)	(0.183, 0.488)
	p-value	0.0004	0.0012	<0.0001
Vascular Disorders	Effect measure	7.615	4.245	0.389
	95% CI	(2.777, 20.883)	(1.916, 9.408)	(0.227, 0.551)
	p-value	0.0001	0.0004	<0.0001
___Flushing	Effect measure	34.774	20.755	0.395
	95% CI	(4.459, 271.17)	(2.905, 148.29)	(0.257, 0.533)
	p-value	0.0007	0.0025	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)

NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Skin And Subcutaneous Tissue Disorders	Effect measure	23.139	16.038	0.301
	95% CI	(2.943, 181.94)	(2.216, 116.09)	(0.169, 0.432)
	p-value	0.0028	0.0060	<0.0001
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	2.425	2.022	0.143
	95% CI	(0.894, 6.576)	(0.900, 4.543)	(-0.012, 0.298)
	p-value	0.0818	0.0884	0.0701
General Disorders And Administration Site Conditions	Effect measure	0.083	0.290	-0.554
	95% CI	(0.033, 0.209)	(0.173, 0.488)	(-0.714, -0.393)
	p-value	<0.0001	<0.0001	<0.0001
___Influenza Like Illness	Effect measure	0.036	0.073	-0.482
	95% CI	(0.008, 0.165)	(0.018, 0.290)	(-0.630, -0.335)
	p-value	<0.0001	0.0002	<0.0001
___Pyrexia	Effect measure	0.157	0.189	-0.162
	95% CI	(0.033, 0.757)	(0.043, 0.819)	(-0.284, -0.040)
	p-value	0.0210	0.0260	0.0092

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA

SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Injury, Poisoning And Procedural Complications	Effect measure	3.366	2.830	0.146
	95% CI	(1.006, 11.257)	(0.977, 8.198)	(0.011, 0.282)
	p-value	0.0488	0.0552	0.0341

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_female

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for Female sex

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.471	0.640	-0.180
	95% CI	(0.205, 1.078)	(0.389, 1.052)	(-0.374, 0.014)
	p-value	0.0747	0.0783	0.0688
Gastrointestinal Disorders	Effect measure	8.104	2.563	0.476
	95% CI	(3.237, 20.288)	(1.616, 4.064)	(0.300, 0.651)
	p-value	<0.0001	0.0001	<0.0001
___Abdominal Pain	Effect measure	6.985	4.232	0.351
	95% CI	(2.367, 20.616)	(1.755, 10.206)	(0.186, 0.516)
	p-value	0.0004	0.0013	<0.0001
___Vomiting	Effect measure	3.689	2.990	0.173
	95% CI	(1.106, 12.305)	(1.050, 8.516)	(0.027, 0.319)
	p-value	0.0337	0.0403	0.0205
___Diarrhoea	Effect measure	11.250	9.200	0.178
	95% CI	(1.379, 91.804)	(1.225, 69.093)	(0.060, 0.297)
	p-value	0.0238	0.0310	0.0032

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.

NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Vascular Disorders	Effect measure	8.200	4.600	0.391
	95% CI	(2.781, 24.179)	(1.922, 11.010)	(0.226, 0.557)
	p-value	0.0001	0.0006	<0.0001
___Flushing	Effect measure	27.581	17.480	0.358
	95% CI	(3.507, 216.89)	(2.436, 125.42)	(0.217, 0.499)
	p-value	0.0016	0.0044	<0.0001
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	4.224	3.128	0.231
	95% CI	(1.410, 12.658)	(1.255, 7.796)	(0.072, 0.390)
	p-value	0.0101	0.0144	0.0044
Skin And Subcutaneous Tissue Disorders	Effect measure	6.745	4.907	0.255
	95% CI	(1.815, 25.063)	(1.529, 15.751)	(0.107, 0.402)
	p-value	0.0044	0.0075	0.0007
General Disorders And Administration Site Conditions	Effect measure	0.100	0.298	-0.519
	95% CI	(0.039, 0.254)	(0.172, 0.516)	(-0.690, -0.348)
	p-value	<0.0001	<0.0001	<0.0001

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
___Pyrexia	Effect measure	0.203	0.251	-0.179
	95% CI	(0.053, 0.783)	(0.075, 0.843)	(-0.319, -0.039)
	p-value	0.0206	0.0254	0.0120
___Influenza Like Illness	Effect measure	0.019	0.038	-0.502
	95% CI	(0.002, 0.147)	(0.005, 0.272)	(-0.651, -0.352)
	p-value	0.0002	0.0011	<0.0001
Injury, Poisoning And Procedural Complications	Effect measure	3.583	3.067	0.135
	95% CI	(0.920, 13.963)	(0.900, 10.455)	(0.003, 0.267)
	p-value	0.0659	0.0733	0.0451

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_EFFECTMEASURES_male

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). OR, RR, ARR for having at least 1 of each type of AE by study arm. Subgroup analysis for Male sex

	Result	OR	RR	ARR
___Multiple Sclerosis Relapse	Effect measure	0.400	0.571	-0.214
	95% CI	(0.107, 1.502)	(0.252, 1.296)	(-0.515, 0.087)
	p-value	0.1746	0.1805	0.1631
Gastrointestinal Disorders	Effect measure	4.000	2.000	0.333
	95% CI	(1.052, 15.207)	(0.974, 4.109)	(0.037, 0.630)
	p-value	0.0419	0.0592	0.0277
___Abdominal Pain	Effect measure	12.333	9.465	0.238
	95% CI	(0.633, 240.44)	(0.560, 160.00)	(0.004, 0.472)
	p-value	0.0973	0.1192	0.0448
___Diarrhoea	Effect measure	1.176	1.143	0.024
	95% CI	(0.226, 6.127)	(0.294, 4.444)	(-0.217, 0.264)
	p-value	0.8469	0.8472	0.8462
___Vomiting	Effect measure	2.833	2.571	0.087
	95% CI	(0.268, 29.955)	(0.292, 22.608)	(-0.096, 0.271)
	p-value	0.3867	0.3945	0.3506

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Vascular Disorders	Effect measure	12.750	7.714	0.373
	95% CI	(1.421, 114.40)	(1.078, 55.191)	(0.136, 0.610)
	p-value	0.0230	0.0418	0.0020
___Flushing	Effect measure	28.120	16.349	0.429
	95% CI	(1.497, 528.18)	(1.019, 262.23)	(0.165, 0.692)
	p-value	0.0258	0.0484	0.0005
General Disorders And Administration Site Conditions	Effect measure	0.080	0.343	-0.548
	95% CI	(0.017, 0.381)	(0.169, 0.695)	(-0.806, -0.289)
	p-value	0.0015	0.0030	<0.0001
___Pyrexia	Effect measure	0.526	0.571	-0.071
	95% CI	(0.078, 3.565)	(0.107, 3.050)	(-0.285, 0.142)
	p-value	0.5108	0.5125	0.5112
___Influenza Like Illness	Effect measure	0.050	0.095	-0.452
	95% CI	(0.005, 0.456)	(0.013, 0.681)	(-0.701, -0.204)
	p-value	0.0079	0.0192	0.0004

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value (p<0.05) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Result	OR	RR	ARR
Injury, Poisoning And Procedural Complications	Effect measure	6.800	5.143	0.230
	95% CI	(0.733, 63.110)	(0.681, 38.816)	(0.010, 0.450)
	p-value	0.0917	0.1123	0.0406
Respiratory, Thoracic And Mediastinal Disorders	Effect measure	2.000	1.714	0.119
	95% CI	(0.420, 9.516)	(0.499, 5.892)	(-0.140, 0.378)
	p-value	0.3838	0.3922	0.3673
Skin And Subcutaneous Tissue Disorders	Effect measure	15.516	11.186	0.286
	95% CI	(0.808, 297.80)	(0.674, 185.52)	(0.041, 0.531)
	p-value	0.0689	0.0920	0.0176

NOTE1: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE2: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
NOTE3: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE4: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE5: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE6: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE7: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_age13to14

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for Ages 13 to 14

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
___Multiple Sclerosis Relapse				
	Yes	0 (0)	9 (64)	9 (28)
	No	18 (100)	5 (36)	23 (72)
Gastrointestinal Disorders				
	Yes	14 (78)	6 (43)	20 (63)
	No	4 (22)	8 (57)	12 (38)
___Abdominal Pain				
	Yes	6 (33)	1 (7)	7 (22)
	No	12 (67)	13 (93)	25 (78)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	8 (44)	1 (7)	9 (28)
	No	10 (56)	13 (93)	23 (72)
Vascular Disorders				
	Yes	7 (39)	0 (0)	7 (22)
	No	11 (61)	14 (100)	25 (78)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
___Flushing				
	Yes	6 (33)	0 (0)	6 (19)
	No	12 (67)	14 (100)	26 (81)
General Disorders And Administration Site Conditions				
	Yes	5 (28)	10 (71)	15 (47)
	No	13 (72)	4 (29)	17 (53)
___Pyrexia				
	Yes	3 (17)	4 (29)	7 (22)
	No	15 (83)	10 (71)	25 (78)
___Influenza Like Illness				
	Yes	0 (0)	7 (50)	7 (22)
	No	18 (100)	7 (50)	25 (78)
Skin And Subcutaneous Tissue Disorders				
	Yes	5 (28)	2 (14)	7 (22)
	No	13 (72)	12 (86)	25 (78)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 18)	IFN B-1a (N= 14)	Total (N= 32)
Injury, Poisoning And Procedural Complications				
	Yes	4 (22)	0 (0)	4 (13)
	No	14 (78)	14 (100)	28 (88)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_age15to17

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for Ages 15 to 17

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
___Multiple Sclerosis Relapse				
	Yes	22 (42)	23 (46)	45 (44)
	No	31 (58)	27 (54)	58 (56)
Gastrointestinal Disorders				
	Yes	39 (74)	14 (28)	53 (51)
	No	14 (26)	36 (72)	50 (49)
___Abdominal Pain				
	Yes	22 (42)	4 (8)	26 (25)
	No	31 (58)	46 (92)	77 (75)
Vascular Disorders				
	Yes	27 (51)	6 (12)	33 (32)
	No	26 (49)	44 (88)	70 (68)
___Flushing				
	Yes	22 (42)	1 (2)	23 (22)
	No	31 (58)	49 (98)	80 (78)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Skin And Subcutaneous Tissue Disorders				
	Yes	17 (32)	1 (2)	18 (17)
	No	36 (68)	49 (98)	85 (83)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	15 (28)	7 (14)	22 (21)
	No	38 (72)	43 (86)	81 (79)
General Disorders And Administration Site Conditions				
	Yes	12 (23)	39 (78)	51 (50)
	No	41 (77)	11 (22)	52 (50)
___Influenza Like Illness				
	Yes	2 (4)	26 (52)	28 (27)
	No	51 (96)	24 (48)	75 (73)
___Pyrexia				
	Yes	2 (4)	10 (20)	12 (12)
	No	51 (96)	40 (80)	91 (88)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 53)	IFN B-1a (N= 50)	Total (N= 103)
Injury, Poisoning And Procedural Complications				
	Yes	12 (23)	4 (8)	16 (16)
	No	41 (77)	46 (92)	87 (84)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_female

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for Female sex

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Multiple Sclerosis Relapse				
	Yes	16 (32)	23 (50)	39 (41)
	No	34 (68)	23 (50)	57 (59)
Gastrointestinal Disorders				
	Yes	39 (78)	14 (30)	53 (55)
	No	11 (22)	32 (70)	43 (45)
___Abdominal Pain				
	Yes	23 (46)	5 (11)	28 (29)
	No	27 (54)	41 (89)	68 (71)
___Vomiting				
	Yes	13 (26)	4 (9)	17 (18)
	No	37 (74)	42 (91)	79 (82)
___Diarrhoea				
	Yes	10 (20)	1 (2)	11 (11)
	No	40 (80)	45 (98)	85 (89)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
Vascular Disorders				
	Yes	25 (50)	5 (11)	30 (31)
	No	25 (50)	41 (89)	66 (69)
___Flushing				
	Yes	19 (38)	1 (2)	20 (21)
	No	31 (62)	45 (98)	76 (79)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	17 (34)	5 (11)	22 (23)
	No	33 (66)	41 (89)	74 (77)
Skin And Subcutaneous Tissue Disorders				
	Yes	16 (32)	3 (7)	19 (20)
	No	34 (68)	43 (93)	77 (80)
General Disorders And Administration Site Conditions				
	Yes	11 (22)	34 (74)	45 (47)
	No	39 (78)	12 (26)	51 (53)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 50)	IFN B-1a (N= 46)	Total (N= 96)
___Pyrexia				
	Yes	3 (6)	11 (24)	14 (15)
	No	47 (94)	35 (76)	82 (85)
___Influenza Like Illness				
	Yes	1 (2)	24 (52)	25 (26)
	No	49 (98)	22 (48)	71 (74)
Injury, Poisoning And Procedural Complications				
	Yes	10 (20)	3 (7)	13 (14)
	No	40 (80)	43 (93)	83 (86)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

109MS306_Table55_56_57_AE_SOCPT_NPERCENT_event_male

Tables 55, 56, 57: Treatment emergent AE by SOC and PT - ITT Population, Aged 13 years and older (n=135). N(%) for having at least 1 of each type of AE by study arm. Subgroup analysis for Male sex

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
___Multiple Sclerosis Relapse				
	Yes	6 (29)	9 (50)	15 (38)
	No	15 (71)	9 (50)	24 (62)
Gastrointestinal Disorders				
	Yes	14 (67)	6 (33)	20 (51)
	No	7 (33)	12 (67)	19 (49)
___Abdominal Pain				
	Yes	5 (24)	0 (0)	5 (13)
	No	16 (76)	18 (100)	34 (87)
___Diarrhoea				
	Yes	4 (19)	3 (17)	7 (18)
	No	17 (81)	15 (83)	32 (82)
___Vomiting				
	Yes	3 (14)	1 (6)	4 (10)
	No	18 (86)	17 (94)	35 (90)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Vascular Disorders				
	Yes	9 (43)	1 (6)	10 (26)
	No	12 (57)	17 (94)	29 (74)
___Flushing				
	Yes	9 (43)	0 (0)	9 (23)
	No	12 (57)	18 (100)	30 (77)
General Disorders And Administration Site Conditions				
	Yes	6 (29)	15 (83)	21 (54)
	No	15 (71)	3 (17)	18 (46)
___Pyrexia				
	Yes	2 (10)	3 (17)	5 (13)
	No	19 (90)	15 (83)	34 (87)
___Influenza Like Illness				
	Yes	1 (5)	9 (50)	10 (26)
	No	20 (95)	9 (50)	29 (74)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

	Event	DMF (N= 21)	IFN B-1a (N= 18)	Total (N= 39)
Injury, Poisoning And Procedural Complications				
	Yes	6 (29)	1 (6)	7 (18)
	No	15 (71)	17 (94)	32 (82)
Respiratory, Thoracic And Mediastinal Disorders				
	Yes	6 (29)	3 (17)	9 (23)
	No	15 (71)	15 (83)	30 (77)
Skin And Subcutaneous Tissue Disorders				
	Yes	6 (29)	0 (0)	6 (15)
	No	15 (71)	18 (100)	33 (85)

NOTE1: Responder rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: The only AEs reported here are from subgroups that fulfill the criteria of >=10 patients in every arm and subgroup AND >=10 AEs in at least one arm AND significant RR p-value ($p<0.05$) in the main non-subgroup analyses
NOTE3: Since we are only including PTs and SOCs that meet subgroup criteria mentioned above, the sum of events in all PTs reported does NOT add up necessarily to the number of events in their respective SOC
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table55_56_57_AE_by_SOC_PT_3pvalues_n=135_subgroups_ah_ban030422.sas date: 30MAR2022

SAE

109MS306_table13_AE_SOCPT_EFFECTMEASURES

Table 13: Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term - ITT Population(n=135)
OR, RR, RD FOR HAVING AT LEAST 1 OF EACH TYPE OF SERIOUS ADVERSE EVENT BY STUDY ARM
The only SERIOUS AEs reported here are those with >=5% in either study arm
ANALYSIS NOT USING SUBGROUPS

	Result	OR	RR	ARR
Serious adverse event	Effect measure	0.540	0.631	-0.115
	95% CI	(0.246, 1.188)	(0.349, 1.142)	(-0.262, 0.031)
	p-value	0.1258	0.1284	0.1229
Nervous system disorders	Effect measure	0.573	0.651	-0.098
	95% CI	(0.254, 1.290)	(0.347, 1.220)	(-0.240, 0.044)
	p-value	0.1784	0.1806	0.1762
___Multiple sclerosis relapse	Effect measure	0.453	0.530	-0.125
	95% CI	(0.190, 1.081)	(0.262, 1.072)	(-0.260, 0.010)
	p-value	0.0742	0.0775	0.0703

NOTE1: Only SOCs and PTs >=5% in either arm are presented.
NOTE2: Odds ratios (OR) and Risk ratios (RR) are represented as DMF/(IFN B-1a)
NOTE3: Absolute risk reductions (ARR) are represented as DMF - (IFN B-1a)
NOTE4: When there is 1 zero cell, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used.
NOTE5: When there is 1 zero cell, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used.
NOTE6: When there are >=2 zero cells, no effect measures or p-values are calculated and thus given values of NA
SOURCE: /bdh-gxp/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table13_t-ae-ser-socpt_n=135_bb_ban012822.sas

109MS306_table13_AE_SOCPT_NPERCENT_EVENT

Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term - ITT Population(n=135)
N(%) FOR HAVING AT LEAST 1 OF EACH TYPE OF SERIOUS ADVERSE EVENT BY STUDY ARM
The only SERIOUS AEs reported here are those with >=5% in either study arm
ANALYSIS NOT USING SUBGROUPS

	Event (n (%))	DMF (N= 71)	IFN B-1a (N= 64)	Total (N= 135)
Serious adverse event				
	Yes	14 (20)	20 (31)	34 (25)
	No	57 (80)	44 (69)	101 (75)
Nervous system disorders				
	Yes	13 (18)	18 (28)	31 (23)
	No	58 (82)	46 (72)	104 (77)
___Multiple sclerosis relapse				
	Yes	10 (14)	17 (27)	27 (20)
	No	61 (86)	47 (73)	108 (80)

NOTE1: Responder (event) rates are yes when a patient has at least 1 of the adverse events of interest
NOTE2: Only SOCs and PTs >=5% in either arm are presented.
SOURCE: /gma/tec/German Reimbursement/109MS306/stats/bn/programs/109MS306_table13_t-ae-ser-socpt_n=135_bb_ban012822.sas

AE discontinuation

109MS306_table73_AE_PT_NPERCENT_event

Table 73: Treatment Emergent Adverse Events That Led to Discontinuation of Study Drug by System Organ Class andPreferred Term - ITT Population, Aged 13 years and older (n=135)

Number of patients with therapy discontinuations due to AE by PT, Aged 13 years and older (n=135)

	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with any event that led to discontinuation	5 (7)	8 (13)	13 (10)
Asthenia	0	1 (2)	1 (<1)
Flushing	2 (3)	0	2 (1)
Headache	0	1 (2)	1 (<1)
Hepatocellular injury	0	1 (2)	1 (<1)
Influenza like illness	0	1 (2)	1 (<1)
Limb discomfort	1 (1)	0	1 (<1)
Mood altered	0	1 (2)	1 (<1)
Multiple sclerosis relapse	2 (3)	3 (5)	5 (4)
Tremor	0	1 (2)	1 (<1)
Vomiting	0	1 (2)	1 (<1)

NOTE 1: Numbers in parentheses are percentages
NOTE 2: A subject was counted only once within each system organ class and preferred term
NOTE 3: System organ class and preferred term are presented in decreasing frequency of the total column
Source: bg12ms/109ms306/csr/t-ae-disc-socpt.sas Run Date: 25MAR2021

109MS306_table73_AE_SOC_NPERCENT_event

Table 73: Treatment Emergent Adverse Events That Led to Discontinuation of Study Drug by System Organ Class andPreferred Term - mITT Population, Aged 13 years and older (n=135)

Number of patients with therapy discontinuations due to AE by SOC, Aged 13 years and older (n=135)

	DMF (N=71)	**IFN B-1a (N=64)**	**Total (N=135)**
Number of subjects with any event that led to discontinuation	5 (7)	8 (13)	13 (10)
Nervous system disorders	2 (3)	5 (8)	7 (5)
General disorders and administration site conditions	0	2 (3)	2 (1)
Vascular disorders	2 (3)	0	2 (1)
Gastrointestinal disorders	0	1 (2)	1 (<1)
Hepatobiliary disorders	0	1 (2)	1 (<1)
Musculoskeletal and connective tissue disorders	1 (1)	0	1 (<1)
Psychiatric disorders	0	1 (2)	1 (<1)

NOTE 1: Numbers in parentheses are percentages
NOTE 2: A subject was counted only once within each system organ class and preferred term
NOTE 3: System organ class and preferred term are presented in decreasing frequency of the total column
Source: bg12ms/109ms306/csr/t-ae-disc-socpt.sas Run Date: 25MAR2021

AESI severity

AESI any

109MS306_table75_any_AESI_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 any AESI, related to CSR Table 75

	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	6.059	1.285	0.209
	95% CI	(1.916 , 19.158)	(1.097 , 1.505)	(0.089 , 0.33)
	p-value	0.002	0.002	0.001
Gastrointestinal disorders	Effect measure	6.478	2.389	0.434
	95% CI	(3.054 , 13.739)	(1.621 , 3.521)	(0.282 , 0.586)
	p-value	0	0	0
Abdominal pain	Effect measure	7.684	5.048	0.316
	95% CI	(2.744 , 21.512)	(2.074 , 12.287)	(0.185 , 0.448)
	p-value	0	0	0
Vomiting	Effect measure	3.433	2.885	0.147
	95% CI	(1.178 , 10)	(1.12 , 7.426)	(0.03 , 0.265)
	p-value	0.024	0.028	0.014
Diarrhoea	Effect measure	3.684	3.155	0.135
	95% CI	(1.145 , 11.857)	(1.095 , 9.094)	(0.025 , 0.245)
	p-value	0.029	0.033	0.016
Nausea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708 , 6.607)	(0.728 , 5.4)	(-0.03 , 0.184)
	p-value	0.176	0.18	0.159
Abdominal pain upper	Effect measure	12.814	10.817	0.153
	95% CI	(1.616 , 101.613)	(1.447 , 80.878)	(0.061 , 0.246)
	p-value	0.016	0.02	0.001
Dyspepsia	Effect measure	6.891	6.31	0.083
	95% CI	(0.824 , 57.635)	(0.798 , 49.898)	(0.007 , 0.159)
	p-value	0.075	0.081	0.032
Constipation	Effect measure	1.851	1.803	0.025
	95% CI	(0.327 , 10.462)	(0.342 , 9.514)	(-0.043 , 0.094)
	p-value	0.486	0.487	0.473
Toothache	Effect measure	0.29	0.3	-0.033
	95% CI	(0.029 , 2.866)	(0.032 , 2.816)	(-0.091 , 0.026)
	p-value	0.29	0.292	0.273
Dental caries	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Dry mouth	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Abdominal pain lower	Effect measure	0.296	0.301	-0.016

	Result	OR	RR	ARR
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Frequent bowel movements	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gastritis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gingival bleeding	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Oesophagitis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Infections and infestations	Effect measure	1.67	1.302	0.127
	95% CI	(0.845 , 3.302)	(0.912 , 1.859)	(-0.04 , 0.295)
	p-value	0.14	0.146	0.136
Nasopharyngitis	Effect measure	1.778	1.603	0.085
	95% CI	(0.724 , 4.364)	(0.762 , 3.371)	(-0.044 , 0.214)
	p-value	0.209	0.214	0.199
Gastroenteritis	Effect measure	1.713	1.623	0.049
	95% CI	(0.542 , 5.409)	(0.574 , 4.589)	(-0.053 , 0.15)
	p-value	0.359	0.362	0.348
Upper respiratory tract infection	Effect measure	2.952	2.704	0.08
	95% CI	(0.762 , 11.427)	(0.765 , 9.555)	(-0.013 , 0.173)
	p-value	0.117	0.122	0.093
Pharyngitis	Effect measure	1.136	1.127	0.008
	95% CI	(0.292 , 4.43)	(0.316 , 4.015)	(-0.076 , 0.092)
	p-value	0.854	0.854	0.853
Tonsillitis	Effect measure	0.896	0.901	-0.006
	95% CI	(0.215 , 3.738)	(0.235 , 3.457)	(-0.086 , 0.074)
	p-value	0.88	0.88	0.88
Sinusitis	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Urinary tract infection	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Viral infection	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Cystitis	Effect measure	8.6	8.119	0.056
	95% CI	(0.454 , 162.938)	(0.446 , 147.892)	(-0.012 , 0.125)
	p-value	0.152	0.157	0.13
Ear infection	Effect measure	6.591	6.315	0.042
	95% CI	(0.334 , 130.11)	(0.332 , 119.928)	(-0.019 , 0.104)
	p-value	0.215	0.22	0.251
Bronchitis	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Gastroenteritis viral	Effect measure	0.9	0.901	-0.002

	Result	OR	RR	ARR
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Laryngitis	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Oral herpes	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Viral upper respiratory tract infection	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Bacteriuria	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Chronic sinusitis	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Eye infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Fungal skin infection	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gastrointestinal infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Otitis externa	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Otitis media	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Otitis media acute	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonia	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonia pneumococcal	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Respiratory tract infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Vascular disorders	Effect measure	10.843	6.13	0.401
	95% CI	(3.891 , 30.215)	(2.553 , 14.717)	(0.267 , 0.534)

	Result	OR	RR	ARR
	p-value	0	0	0
Flushing	Effect measure	41.023	25.239	0.379
	95% CI	(5.377 , 312.975)	(3.534 , 180.232)	(0.261 , 0.496)
	p-value	0	0.001	0
Hot flush	Effect measure	6.891	6.31	0.083
	95% CI	(0.824 , 57.635)	(0.798 , 49.898)	(0.007 , 0.159)
	p-value	0.075	0.081	0.032
Hypertension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hypotension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Orthostatic hypotension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
General disorders and administration site conditions	Effect measure	0.251	0.367	-0.267
	95% CI	(0.112 , 0.566)	(0.199 , 0.679)	(-0.414 , -0.12)
	p-value	0.001	0.001	0
Pyrexia	Effect measure	0.213	0.258	-0.162
	95% CI	(0.066 , 0.687)	(0.089 , 0.742)	(-0.277 , -0.048)
	p-value	0.01	0.012	0.005
Asthenia	Effect measure	0.28	0.3	-0.066
	95% CI	(0.054 , 1.441)	(0.063 , 1.436)	(-0.147 , 0.016)
	p-value	0.128	0.132	0.113
Fatigue	Effect measure	0.116	0.129	-0.095
	95% CI	(0.014 , 0.973)	(0.016 , 1.018)	(-0.177 , -0.014)
	p-value	0.047	0.052	0.021
Chills	Effect measure	0.094	0.1	-0.062
	95% CI	(0.005 , 1.781)	(0.006 , 1.826)	(-0.137 , 0.012)
	p-value	0.115	0.12	0.115
Pain	Effect measure	0.123	0.129	-0.047
	95% CI	(0.006 , 2.426)	(0.007 , 2.448)	(-0.114 , 0.02)
	p-value	0.168	0.173	0.226
Chest discomfort	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Chest pain	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Feeling hot	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Generalised oedema	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Oedema peripheral	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)

	Result	OR	RR	ARR
	p-value	0.459	0.459	0.96
Respiratory, thoracic and mediastinal disorders	Effect measure	4.627	3.606	0.204
	95% CI	(1.621 , 13.213)	(1.437 , 9.047)	(0.08 , 0.327)
	p-value	0.004	0.006	0.001
Oropharyngeal pain	Effect measure	3.051	2.704	0.107
	95% CI	(0.931 , 10.001)	(0.918 , 7.963)	(0.001 , 0.212)
	p-value	0.066	0.071	0.048
Cough	Effect measure	5.082	4.507	0.11
	95% CI	(1.069 , 24.155)	(1.026 , 19.802)	(0.018 , 0.201)
	p-value	0.041	0.046	0.019
Dyspnoea	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonitis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Tonsillar erythema	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Skin and subcutaneous tissue disorders	Effect measure	23.019	17.127	0.252
	95% CI	(2.981 , 177.766)	(2.359 , 124.33)	(0.145 , 0.359)
	p-value	0.003	0.005	0
Rash	Effect measure	9.145	8.113	0.111
	95% CI	(1.125 , 74.347)	(1.057 , 62.278)	(0.028 , 0.194)
	p-value	0.038	0.044	0.009
Erythema	Effect measure	12.802	11.727	0.085
	95% CI	(0.707 , 231.94)	(0.674 , 204.098)	(0.005 , 0.164)
	p-value	0.085	0.091	0.035
Pruritus	Effect measure	8.6	8.119	0.056
	95% CI	(0.454 , 162.938)	(0.446 , 147.892)	(-0.012 , 0.125)
	p-value	0.152	0.157	0.13
Dry skin	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Ecchymosis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Rash pruritic	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Musculoskeletal and connective tissue disorders	Effect measure	0.1	0.113	-0.111

	Result	OR	RR	ARR
	95% CI	(0.012 , 0.823)	(0.014 , 0.876)	(-0.196 , -0.025)
	p-value	0.032	0.037	0.011
Myalgia	Effect measure	0.1	0.113	-0.111
	95% CI	(0.012 , 0.823)	(0.014 , 0.876)	(-0.196 , -0.025)
	p-value	0.032	0.037	0.011
Renal and urinary disorders	Effect measure	0.426	0.451	-0.051
	95% CI	(0.102 , 1.781)	(0.118 , 1.728)	(-0.137 , 0.034)
	p-value	0.243	0.245	0.237
Proteinuria	Effect measure	0.29	0.3	-0.033
	95% CI	(0.029 , 2.866)	(0.032 , 2.816)	(-0.091 , 0.026)
	p-value	0.29	0.292	0.273
Dysuria	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Bladder discomfort	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Renal cyst	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Renal pain	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Investigations	Effect measure	0.899	0.901	-0.003
	95% CI	(0.123 , 6.572)	(0.131 , 6.214)	(-0.061 , 0.054)
	p-value	0.916	0.916	0.916
Alanine aminotransferase increased	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Aspartate aminotransferase increased	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Blood bilirubin increased	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Blood glucose increased	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Cardiac disorders	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Palpitations	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Hepatobiliary disorders	Effect measure	0.9	0.901	-0.002

	Result	OR	RR	ARR
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Hepatocellular injury	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Blood and lymphatic system disorders	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Lymphopenia	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Nervous system disorders	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Burning sensation	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_any_AESI_NPERCENT

Overall rate and effect measures of patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with any AESI	67 (94)	47 (73)	114 (84)
Gastrointestinal disorders	53 (75)	20 (31)	73 (54)
Abdominal pain	28 (39)	5 (8)	33 (24)
Vomiting	16 (23)	5 (8)	21 (16)
Diarrhoea	14 (20)	4 (6)	18 (13)
Nausea	11 (15)	5 (8)	16 (12)
Abdominal pain upper	12 (17)	1 (2)	13 (10)
Dyspepsia	7 (10)	1 (2)	8 (6)
Constipation	4 (6)	2 (3)	6 (4)
Toothache	1 (1)	3 (5)	4 (3)
Dental caries	0	2 (3)	2 (1)
Dry mouth	1 (1)	1 (2)	2 (1)
Abdominal pain lower	0	1 (2)	1 (1)
Frequent bowel movements	1 (1)	0	1 (1)
Gastritis	1 (1)	0	1 (1)
Gingival bleeding	0	1 (2)	1 (1)
Oesophagitis	1 (1)	0	1 (1)
Infections and infestations	39 (55)	27 (42)	66 (49)
Nasopharyngitis	16 (23)	9 (14)	25 (19)
Gastroenteritis	9 (13)	5 (8)	14 (10)
Upper respiratory tract infection	9 (13)	3 (5)	12 (9)
Pharyngitis	5 (7)	4 (6)	9 (7)
Tonsillitis	4 (6)	4 (6)	8 (6)
Sinusitis	3 (4)	2 (3)	5 (4)
Urinary tract infection	3 (4)	2 (3)	5 (4)
Viral infection	3 (4)	2 (3)	5 (4)
Cystitis	4 (6)	0	4 (3)
Ear infection	3 (4)	0	3 (2)
Bronchitis	0	2 (3)	2 (1)
Gastroenteritis viral	1 (1)	1 (2)	2 (1)
Laryngitis	2 (3)	0	2 (1)
Oral herpes	2 (3)	0	2 (1)
Viral upper respiratory tract infection	0	2 (3)	2 (1)
Bacteriuria	1 (1)	0	1 (1)
Chronic sinusitis	0	1 (2)	1 (1)
Eye infection	0	1 (2)	1 (1)
Fungal skin infection	1 (1)	0	1 (1)
Gastrointestinal infection	0	1 (2)	1 (1)
Otitis externa	1 (1)	0	1 (1)
Otitis media	0	1 (2)	1 (1)
Otitis media acute	1 (1)	0	1 (1)
Pneumonia	1 (1)	0	1 (1)
Pneumonia pneumococcal	1 (1)	0	1 (1)
Respiratory tract infection	0	1 (2)	1 (1)
Vascular disorders	34 (48)	5 (8)	39 (29)
Flushing	28 (39)	1 (2)	29 (21)
Hot flush	7 (10)	1 (2)	8 (6)
Hypertension	0	1 (2)	1 (1)
Hypotension	0	1 (2)	1 (1)
Orthostatic hypotension	0	1 (2)	1 (1)

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
General disorders and administration site conditions	11 (15)	27 (42)	38 (28)
Pyrexia	4 (6)	14 (22)	18 (13)
Asthenia	2 (3)	6 (9)	8 (6)
Fatigue	1 (1)	7 (11)	8 (6)
Chills	0	4 (6)	4 (3)
Pain	0	3 (5)	3 (2)
Chest discomfort	1 (1)	0	1 (1)
Chest pain	1 (1)	0	1 (1)
Feeling hot	1 (1)	0	1 (1)
Generalised oedema	1 (1)	0	1 (1)
Oedema peripheral	0	1 (2)	1 (1)
Respiratory, thoracic and mediastinal disorders	20 (28)	5 (8)	25 (19)
Oropharyngeal pain	12 (17)	4 (6)	16 (12)
Cough	10 (14)	2 (3)	12 (9)
Dyspnoea	1 (1)	0	1 (1)
Pneumonitis	1 (1)	0	1 (1)
Tonsillar erythema	0	1 (2)	1 (1)
Skin and subcutaneous tissue disorders	19 (27)	1 (2)	20 (15)
Rash	9 (13)	1 (2)	10 (7)
Erythema	6 (8)	0	6 (4)
Pruritus	4 (6)	0	4 (3)
Dry skin	1 (1)	0	1 (1)
Ecchymosis	1 (1)	0	1 (1)
Rash pruritic	1 (1)	0	1 (1)
Musculoskeletal and connective tissue disorders	1 (1)	8 (13)	9 (7)
Myalgia	1 (1)	8 (13)	9 (7)
Renal and urinary disorders	3 (4)	6 (9)	9 (7)
Proteinuria	1 (1)	3 (5)	4 (3)
Dysuria	1 (1)	1 (2)	2 (1)
Bladder discomfort	0	1 (2)	1 (1)
Renal cyst	1 (1)	0	1 (1)
Renal pain	0	1 (2)	1 (1)
Investigations	2 (3)	2 (3)	4 (3)
Alanine aminotransferase increased	1 (1)	1 (2)	2 (1)
Aspartate aminotransferase increased	0	1 (2)	1 (1)
Blood bilirubin increased	1 (1)	0	1 (1)
Blood glucose increased	1 (1)	0	1 (1)
Cardiac disorders	2 (3)	0	2 (1)
Palpitations	2 (3)	0	2 (1)
Hepatobiliary disorders	1 (1)	1 (2)	2 (1)
Hepatocellular injury	1 (1)	1 (2)	2 (1)
Blood and lymphatic system disorders	1 (1)	0	1 (1)
Lymphopenia	1 (1)	0	1 (1)
Nervous system disorders	0	1 (2)	1 (1)
Burning sensation	0	1 (2)	1 (1)

Sub groups

109MS306_table75_any_Age1314_AESI_EFFECTMEASURES

Overall rate and effect measures of Aged 13-14 patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	11.261	1.261	0.214
-	95% CI	(0.532 , 238.544)	(0.969 , 1.64)	(-0.064 , 0.493)
-	p-value	0.12	0.084	0.169
Gastrointestinal disorders	Effect measure	4.667	1.815	0.349
-	95% CI	(1.006 , 21.652)	(0.944 , 3.488)	(0.027 , 0.672)
-	p-value	0.049	0.074	0.034
Abdominal pain	Effect measure	6.5	4.667	0.262
-	95% CI	(0.68 , 62.149)	(0.633 , 34.43)	(0.006 , 0.518)
-	p-value	0.104	0.131	0.045
Infections and infestations	Effect measure	3.929	2.139	0.325
-	95% CI	(0.879 , 17.563)	(0.864 , 5.295)	(-0.001 , 0.652)
-	p-value	0.073	0.1	0.051
Nasopharyngitis	Effect measure	6.5	4.667	0.262
-	95% CI	(0.68 , 62.149)	(0.633 , 34.43)	(0.006 , 0.518)
-	p-value	0.104	0.131	0.045
Vascular disorders	Effect measure	18.913	11.757	0.389
-	95% CI	(0.975 , 366.99)	(0.73 , 189.308)	(0.1 , 0.678)
-	p-value	0.052	0.082	0.005
Flushing	Effect measure	15.08	10.189	0.333
-	95% CI	(0.77 , 295.19)	(0.624 , 166.403)	(0.052 , 0.615)
-	p-value	0.074	0.103	0.015
General disorders and administration site conditions	Effect measure	0.385	0.556	-0.222
-	95% CI	(0.088 , 1.673)	(0.223 , 1.381)	(-0.556 , 0.112)
-	p-value	0.203	0.206	0.192
Pyrexia	Effect measure	0.312	0.389	-0.175
-	95% CI	(0.048 , 2.032)	(0.083 , 1.827)	(-0.452 , 0.103)
-	p-value	0.223	0.231	0.218
Respiratory, thoracic and mediastinal disorders	Effect measure	10.4	6.222	0.373
-	95% CI	(1.111 , 97.335)	(0.878 , 44.086)	(0.107 , 0.639)
-	p-value	0.04	0.067	0.006
Skin and subcutaneous tissue disorders	Effect measure	3.714	3.111	0.151
-	95% CI	(0.366 , 37.708)	(0.39 , 24.829)	(-0.084 , 0.385)
-	p-value	0.267	0.284	0.208

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Age1314_AESI_NPERCENT

Overall rate and effect measures of Aged 13-14 patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Number of subjects with any AESI	18 (100)	11 (79)	29 (91)
Gastrointestinal disorders	14 (78)	6 (43)	20 (63)
Abdominal pain	6 (33)	1 (7)	7 (22)
Infections and infestations	11 (61)	4 (29)	15 (47)
Nasopharyngitis	6 (33)	1 (7)	7 (22)
Vascular disorders	7 (39)	0	7 (22)
Flushing	6 (33)	0	6 (19)
General disorders and administration site conditions	5 (28)	7 (50)	12 (38)
Pyrexia	2 (11)	4 (29)	6 (19)
Respiratory, thoracic and mediastinal disorders	8 (44)	1 (7)	9 (28)
Skin and subcutaneous tissue disorders	4 (22)	1 (7)	5 (16)

NOTE1: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Age1517_AESI_EFFECTMEASURES

Overall rate and effect measures of Aged 15-17 patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	4.764	1.284	0.205
-	95% CI	(1.447 , 15.684)	(1.063 , 1.552)	(0.061 , 0.348)
-	p-value	0.01	0.01	0.005
Gastrointestinal disorders	Effect measure	7.163	2.628	0.456
-	95% CI	(3.006 , 17.069)	(1.638 , 4.217)	(0.284 , 0.628)
-	p-value	0	0	0
Abdominal pain	Effect measure	8.161	5.189	0.335
-	95% CI	(2.562 , 25.998)	(1.923 , 14.003)	(0.183 , 0.488)
-	p-value	0	0.001	0
Infections and infestations	Effect measure	1.315	1.148	0.068
-	95% CI	(0.606 , 2.853)	(0.775 , 1.702)	(-0.124 , 0.261)
-	p-value	0.489	0.491	0.487
Nasopharyngitis	Effect measure	1.221	1.179	0.029
-	95% CI	(0.439 , 3.394)	(0.506 , 2.747)	(-0.118 , 0.175)
-	p-value	0.702	0.702	0.701
Vascular disorders	Effect measure	9.346	5.094	0.409
-	95% CI	(3.208 , 27.232)	(2.129 , 12.19)	(0.251 , 0.568)
-	p-value	0	0	0
Flushing	Effect measure	34.774	20.755	0.395
-	95% CI	(4.459 , 271.17)	(2.905 , 148.292)	(0.257 , 0.533)
-	p-value	0.001	0.003	0
General disorders and administration site conditions	Effect measure	0.191	0.283	-0.287
-	95% CI	(0.069 , 0.531)	(0.124 , 0.647)	(-0.447 , -0.126)
-	p-value	0.002	0.003	0
Pyrexia	Effect measure	0.157	0.189	-0.162
-	95% CI	(0.033 , 0.757)	(0.043 , 0.819)	(-0.284 , -0.04)
-	p-value	0.021	0.026	0.009
Respiratory, thoracic and mediastinal disorders	Effect measure	3.366	2.83	0.146
-	95% CI	(1.006 , 11.257)	(0.977 , 8.198)	(0.011 , 0.282)
-	p-value	0.049	0.055	0.034
Skin and subcutaneous tissue disorders	Effect measure	40.662	29.262	0.283
-	95% CI	(2.359 , 701.003)	(1.798 , 476.306)	(0.142 , 0.424)
-	p-value	0.011	0.018	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Age1517_AESI_NPERCENT

Overall rate and effect measures of Aged 15-17 patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Number of subjects with any AESI	49 (92)	36 (72)	85 (83)
Gastrointestinal disorders	39 (74)	14 (28)	53 (51)
Abdominal pain	22 (42)	4 (8)	26 (25)
Infections and infestations	28 (53)	23 (46)	51 (50)
Nasopharyngitis	10 (19)	8 (16)	18 (17)
Vascular disorders	27 (51)	5 (10)	32 (31)
Flushing	22 (42)	1 (2)	23 (22)
General disorders and administration site conditions	6 (11)	20 (40)	26 (25)
Pyrexia	2 (4)	10 (20)	12 (12)
Respiratory, thoracic and mediastinal disorders	12 (23)	4 (8)	16 (16)
Skin and subcutaneous tissue disorders	15 (28)	0	15 (15)

NOTE1: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Female_AESI_EFFECTMEASURES

Overall rate and effect measures of female patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	10.5	1.38	0.264
-	95% CI	(2.234 , 49.354)	(1.131 , 1.684)	(0.121 , 0.408)
-	p-value	0.003	0.002	0
Gastrointestinal disorders	Effect measure	8.104	2.563	0.476
-	95% CI	(3.237 , 20.288)	(1.616 , 4.064)	(0.3 , 0.651)
-	p-value	0	0	0
Abdominal pain	Effect measure	6.985	4.232	0.351
-	95% CI	(2.367 , 20.616)	(1.755 , 10.206)	(0.186 , 0.516)
-	p-value	0	0.001	0
Vomiting	Effect measure	3.689	2.99	0.173
-	95% CI	(1.106 , 12.305)	(1.05 , 8.516)	(0.027 , 0.319)
-	p-value	0.034	0.04	0.02
Diarrhoea	Effect measure	11.25	9.2	0.178
-	95% CI	(1.379 , 91.804)	(1.225 , 69.093)	(0.06 , 0.297)
-	p-value	0.024	0.031	0.003
Infections and infestations	Effect measure	1.848	1.407	0.15
-	95% CI	(0.817 , 4.18)	(0.887 , 2.233)	(-0.046 , 0.347)
-	p-value	0.14	0.147	0.134
Nasopharyngitis	Effect measure	4.043	3.373	0.155
-	95% CI	(1.05 , 15.566)	(1.004 , 11.337)	(0.02 , 0.29)
-	p-value	0.042	0.049	0.025
Vascular disorders	Effect measure	10.5	5.75	0.413
-	95% CI	(3.272 , 33.69)	(2.165 , 15.268)	(0.252 , 0.574)
-	p-value	0	0	0
Flushing	Effect measure	27.581	17.48	0.358
-	95% CI	(3.507 , 216.887)	(2.436 , 125.42)	(0.217 , 0.499)
-	p-value	0.002	0.004	0
General disorders and administration site conditions	Effect measure	0.231	0.339	-0.273
-	95% CI	(0.086 , 0.623)	(0.157 , 0.731)	(-0.445 , -0.101)
-	p-value	0.004	0.006	0.002
Pyrexia	Effect measure	0.133	0.167	-0.199
-	95% CI	(0.028 , 0.636)	(0.039 , 0.715)	(-0.334 , -0.064)
-	p-value	0.012	0.016	0.004
Respiratory, thoracic and mediastinal disorders	Effect measure	6.143	4.6	0.235
-	95% CI	(1.645 , 22.937)	(1.423 , 14.868)	(0.089 , 0.38)
-	p-value	0.007	0.011	0.002

AESI	Result	OR	RR	ARR
Skin and subcutaneous tissue disorders	Effect measure	17.5	12.88	0.258
-	95% CI	(2.196 , 139.457)	(1.763 , 94.115)	(0.127 , 0.39)
-	p-value	0.007	0.012	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used. NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used. NOTE5: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Female_AESI_NPERCENT

Overall rate and effect measures of female patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Number of subjects with any AESI	48 (96)	32 (70)	80 (83)
Gastrointestinal disorders	39 (78)	14 (30)	53 (55)
Abdominal pain	23 (46)	5 (11)	28 (29)
Vomiting	13 (26)	4 (9)	17 (18)
Diarrhoea	10 (20)	1 (2)	11 (11)
Infections and infestations	26 (52)	17 (37)	43 (45)
Nasopharyngitis	11 (22)	3 (7)	14 (15)
Vascular disorders	25 (50)	4 (9)	29 (30)
Flushing	19 (38)	1 (2)	20 (21)
General disorders and administration site conditions	7 (14)	19 (41)	26 (27)
Pyrexia	2 (4)	11 (24)	13 (14)
Respiratory, thoracic and mediastinal disorders	15 (30)	3 (7)	18 (19)
Skin and subcutaneous tissue disorders	14 (28)	1 (2)	15 (16)

NOTE1: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Male_AESI_EFFECTMEASURES

Overall rate and effect measures of male patients with ≥1 any AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	1.9	1.086	0.071
-	95% CI	(0.281 , 12.869)	(0.847 , 1.393)	(-0.142 , 0.285)
-	p-value	0.511	0.517	0.511
Gastrointestinal disorders	Effect measure	4	2	0.333
-	95% CI	(1.052 , 15.207)	(0.974 , 4.109)	(0.037 , 0.63)
-	p-value	0.042	0.059	0.028
Abdominal pain	Effect measure	12.333	9.465	0.238
-	95% CI	(0.633 , 240.438)	(0.56 , 159.998)	(0.004 , 0.472)
-	p-value	0.097	0.119	0.045
Vomiting	Effect measure	2.833	2.571	0.087
-	95% CI	(0.268 , 29.955)	(0.292 , 22.608)	(-0.096 , 0.271)
-	p-value	0.387	0.394	0.351
Diarrhoea	Effect measure	1.176	1.143	0.024
-	95% CI	(0.226 , 6.127)	(0.294 , 4.444)	(-0.217 , 0.264)
-	p-value	0.847	0.847	0.846
Infections and infestations	Effect measure	1.3	1.114	0.063
-	95% CI	(0.361 , 4.679)	(0.654 , 1.897)	(-0.246 , 0.373)
-	p-value	0.688	0.69	0.688
Nasopharyngitis	Effect measure	0.625	0.714	-0.095
-	95% CI	(0.154 , 2.542)	(0.261 , 1.953)	(-0.379 , 0.189)
-	p-value	0.511	0.512	0.511
Vascular disorders	Effect measure	12.75	7.714	0.373
-	95% CI	(1.421 , 114.4)	(1.078 , 55.191)	(0.136 , 0.61)
-	p-value	0.023	0.042	0.002
Flushing	Effect measure	28.12	16.349	0.429
-	95% CI	(1.497 , 528.181)	(1.019 , 262.229)	(0.165 , 0.692)
-	p-value	0.026	0.048	0
General disorders and administration site conditions	Effect measure	0.294	0.429	-0.254
-	95% CI	(0.07 , 1.232)	(0.154 , 1.191)	(-0.538 , 0.03)
-	p-value	0.094	0.104	0.08
Pyrexia	Effect measure	0.526	0.571	-0.071
-	95% CI	(0.078 , 3.565)	(0.107 , 3.05)	(-0.285 , 0.142)
-	p-value	0.511	0.513	0.511
Respiratory, thoracic and mediastinal disorders	Effect measure	2.5	2.143	0.127
-	95% CI	(0.422 , 14.828)	(0.471 , 9.741)	(-0.106 , 0.36)
-	p-value	0.313	0.324	0.285
Skin and subcutaneous tissue disorders	Effect measure	12.333	9.465	0.238
-	95% CI	(0.633 , 240.438)	(0.56 , 159.998)	(0.004 , 0.472)
-	p-value	0.097	0.119	0.045

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a

NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with ≥10 events in either treatment arm are shown in this table

109MS306_table75_any_Male_AESI_NPERCENT

Overall rate and effect measures of male patients with ≥1 any AESI, related to CSR Table 75

AESI	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Number of subjects with any AESI	19 (90)	15 (83)	34 (87)
Gastrointestinal disorders	14 (67)	6 (33)	20 (51)
Abdominal pain	5 (24)	0	5 (13)
Vomiting	3 (14)	1 (6)	4 (10)
Diarrhoea	4 (19)	3 (17)	7 (18)
Infections and infestations	13 (62)	10 (56)	23 (59)
Nasopharyngitis	5 (24)	6 (33)	11 (28)
Vascular disorders	9 (43)	1 (6)	10 (26)
Flushing	9 (43)	0	9 (23)
General disorders and administration site conditions	4 (19)	8 (44)	12 (31)
Pyrexia	2 (10)	3 (17)	5 (13)
Respiratory, thoracic and mediastinal disorders	5 (24)	2 (11)	7 (18)
Skin and subcutaneous tissue disorders	5 (24)	0	5 (13)

NOTE1: Only AESIs with ≥10 events in either treatment arm are shown in this table

mild AESI

109MS306_table75_MILD_AESI_NPERCENT_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 mild AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Number of subjects with any AESI	61 (86)	45 (70)	106 (79)	2.576 (1.093 , 6.069) 0.031	1.222 (1.016 , 1.47) 0.034	0.156 (0.018 , 0.294) 0.027
Gastrointestinal disorders	47 (66)	17 (27)	64 (47)	5.414 (2.58 , 11.362) 0	2.492 (1.605 , 3.869) 0	0.396 (0.242 , 0.551) 0
Abdominal pain	27 (38)	5 (8)	32 (24)	7.241 (2.582 , 20.303) 0	4.868 (1.994 , 11.882) 0.001	0.302 (0.171 , 0.433) 0
Vomiting	14 (20)	3 (5)	17 (13)	4.994 (1.364 , 18.292) 0.015	4.207 (1.267 , 13.971) 0.019	0.15 (0.044 , 0.256) 0.005
Diarrhoea	11 (15)	4 (6)	15 (11)	2.75 (0.829 , 9.121) 0.098	2.479 (0.831 , 7.398) 0.104	0.092 (-0.011 , 0.195) 0.078
Nausea	10 (14)	5 (8)	15 (11)	1.934 (0.624 , 5.998) 0.253	1.803 (0.651 , 4.994) 0.257	0.063 (-0.042 , 0.167) 0.238
Abdominal pain upper	11 (15)	1 (2)	12 (9)	11.55 (1.447 , 92.214) 0.021	9.915 (1.317 , 74.675) 0.026	0.139 (0.05 , 0.229) 0.002
Constipation	4 (6)	2 (3)	6 (4)	1.851 (0.327 , 10.462) 0.486	1.803 (0.342 , 9.514) 0.487	0.025 (-0.043 , 0.094) 0.473
Dyspepsia	4 (6)	1 (2)	5 (4)	3.761 (0.409 , 34.566) 0.242	3.606 (0.414 , 31.425) 0.246	0.041 (-0.021 , 0.102) 0.195
Toothache	1 (1)	2 (3)	3 (2)	0.443 (0.039 , 5.004) 0.51	0.451 (0.042 , 4.853) 0.511	-0.017 (-0.068 , 0.034) 0.507
Dental caries	0	2 (3)	2 (1)	0.175 (0.008 , 3.711) 0.263	0.18 (0.009 , 3.688) 0.266	-0.031 (-0.089 , 0.026) 0.451
Dry mouth	1 (1)	1 (2)	2 (1)	0.9 (0.055 , 14.691) 0.941	0.901 (0.058 , 14.117) 0.941	-0.002 (-0.042 , 0.039) 0.941

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Abdominal pain lower	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Frequent bowel movements	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Oesophagitis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Infections and infestations	33 (46)	22 (34)	55 (41)	1.658 (0.827 , 3.323) 0.154	1.352 (0.888 , 2.059) 0.16	0.121 (-0.043 , 0.285) 0.149
Nasopharyngitis	16 (23)	7 (11)	23 (17)	2.369 (0.905 , 6.201) 0.079	2.06 (0.906 , 4.685) 0.085	0.116 (-0.008 , 0.24) 0.066
Gastroenteritis	7 (10)	4 (6)	11 (8)	1.641 (0.457 , 5.889) 0.448	1.577 (0.484 , 5.139) 0.449	0.036 (-0.055 , 0.127) 0.438
Upper respiratory tract infection	7 (10)	3 (5)	10 (7)	2.224 (0.55 , 8.994) 0.262	2.103 (0.568 , 7.792) 0.266	0.052 (-0.035 , 0.138) 0.242
Pharyngitis	4 (6)	4 (6)	8 (6)	0.896 (0.215 , 3.738) 0.88	0.901 (0.235 , 3.457) 0.88	-0.006 (-0.086 , 0.074) 0.88
Tonsillitis	3 (4)	4 (6)	7 (5)	0.662 (0.142 , 3.077) 0.598	0.676 (0.157 , 2.906) 0.599	-0.02 (-0.096 , 0.055) 0.599
Sinusitis	3 (4)	2 (3)	5 (4)	1.368 (0.221 , 8.458) 0.736	1.352 (0.233 , 7.836) 0.736	0.011 (-0.052 , 0.074) 0.733
Viral infection	3 (4)	2 (3)	5 (4)	1.368 (0.221 , 8.458) 0.736	1.352 (0.233 , 7.836) 0.736	0.011 (-0.052 , 0.074) 0.733
Urinary tract infection	2 (3)	2 (3)	4 (3)	0.899 (0.123 , 6.572) 0.916	0.901 (0.131 , 6.214) 0.916	-0.003 (-0.061 , 0.054) 0.916
Cystitis	3 (4)	0	3 (2)	6.591 (0.334 , 130.11) 0.215	6.315 (0.332 , 119.928) 0.22	0.042 (-0.019 , 0.104) 0.251
Ear infection	3 (4)	0	3 (2)	6.591 (0.334 , 130.11) 0.215	6.315 (0.332 , 119.928) 0.22	0.042 (-0.019 , 0.104) 0.251

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Oral herpes	2 (3)	0	2 (1)	4.64 (0.219 , 98.493) 0.325	4.51 (0.221 , 92.209) 0.328	0.028 (-0.025 , 0.082) 0.498
Viral upper respiratory tract infection	0	2 (3)	2 (1)	0.175 (0.008 , 3.711) 0.263	0.18 (0.009 , 3.688) 0.266	-0.031 (-0.089 , 0.026) 0.451
Bacteriuria	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Bronchitis	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Eye infection	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Fungal skin infection	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Gastroenteritis viral	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Gastrointestinal infection	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Laryngitis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Otitis externa	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Otitis media acute	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
General disorders and administration site conditions	10 (14)	24 (38)	34 (25)	0.273 (0.118 , 0.632) 0.002	0.376 (0.195 , 0.724) 0.003	-0.234 (-0.378 , -0.091) 0.001
Pyrexia	3 (4)	11 (17)	14 (10)	0.213 (0.056 , 0.801) 0.022	0.246 (0.072 , 0.842) 0.025	-0.13 (-0.233 , -0.026) 0.014
Asthenia	2 (3)	6 (9)	8 (6)	0.28 (0.054 , 1.441) 0.128	0.3 (0.063 , 1.436) 0.132	-0.066 (-0.147 , 0.016) 0.113

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Fatigue	1 (1)	4 (6)	5 (4)	0.214 (0.023 , 1.97) 0.173	0.225 (0.026 , 1.964) 0.177	-0.048 (-0.114 , 0.017) 0.146
Chills	0	4 (6)	4 (3)	0.094 (0.005 , 1.781) 0.115	0.1 (0.006 , 1.826) 0.12	-0.062 (-0.137 , 0.012) 0.115
Pain	0	2 (3)	2 (1)	0.175 (0.008 , 3.711) 0.263	0.18 (0.009 , 3.688) 0.266	-0.031 (-0.089 , 0.026) 0.451
Chest discomfort	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Chest pain	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Feeling hot	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Generalised oedema	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Oedema peripheral	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Vascular disorders	28 (39)	5 (8)	33 (24)	7.684 (2.744 , 21.512) 0	5.048 (2.074 , 12.287) 0	0.316 (0.185 , 0.448) 0
Flushing	22 (31)	1 (2)	23 (17)	28.286 (3.684 , 217.206) 0.001	19.831 (2.751 , 142.962) 0.003	0.294 (0.182 , 0.406) 0
Hot flush	7 (10)	1 (2)	8 (6)	6.891 (0.824 , 57.635) 0.075	6.31 (0.798 , 49.898) 0.081	0.083 (0.007 , 0.159) 0.032
Hypertension	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Hypotension	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Orthostatic hypotension	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Respiratory, thoracic and mediastinal disorders	19 (27)	5 (8)	24 (18)	4.312 (1.504 , 12.362) 0.007	3.425 (1.358 , 8.642) 0.009	0.189 (0.067 , 0.312) 0.002
Oropharyngeal pain	11 (15)	4 (6)	15 (11)	2.75 (0.829 , 9.121) 0.098	2.479 (0.831 , 7.398) 0.104	0.092 (-0.011 , 0.195) 0.078
Cough	9 (13)	2 (3)	11 (8)	4.5 (0.934 , 21.675) 0.061	4.056 (0.91 , 18.079) 0.066	0.096 (0.007 , 0.184) 0.034
Dyspnoea	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Pneumonitis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Tonsillar erythema	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Skin and subcutaneous tissue disorders	17 (24)	1 (2)	18 (13)	19.833 (2.555 , 153.952) 0.004	15.324 (2.098 , 111.911) 0.007	0.224 (0.12 , 0.328) 0
Rash	9 (13)	1 (2)	10 (7)	9.145 (1.125 , 74.347) 0.038	8.113 (1.057 , 62.278) 0.044	0.111 (0.028 , 0.194) 0.009
Erythema	5 (7)	0	5 (4)	10.669 (0.578 , 196.883) 0.111	9.923 (0.56 , 175.966) 0.118	0.07 (-0.004 , 0.145) 0.067
Pruritus	3 (4)	0	3 (2)	6.591 (0.334 , 130.11) 0.215	6.315 (0.332 , 119.928) 0.22	0.042 (-0.019 , 0.104) 0.251
Dry skin	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Ecchymosis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Rash pruritic	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Musculoskeletal and connective tissue disorders	1 (1)	8 (13)	9 (7)	0.1 (0.012 , 0.823) 0.032	0.113 (0.014 , 0.876) 0.037	-0.111 (-0.196 , -0.025) 0.011

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Myalgia	1 (1)	8 (13)	9 (7)	0.1 (0.012 , 0.823) 0.032	0.113 (0.014 , 0.876) 0.037	-0.111 (-0.196 , -0.025) 0.011
Renal and urinary disorders	3 (4)	6 (9)	9 (7)	0.426 (0.102 , 1.781) 0.243	0.451 (0.118 , 1.728) 0.245	-0.051 (-0.137 , 0.034) 0.237
Proteinuria	1 (1)	3 (5)	4 (3)	0.29 (0.029 , 2.866) 0.29	0.3 (0.032 , 2.816) 0.292	-0.033 (-0.091 , 0.026) 0.273
Dysuria	1 (1)	1 (2)	2 (1)	0.9 (0.055 , 14.691) 0.941	0.901 (0.058 , 14.117) 0.941	-0.002 (-0.042 , 0.039) 0.941
Bladder discomfort	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Renal cyst	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Renal pain	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Investigations	2 (3)	2 (3)	4 (3)	0.899 (0.123 , 6.572) 0.916	0.901 (0.131 , 6.214) 0.916	-0.003 (-0.061 , 0.054) 0.916
Alanine aminotransferase increased	1 (1)	1 (2)	2 (1)	0.9 (0.055 , 14.691) 0.941	0.901 (0.058 , 14.117) 0.941	-0.002 (-0.042 , 0.039) 0.941
Aspartate aminotransferase increased	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Blood bilirubin increased	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Blood glucose increased	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Cardiac disorders	2 (3)	0	2 (1)	4.64 (0.219 , 98.493) 0.325	4.51 (0.221 , 92.209) 0.328	0.028 (-0.025 , 0.082) 0.498
Palpitations	2 (3)	0	2 (1)	4.64 (0.219 , 98.493) 0.325	4.51 (0.221 , 92.209) 0.328	0.028 (-0.025 , 0.082) 0.498

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Hepatobiliary disorders	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Hepatocellular injury	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Nervous system disorders	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Burning sensation	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

AESI moderate

109MS306_table75_moderate_AESI_NPERCENT_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 moderate AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Number of subjects with any AESI	25 (35)	18 (28)	43 (32)	1.389	1.252	0.071
				(0.669 , 2.884)	(0.757 , 2.07)	(-0.086 , 0.227)
				0.378	0.381	0.375
Gastrointestinal disorders	13 (18)	7 (11)	20 (15)	1.825	1.674	0.074
				(0.679 , 4.906)	(0.712 , 3.934)	(-0.044 , 0.192)
				0.233	0.237	0.221
Vomiting	4 (6)	3 (5)	7 (5)	1.214	1.202	0.009
				(0.261 , 5.643)	(0.28 , 5.167)	(-0.065 , 0.084)
				0.805	0.805	0.804
Abdominal pain	4 (6)	1 (2)	5 (4)	3.761	3.606	0.041
				(0.409 , 34.566)	(0.414 , 31.425)	(-0.021 , 0.102)
				0.242	0.246	0.195
Diarrhoea	5 (7)	0	5 (4)	10.669	9.923	0.07
				(0.578 , 196.883)	(0.56 , 175.966)	(-0.004 , 0.145)
				0.111	0.118	0.067
Dyspepsia	3 (4)	0	3 (2)	6.591	6.315	0.042
				(0.334 , 130.11)	(0.332 , 119.928)	(-0.019 , 0.104)
				0.215	0.22	0.251
Abdominal pain upper	2 (3)	0	2 (1)	4.64	4.51	0.028
				(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
				0.325	0.328	0.498
Nausea	1 (1)	1 (2)	2 (1)	0.9	0.901	-0.002
				(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
				0.941	0.941	0.941
Constipation	1 (1)	0	1 (1)	2.745	2.706	0.014
				(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
				0.539	0.54	0.956

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Gastritis	1 (1)	0	1 (1)	2.745	2.706	0.014
				(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
				0.539	0.54	0.956
Gingival bleeding	0	1 (2)	1 (1)	0.296	0.301	-0.016
				(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
				0.459	0.459	0.96
Toothache	0	1 (2)	1 (1)	0.296	0.301	-0.016
				(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
				0.459	0.459	0.96
Infections and infestations	10 (14)	8 (13)	18 (13)	1.148	1.127	0.016
				(0.423 , 3.113)	(0.474 , 2.679)	(-0.099 , 0.13)
				0.787	0.787	0.786
Gastroenteritis	2 (3)	1 (2)	3 (2)	1.826	1.803	0.013
				(0.162 , 20.631)	(0.167 , 19.412)	(-0.036 , 0.062)
				0.626	0.627	0.616
Upper respiratory tract infection	3 (4)	0	3 (2)	6.591	6.315	0.042
				(0.334 , 130.11)	(0.332 , 119.928)	(-0.019 , 0.104)
				0.215	0.22	0.251
Nasopharyngitis	0	2 (3)	2 (1)	0.175	0.18	-0.031
				(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
				0.263	0.266	0.451
Bronchitis	0	1 (2)	1 (1)	0.296	0.301	-0.016
				(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
				0.459	0.459	0.96
Chronic sinusitis	0	1 (2)	1 (1)	0.296	0.301	-0.016
				(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
				0.459	0.459	0.96
Cystitis	1 (1)	0	1 (1)	2.745	2.706	0.014
				(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
				0.539	0.54	0.956
Gastroenteritis viral	0	1 (2)	1 (1)	0.296	0.301	-0.016
				(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
				0.459	0.459	0.96
Laryngitis	1 (1)	0	1 (1)	2.745	2.706	0.014
				(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
				0.539	0.54	0.956

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Otitis media	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Pharyngitis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Pneumonia	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Pneumonia pneumococcal	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Respiratory tract infection	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Tonsillitis	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Urinary tract infection	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
General disorders and administration site conditions	3 (4)	7 (11)	10 (7)	0.359 (0.089 , 1.453) 0.151	0.386 (0.104 , 1.431) 0.155	-0.067 (-0.157 , 0.023) 0.142
Fatigue	1 (1)	4 (6)	5 (4)	0.214 (0.023 , 1.97) 0.173	0.225 (0.026 , 1.964) 0.177	-0.048 (-0.114 , 0.017) 0.146
Pyrexia	2 (3)	3 (5)	5 (4)	0.589 (0.095 , 3.645) 0.57	0.601 (0.104 , 3.482) 0.57	-0.019 (-0.083 , 0.046) 0.57
Pain	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Vascular disorders	8 (11)	1 (2)	9 (7)	8 (0.972 , 65.853) 0.053	7.211 (0.927 , 56.085) 0.059	0.097 (0.017 , 0.177) 0.017

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Flushing	8 (11)	1 (2)	9 (7)	8 (0.972 , 65.853) 0.053	7.211 (0.927 , 56.085) 0.059	0.097 (0.017 , 0.177) 0.017
Respiratory, thoracic and mediastinal disorders	2 (3)	0	2 (1)	4.64 (0.219 , 98.493) 0.325	4.51 (0.221 , 92.209) 0.328	0.028 (-0.025 , 0.082) 0.498
Cough	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Oropharyngeal pain	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Skin and subcutaneous tissue disorders	2 (3)	0	2 (1)	4.64 (0.219 , 98.493) 0.325	4.51 (0.221 , 92.209) 0.328	0.028 (-0.025 , 0.082) 0.498
Erythema	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Pruritus	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Blood and lymphatic system disorders	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Lymphopenia	1 (1)	0	1 (1)	2.745 (0.11 , 68.583) 0.539	2.706 (0.112 , 65.264) 0.54	0.014 (-0.028 , 0.056) 0.956
Hepatobiliary disorders	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Hepatocellular injury	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96
Musculoskeletal and connective tissue disorders	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)	OR	RR	ARR
Myalgia	0	1 (2)	1 (1)	0.296 (0.012 , 7.397) 0.459	0.301 (0.012 , 7.252) 0.459	-0.016 (-0.061 , 0.03) 0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

AESI NonSevere

109MS306_table75_NonSevere_AESI_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 non-severe (mild or moderate) AESI, related to CSR Table 75

	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	6.059	1.285	0.209
	95% CI	(1.916 , 19.158)	(1.097 , 1.505)	(0.089 , 0.33)
	p-value	0.002	0.002	0.001
Gastrointestinal disorders	Effect measure	6.478	2.389	0.434
	95% CI	(3.054 , 13.739)	(1.621 , 3.521)	(0.282 , 0.586)
	p-value	0	0	0
Abdominal pain	Effect measure	7.684	5.048	0.316
	95% CI	(2.744 , 21.512)	(2.074 , 12.287)	(0.185 , 0.448)
	p-value	0	0	0
Vomiting	Effect measure	3.433	2.885	0.147
	95% CI	(1.178 , 10)	(1.12 , 7.426)	(0.03 , 0.265)
	p-value	0.024	0.028	0.014
Diarrhoea	Effect measure	3.684	3.155	0.135
	95% CI	(1.145 , 11.857)	(1.095 , 9.094)	(0.025 , 0.245)
	p-value	0.029	0.033	0.016
Nausea	Effect measure	2.163	1.983	0.077
	95% CI	(0.708 , 6.607)	(0.728 , 5.4)	(-0.03 , 0.184)
	p-value	0.176	0.18	0.159
Abdominal pain upper	Effect measure	12.814	10.817	0.153
	95% CI	(1.616 , 101.613)	(1.447 , 80.878)	(0.061 , 0.246)
	p-value	0.016	0.02	0.001
Dyspepsia	Effect measure	6.891	6.31	0.083
	95% CI	(0.824 , 57.635)	(0.798 , 49.898)	(0.007 , 0.159)
	p-value	0.075	0.081	0.032
Constipation	Effect measure	1.851	1.803	0.025
	95% CI	(0.327 , 10.462)	(0.342 , 9.514)	(-0.043 , 0.094)
	p-value	0.486	0.487	0.473
Toothache	Effect measure	0.29	0.3	-0.033
	95% CI	(0.029 , 2.866)	(0.032 , 2.816)	(-0.091 , 0.026)
	p-value	0.29	0.292	0.273
Dental caries	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Dry mouth	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Abdominal pain lower	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

	Result	OR	RR	ARR
Frequent bowel movements	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gastritis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gingival bleeding	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Oesophagitis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Infections and infestations	Effect measure	1.67	1.302	0.127
	95% CI	(0.845 , 3.302)	(0.912 , 1.859)	(-0.04 , 0.295)
	p-value	0.14	0.146	0.136
Nasopharyngitis	Effect measure	1.778	1.603	0.085
	95% CI	(0.724 , 4.364)	(0.762 , 3.371)	(-0.044 , 0.214)
	p-value	0.209	0.214	0.199
Gastroenteritis	Effect measure	1.713	1.623	0.049
	95% CI	(0.542 , 5.409)	(0.574 , 4.589)	(-0.053 , 0.15)
	p-value	0.359	0.362	0.348
Upper respiratory tract infection	Effect measure	2.952	2.704	0.08
	95% CI	(0.762 , 11.427)	(0.765 , 9.555)	(-0.013 , 0.173)
	p-value	0.117	0.122	0.093
Pharyngitis	Effect measure	1.136	1.127	0.008
	95% CI	(0.292 , 4.43)	(0.316 , 4.015)	(-0.076 , 0.092)
	p-value	0.854	0.854	0.853
Tonsillitis	Effect measure	0.896	0.901	-0.006
	95% CI	(0.215 , 3.738)	(0.235 , 3.457)	(-0.086 , 0.074)
	p-value	0.88	0.88	0.88
Sinusitis	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Urinary tract infection	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Viral infection	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Cystitis	Effect measure	8.6	8.119	0.056
	95% CI	(0.454 , 162.938)	(0.446 , 147.892)	(-0.012 , 0.125)
	p-value	0.152	0.157	0.13
Ear infection	Effect measure	6.591	6.315	0.042
	95% CI	(0.334 , 130.11)	(0.332 , 119.928)	(-0.019 , 0.104)
	p-value	0.215	0.22	0.251
Bronchitis	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Gastroenteritis viral	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)

	Result	OR	RR	ARR
	p-value	0.941	0.941	0.941
Laryngitis	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Oral herpes	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Viral upper respiratory tract infection	Effect measure	0.175	0.18	-0.031
	95% CI	(0.008 , 3.711)	(0.009 , 3.688)	(-0.089 , 0.026)
	p-value	0.263	0.266	0.451
Bacteriuria	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Chronic sinusitis	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Eye infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Fungal skin infection	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Gastrointestinal infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Otitis externa	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Otitis media	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Otitis media acute	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonia	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonia pneumococcal	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Respiratory tract infection	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Vascular disorders	Effect measure	10.843	6.13	0.401
	95% CI	(3.891 , 30.215)	(2.553 , 14.717)	(0.267 , 0.534)
	p-value	0	0	0
Flushing	Effect measure	41.023	25.239	0.379

	Result	OR	RR	ARR
	95% CI	(5.377 , 312.975)	(3.534 , 180.232)	(0.261 , 0.496)
	p-value	0	0.001	0
Hot flush	Effect measure	6.891	6.31	0.083
	95% CI	(0.824 , 57.635)	(0.798 , 49.898)	(0.007 , 0.159)
	p-value	0.075	0.081	0.032
Hypertension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hypotension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Orthostatic hypotension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
General disorders and administration site conditions	Effect measure	0.251	0.367	-0.267
	95% CI	(0.112 , 0.566)	(0.199 , 0.679)	(-0.414 , -0.12)
	p-value	0.001	0.001	0
Pyrexia	Effect measure	0.213	0.258	-0.162
	95% CI	(0.066 , 0.687)	(0.089 , 0.742)	(-0.277 , -0.048)
	p-value	0.01	0.012	0.005
Asthenia	Effect measure	0.28	0.3	-0.066
	95% CI	(0.054 , 1.441)	(0.063 , 1.436)	(-0.147 , 0.016)
	p-value	0.128	0.132	0.113
Fatigue	Effect measure	0.116	0.129	-0.095
	95% CI	(0.014 , 0.973)	(0.016 , 1.018)	(-0.177 , -0.014)
	p-value	0.047	0.052	0.021
Chills	Effect measure	0.094	0.1	-0.062
	95% CI	(0.005 , 1.781)	(0.006 , 1.826)	(-0.137 , 0.012)
	p-value	0.115	0.12	0.115
Pain	Effect measure	0.123	0.129	-0.047
	95% CI	(0.006 , 2.426)	(0.007 , 2.448)	(-0.114 , 0.02)
	p-value	0.168	0.173	0.226
Chest discomfort	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Chest pain	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Feeling hot	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Generalised oedema	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Oedema peripheral	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

	Result	OR	RR	ARR
Respiratory, thoracic and mediastinal disorders	Effect measure	4.627	3.606	0.204
	95% CI	(1.621 , 13.213)	(1.437 , 9.047)	(0.08 , 0.327)
	p-value	0.004	0.006	0.001
Oropharyngeal pain	Effect measure	3.051	2.704	0.107
	95% CI	(0.931 , 10.001)	(0.918 , 7.963)	(0.001 , 0.212)
	p-value	0.066	0.071	0.048
Cough	Effect measure	5.082	4.507	0.11
	95% CI	(1.069 , 24.155)	(1.026 , 19.802)	(0.018 , 0.201)
	p-value	0.041	0.046	0.019
Dyspnoea	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonitis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Tonsillar erythema	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Skin and subcutaneous tissue disorders	Effect measure	23.019	17.127	0.252
	95% CI	(2.981 , 177.766)	(2.359 , 124.33)	(0.145 , 0.359)
	p-value	0.003	0.005	0
Rash	Effect measure	9.145	8.113	0.111
	95% CI	(1.125 , 74.347)	(1.057 , 62.278)	(0.028 , 0.194)
	p-value	0.038	0.044	0.009
Erythema	Effect measure	12.802	11.727	0.085
	95% CI	(0.707 , 231.94)	(0.674 , 204.098)	(0.005 , 0.164)
	p-value	0.085	0.091	0.035
Pruritus	Effect measure	8.6	8.119	0.056
	95% CI	(0.454 , 162.938)	(0.446 , 147.892)	(-0.012 , 0.125)
	p-value	0.152	0.157	0.13
Dry skin	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Ecchymosis	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Rash pruritic	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Musculoskeletal and connective tissue disorders	Effect measure	0.1	0.113	-0.111
	95% CI	(0.012 , 0.823)	(0.014 , 0.876)	(-0.196 , -0.025)

	Result	OR	RR	ARR
	p-value	0.032	0.037	0.011
Myalgia	Effect measure	0.1	0.113	-0.111
	95% CI	(0.012 , 0.823)	(0.014 , 0.876)	(-0.196 , -0.025)
	p-value	0.032	0.037	0.011
Renal and urinary disorders	Effect measure	0.426	0.451	-0.051
	95% CI	(0.102 , 1.781)	(0.118 , 1.728)	(-0.137 , 0.034)
	p-value	0.243	0.245	0.237
Proteinuria	Effect measure	0.29	0.3	-0.033
	95% CI	(0.029 , 2.866)	(0.032 , 2.816)	(-0.091 , 0.026)
	p-value	0.29	0.292	0.273
Dysuria	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Bladder discomfort	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Renal cyst	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Renal pain	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Investigations	Effect measure	0.899	0.901	-0.003
	95% CI	(0.123 , 6.572)	(0.131 , 6.214)	(-0.061 , 0.054)
	p-value	0.916	0.916	0.916
Alanine aminotransferase increased	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Aspartate aminotransferase increased	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Blood bilirubin increased	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Blood glucose increased	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Cardiac disorders	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Palpitations	Effect measure	4.64	4.51	0.028
	95% CI	(0.219 , 98.493)	(0.221 , 92.209)	(-0.025 , 0.082)
	p-value	0.325	0.328	0.498
Hepatobiliary disorders	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941

	Result	OR	RR	ARR
Hepatocellular injury	Effect measure	0.9	0.901	-0.002
	95% CI	(0.055 , 14.691)	(0.058 , 14.117)	(-0.042 , 0.039)
	p-value	0.941	0.941	0.941
Blood and lymphatic system disorders	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Lymphopenia	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Nervous system disorders	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Burning sensation	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_NonSevere_AESI_NPERCENT

Overall rate and effect measures of patients with ≥1 non-severe (mild or moderate) AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with any AESI	67 (94)	47 (73)	114 (84)
Gastrointestinal disorders	53 (75)	20 (31)	73 (54)
Abdominal pain	28 (39)	5 (8)	33 (24)
Vomiting	16 (23)	5 (8)	21 (16)
Diarrhoea	14 (20)	4 (6)	18 (13)
Nausea	11 (15)	5 (8)	16 (12)
Abdominal pain upper	12 (17)	1 (2)	13 (10)
Dyspepsia	7 (10)	1 (2)	8 (6)
Constipation	4 (6)	2 (3)	6 (4)
Toothache	1 (1)	3 (5)	4 (3)
Dental caries	0	2 (3)	2 (1)
Dry mouth	1 (1)	1 (2)	2 (1)
Abdominal pain lower	0	1 (2)	1 (1)
Frequent bowel movements	1 (1)	0	1 (1)
Gastritis	1 (1)	0	1 (1)
Gingival bleeding	0	1 (2)	1 (1)
Oesophagitis	1 (1)	0	1 (1)
Infections and infestations	39 (55)	27 (42)	66 (49)
Nasopharyngitis	16 (23)	9 (14)	25 (19)
Gastroenteritis	9 (13)	5 (8)	14 (10)
Upper respiratory tract infection	9 (13)	3 (5)	12 (9)
Pharyngitis	5 (7)	4 (6)	9 (7)
Tonsillitis	4 (6)	4 (6)	8 (6)
Sinusitis	3 (4)	2 (3)	5 (4)
Urinary tract infection	3 (4)	2 (3)	5 (4)
Viral infection	3 (4)	2 (3)	5 (4)
Cystitis	4 (6)	0	4 (3)
Ear infection	3 (4)	0	3 (2)
Bronchitis	0	2 (3)	2 (1)
Gastroenteritis viral	1 (1)	1 (2)	2 (1)
Laryngitis	2 (3)	0	2 (1)
Oral herpes	2 (3)	0	2 (1)
Viral upper respiratory tract infection	0	2 (3)	2 (1)
Bacteriuria	1 (1)	0	1 (1)
Chronic sinusitis	0	1 (2)	1 (1)
Eye infection	0	1 (2)	1 (1)
Fungal skin infection	1 (1)	0	1 (1)
Gastrointestinal infection	0	1 (2)	1 (1)
Otitis externa	1 (1)	0	1 (1)
Otitis media	0	1 (2)	1 (1)
Otitis media acute	1 (1)	0	1 (1)
Pneumonia	1 (1)	0	1 (1)
Pneumonia pneumococcal	1 (1)	0	1 (1)
Respiratory tract infection	0	1 (2)	1 (1)
Vascular disorders	34 (48)	5 (8)	39 (29)
Flushing	28 (39)	1 (2)	29 (21)
Hot flush	7 (10)	1 (2)	8 (6)
Hypertension	0	1 (2)	1 (1)
Hypotension	0	1 (2)	1 (1)
Orthostatic hypotension	0	1 (2)	1 (1)

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
General disorders and administration site conditions	11 (15)	27 (42)	38 (28)
Pyrexia	4 (6)	14 (22)	18 (13)
Asthenia	2 (3)	6 (9)	8 (6)
Fatigue	1 (1)	7 (11)	8 (6)
Chills	0	4 (6)	4 (3)
Pain	0	3 (5)	3 (2)
Chest discomfort	1 (1)	0	1 (1)
Chest pain	1 (1)	0	1 (1)
Feeling hot	1 (1)	0	1 (1)
Generalised oedema	1 (1)	0	1 (1)
Oedema peripheral	0	1 (2)	1 (1)
Respiratory, thoracic and mediastinal disorders	20 (28)	5 (8)	25 (19)
Oropharyngeal pain	12 (17)	4 (6)	16 (12)
Cough	10 (14)	2 (3)	12 (9)
Dyspnoea	1 (1)	0	1 (1)
Pneumonitis	1 (1)	0	1 (1)
Tonsillar erythema	0	1 (2)	1 (1)
Skin and subcutaneous tissue disorders	19 (27)	1 (2)	20 (15)
Rash	9 (13)	1 (2)	10 (7)
Erythema	6 (8)	0	6 (4)
Pruritus	4 (6)	0	4 (3)
Dry skin	1 (1)	0	1 (1)
Ecchymosis	1 (1)	0	1 (1)
Rash pruritic	1 (1)	0	1 (1)
Musculoskeletal and connective tissue disorders	1 (1)	8 (13)	9 (7)
Myalgia	1 (1)	8 (13)	9 (7)
Renal and urinary disorders	3 (4)	6 (9)	9 (7)
Proteinuria	1 (1)	3 (5)	4 (3)
Dysuria	1 (1)	1 (2)	2 (1)
Bladder discomfort	0	1 (2)	1 (1)
Renal cyst	1 (1)	0	1 (1)
Renal pain	0	1 (2)	1 (1)
Investigations	2 (3)	2 (3)	4 (3)
Alanine aminotransferase increased	1 (1)	1 (2)	2 (1)
Aspartate aminotransferase increased	0	1 (2)	1 (1)
Blood bilirubin increased	1 (1)	0	1 (1)
Blood glucose increased	1 (1)	0	1 (1)
Cardiac disorders	2 (3)	0	2 (1)
Palpitations	2 (3)	0	2 (1)
Hepatobiliary disorders	1 (1)	1 (2)	2 (1)
Hepatocellular injury	1 (1)	1 (2)	2 (1)
Blood and lymphatic system disorders	1 (1)	0	1 (1)
Lymphopenia	1 (1)	0	1 (1)
Nervous system disorders	0	1 (2)	1 (1)
Burning sensation	0	1 (2)	1 (1)

Sub groups

109MS306_table75_Nonsevere_Age1314_AESI_EFFECTMEASURES

Overall rate and effect measures of aged 13-14 patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	11.261	1.261	0.214
-	95% CI	(0.532 , 238.544)	(0.969 , 1.64)	(-0.064 , 0.493)
-	p-value	0.12	0.084	0.169
Gastrointestinal disorders	Effect measure	4.667	1.815	0.349
-	95% CI	(1.006 , 21.652)	(0.944 , 3.488)	(0.027 , 0.672)
-	p-value	0.049	0.074	0.034
Abdominal pain	Effect measure	6.5	4.667	0.262
-	95% CI	(0.68 , 62.149)	(0.633 , 34.43)	(0.006 , 0.518)
-	p-value	0.104	0.131	0.045
Vascular disorders	Effect measure	18.913	11.757	0.389
-	95% CI	(0.975 , 366.99)	(0.73 , 189.308)	(0.1 , 0.678)
-	p-value	0.052	0.082	0.005
Flushing	Effect measure	15.08	10.189	0.333
-	95% CI	(0.77 , 295.19)	(0.624 , 166.403)	(0.052 , 0.615)
-	p-value	0.074	0.103	0.015
General disorders and administration site conditions	Effect measure	0.385	0.556	-0.222
-	95% CI	(0.088 , 1.673)	(0.223 , 1.381)	(-0.556 , 0.112)
-	p-value	0.203	0.206	0.192
Pyrexia	Effect measure	0.312	0.389	-0.175
-	95% CI	(0.048 , 2.032)	(0.083 , 1.827)	(-0.452 , 0.103)
-	p-value	0.223	0.231	0.218
Respiratory, thoracic and mediastinal disorders	Effect measure	10.4	6.222	0.373
-	95% CI	(1.111 , 97.335)	(0.878 , 44.086)	(0.107 , 0.639)
-	p-value	0.04	0.067	0.006
Skin and subcutaneous tissue disorders	Effect measure	3.714	3.111	0.151
-	95% CI	(0.366 , 37.708)	(0.39 , 24.829)	(-0.084 , 0.385)
-	p-value	0.267	0.284	0.208

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Age1314_AESI_NPERCENT

Overall rate and effect measures of aged 13-14 patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	DMF (N=18)	IFN B-1a (N=14)	Total (N=32)
Number of subjects with any AESI	18 (100)	11 (79)	29 (91)
Gastrointestinal disorders	14 (78)	6 (43)	20 (63)
Abdominal pain	6 (33)	1 (7)	7 (22)
Vascular disorders	7 (39)	0	7 (22)
Flushing	6 (33)	0	6 (19)
General disorders and administration site conditions	5 (28)	7 (50)	12 (38)
Pyrexia	2 (11)	4 (29)	6 (19)
Respiratory, thoracic and mediastinal disorders	8 (44)	1 (7)	9 (28)
Skin and subcutaneous tissue disorders	4 (22)	1 (7)	5 (16)

NOTE1: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Age1517_AESI_EFFECTMEASURES

Overall rate and effect measures of aged 15-17 patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	4.764	1.284	0.205
-	95% CI	(1.447 , 15.684)	(1.063 , 1.552)	(0.061 , 0.348)
-	p-value	0.01	0.01	0.005
Gastrointestinal disorders	Effect measure	7.163	2.628	0.456
-	95% CI	(3.006 , 17.069)	(1.638 , 4.217)	(0.284 , 0.628)
-	p-value	0	0	0
Abdominal pain	Effect measure	8.161	5.189	0.335
-	95% CI	(2.562 , 25.998)	(1.923 , 14.003)	(0.183 , 0.488)
-	p-value	0	0.001	0
Vascular disorders	Effect measure	9.346	5.094	0.409
-	95% CI	(3.208 , 27.232)	(2.129 , 12.19)	(0.251 , 0.568)
-	p-value	0	0	0
Flushing	Effect measure	34.774	20.755	0.395
-	95% CI	(4.459 , 271.17)	(2.905 , 148.292)	(0.257 , 0.533)
-	p-value	0.001	0.003	0
General disorders and administration site conditions	Effect measure	0.191	0.283	-0.287
-	95% CI	(0.069 , 0.531)	(0.124 , 0.647)	(-0.447 , -0.126)
-	p-value	0.002	0.003	0
Pyrexia	Effect measure	0.157	0.189	-0.162
-	95% CI	(0.033 , 0.757)	(0.043 , 0.819)	(-0.284 , -0.04)
-	p-value	0.021	0.026	0.009
Respiratory, thoracic and mediastinal disorders	Effect measure	3.366	2.83	0.146
-	95% CI	(1.006 , 11.257)	(0.977 , 8.198)	(0.011 , 0.282)
-	p-value	0.049	0.055	0.034
Skin and subcutaneous tissue disorders	Effect measure	40.662	29.262	0.283
-	95% CI	(2.359 , 701.003)	(1.798 , 476.306)	(0.142 , 0.424)
-	p-value	0.011	0.018	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Age1517_AESI_NPERCENT

Overall rate and effect measures of aged 15-17 patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	DMF (N=53)	IFN B-1a (N=50)	Total (N=103)
Number of subjects with any AESI	49 (92)	36 (72)	85 (83)
Gastrointestinal disorders	39 (74)	14 (28)	53 (51)
Abdominal pain	22 (42)	4 (8)	26 (25)
Vascular disorders	27 (51)	5 (10)	32 (31)
Flushing	22 (42)	1 (2)	23 (22)
General disorders and administration site conditions	6 (11)	20 (40)	26 (25)
Pyrexia	2 (4)	10 (20)	12 (12)
Respiratory, thoracic and mediastinal disorders	12 (23)	4 (8)	16 (16)
Skin and subcutaneous tissue disorders	15 (28)	0	15 (15)

NOTE1: Only AESIs with significant statistical testing (p-value <0.5) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Female_AESI_EFFECTMEASURES

Overall rate and effect measures of female patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	10.5	1.38	0.264
-	95% CI	(2.234 , 49.354)	(1.131 , 1.684)	(0.121 , 0.408)
-	p-value	0.003	0.002	0
Gastrointestinal disorders	Effect measure	8.104	2.563	0.476
-	95% CI	(3.237 , 20.288)	(1.616 , 4.064)	(0.3 , 0.651)
-	p-value	0	0	0
Abdominal pain	Effect measure	6.985	4.232	0.351
-	95% CI	(2.367 , 20.616)	(1.755 , 10.206)	(0.186 , 0.516)
-	p-value	0	0.001	0
Vomiting	Effect measure	3.689	2.99	0.173
-	95% CI	(1.106 , 12.305)	(1.05 , 8.516)	(0.027 , 0.319)
-	p-value	0.034	0.04	0.02
Diarrhoea	Effect measure	11.25	9.2	0.178
-	95% CI	(1.379 , 91.804)	(1.225 , 69.093)	(0.06 , 0.297)
-	p-value	0.024	0.031	0.003
Vascular disorders	Effect measure	10.5	5.75	0.413
-	95% CI	(3.272 , 33.69)	(2.165 , 15.268)	(0.252 , 0.574)
-	p-value	0	0	0
Flushing	Effect measure	27.581	17.48	0.358
-	95% CI	(3.507 , 216.887)	(2.436 , 125.42)	(0.217 , 0.499)
-	p-value	0.002	0.004	0
General disorders and administration site conditions	Effect measure	0.231	0.339	-0.273
-	95% CI	(0.086 , 0.623)	(0.157 , 0.731)	(-0.445 , -0.101)
-	p-value	0.004	0.006	0.002
Pyrexia	Effect measure	0.133	0.167	-0.199
-	95% CI	(0.028 , 0.636)	(0.039 , 0.715)	(-0.334 , -0.064)
-	p-value	0.012	0.016	0.004
Respiratory, thoracic and mediastinal disorders	Effect measure	6.143	4.6	0.235
-	95% CI	(1.645 , 22.937)	(1.423 , 14.868)	(0.089 , 0.38)
-	p-value	0.007	0.011	0.002
Skin and subcutaneous tissue disorders	Effect measure	17.5	12.88	0.258
-	95% CI	(2.196 , 139.457)	(1.763 , 94.115)	(0.127 , 0.39)
-	p-value	0.007	0.012	0

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Female_AESI_NPERCENT

Overall rate and effect measures of female patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	DMF (N=50)	IFN B-1a (N=46)	Total (N=96)
Number of subjects with any AESI	48 (96)	32 (70)	80 (83)
Gastrointestinal disorders	39 (78)	14 (30)	53 (55)
Abdominal pain	23 (46)	5 (11)	28 (29)
Vomiting	13 (26)	4 (9)	17 (18)
Diarrhoea	10 (20)	1 (2)	11 (11)
Vascular disorders	25 (50)	4 (9)	29 (30)
Flushing	19 (38)	1 (2)	20 (21)
General disorders and administration site conditions	7 (14)	19 (41)	26 (27)
Pyrexia	2 (4)	11 (24)	13 (14)
Respiratory, thoracic and mediastinal disorders	15 (30)	3 (7)	18 (19)
Skin and subcutaneous tissue disorders	14 (28)	1 (2)	15 (16)

NOTE1: Only AESIs with significant statistical testing (p-value <0.5) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Male_AESI_EFFECTMEASURES

Overall rate and effect measures of male patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	1.9	1.086	0.071
-	95% CI	(0.281 , 12.869)	(0.847 , 1.393)	(-0.142 , 0.285)
-	p-value	0.511	0.517	0.511
Gastrointestinal disorders	Effect measure	4	2	0.333
-	95% CI	(1.052 , 15.207)	(0.974 , 4.109)	(0.037 , 0.63)
-	p-value	0.042	0.059	0.028
Abdominal pain	Effect measure	12.333	9.465	0.238
-	95% CI	(0.633 , 240.438)	(0.56 , 159.998)	(0.004 , 0.472)
-	p-value	0.097	0.119	0.045
Vomiting	Effect measure	2.833	2.571	0.087
-	95% CI	(0.268 , 29.955)	(0.292 , 22.608)	(-0.096 , 0.271)
-	p-value	0.387	0.394	0.351
Diarrhoea	Effect measure	1.176	1.143	0.024
-	95% CI	(0.226 , 6.127)	(0.294 , 4.444)	(-0.217 , 0.264)
-	p-value	0.847	0.847	0.846
Vascular disorders	Effect measure	12.75	7.714	0.373
-	95% CI	(1.421 , 114.4)	(1.078 , 55.191)	(0.136 , 0.61)
-	p-value	0.023	0.042	0.002
Flushing	Effect measure	28.12	16.349	0.429
-	95% CI	(1.497 , 528.181)	(1.019 , 262.229)	(0.165 , 0.692)
-	p-value	0.026	0.048	0
General disorders and administration site conditions	Effect measure	0.294	0.429	-0.254
-	95% CI	(0.07 , 1.232)	(0.154 , 1.191)	(-0.538 , 0.03)
-	p-value	0.094	0.104	0.08
Pyrexia	Effect measure	0.526	0.571	-0.071
-	95% CI	(0.078 , 3.565)	(0.107 , 3.05)	(-0.285 , 0.142)
-	p-value	0.511	0.513	0.511
Respiratory, thoracic and mediastinal disorders	Effect measure	2.5	2.143	0.127
-	95% CI	(0.422 , 14.828)	(0.471 , 9.741)	(-0.106 , 0.36)
-	p-value	0.313	0.324	0.285
Skin and subcutaneous tissue disorders	Effect measure	12.333	9.465	0.238
-	95% CI	(0.633 , 240.438)	(0.56 , 159.998)	(0.004 , 0.472)
-	p-value	0.097	0.119	0.045

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used
NOTE5: Only AESIs with significant statistical testing (p-value <0.05) in RR AND ≥10 events in either treatment arm are shown in this table

109MS306_table75_Nonsevere_Male_AESI_NPERCENT

Overall rate and effect measures of male patients with ≥1 non-severe AESI, related to CSR Table 75

AESI	DMF (N=21)	IFN B-1a (N=18)	Total (N=39)
Number of subjects with any AESI	19 (90)	15 (83)	34 (87)
Gastrointestinal disorders	14 (67)	6 (33)	20 (51)
Abdominal pain	5 (24)	0	5 (13)
Vomiting	3 (14)	1 (6)	4 (10)
Diarrhoea	4 (19)	3 (17)	7 (18)
Vascular disorders	9 (43)	1 (6)	10 (26)
Flushing	9 (43)	0	9 (23)
General disorders and administration site conditions	4 (19)	8 (44)	12 (31)
Pyrexia	2 (10)	3 (17)	5 (13)
Respiratory, thoracic and mediastinal disorders	5 (24)	2 (11)	7 (18)
Skin and subcutaneous tissue disorders	5 (24)	0	5 (13)

NOTE1: Only AESIs with significant statistical testing (p-value <0.5) in RR AND ≥10 events in either treatment arm are shown in this table

AESI severe

109MS306_table75_severe_AESI_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 severe AESI, related to CSR Table 75

	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hepatobiliary disorders	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hepatocellular injury	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_severe_AESI_NPERCENT

Overall rate and effect measures of patients with ≥1 severe AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with any AESI	0	1 (2)	1 (1)
Hepatobiliary disorders	0	1 (2)	1 (1)
Hepatocellular injury	0	1 (2)	1 (1)

AESI serious

109MS306_table75_serious_AESI_EFFECTMEASURES

Overall rate and effect measures of patients with ≥1 serious AESI, related to CSR Table 75

	Result	OR	RR	ARR
Number of subjects with any AESI	Effect measure	1.368	1.352	0.011
	95% CI	(0.221 , 8.458)	(0.233 , 7.836)	(-0.052 , 0.074)
	p-value	0.736	0.736	0.733
Gastrointestinal disorders	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Abdominal pain upper	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Hepatobiliary disorders	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hepatocellular injury	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Infections and infestations	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Pneumonia pneumococcal	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Skin and subcutaneous tissue disorders	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Rash pruritic	Effect measure	2.745	2.706	0.014
	95% CI	(0.11 , 68.583)	(0.112 , 65.264)	(-0.028 , 0.056)
	p-value	0.539	0.54	0.956
Vascular disorders	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96
Hypertension	Effect measure	0.296	0.301	-0.016
	95% CI	(0.012 , 7.397)	(0.012 , 7.252)	(-0.061 , 0.03)
	p-value	0.459	0.459	0.96

NOTE1: Odds ratios and Risk ratios are represented as DMF/IFN B-1a
NOTE2: Absolute Risk Reductions are represented as DMF - IFN B-1a
NOTE3: When there are zero cells, Odds ratios, Risk ratios, confidence limits and p-values are calculated using the modified Wald Method (Haldane (1955)). Otherwise standard Wald methods are used
NOTE4: When there are zero cells, Absolute risk reductions, confidence limits and p-values are calculated using the corrected Wald Method (Fleiss, Levin and Paik (2003)). Otherwise standard Wald methods are used

109MS306_table75_serious_AESI_NPERCENT

Overall rate and effect measures of patients with ≥1 serious AESI, related to CSR Table 75

AESI	DMF (N=71)	IFN B-1a (N=64)	Total (N=135)
Number of subjects with any AESI	3 (4)	2 (3)	5 (4)
Gastrointestinal disorders	1 (1)	0	1 (1)
Abdominal pain upper	1 (1)	0	1 (1)
Hepatobiliary disorders	0	1 (2)	1 (1)
Hepatocellular injury	0	1 (2)	1 (1)
Infections and infestations	1 (1)	0	1 (1)
Pneumonia pneumococcal	1 (1)	0	1 (1)
Skin and subcutaneous tissue disorders	1 (1)	0	1 (1)
Rash pruritic	1 (1)	0	1 (1)
Vascular disorders	0	1 (2)	1 (1)
Hypertension	0	1 (2)	1 (1)

Sub groups: interaction tests

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS (0/>0)	Baseline
Adjusted ARR	0.506	1.000	0.534	
EDSS01-Expanded Disability Score at Week 12	0.8462	0.5580	0.7240	
EDSS01-Expanded Disability Score at Week 24	0.9269	0.1812	0.1797	
EDSS01-Expanded Disability Score at Week 36	0.7457	0.6726	0.7933	
EDSS01-Expanded Disability Score at Week 48	0.9381	0.9277	0.2854	
EDSS01-Expanded Disability Score at Week 60	0.0905	IFN B-1a in 13-14=9 IFN B-1a in 15-17=38 DMF in 13-14=16 DMF in 15-17=46	0.0997	
EDSS01-Expanded Disability Score at Week 72	0.9780	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=45	0.6933	
EDSS01-Expanded Disability Score at Week 96	0.5436	IFN B-1a in 13-14=7 IFN B-1a in 15-17=32 DMF in 13-14=16 DMF in 15-17=38	0.6462	
EDSS01-Expanded Disability Score Change from Baseline at Week 12	0.6476	0.8437	0.4861	
EDSS01-Expanded Disability Score Change from Baseline at Week 24	0.8578	0.2848	0.0927	
EDSS01-Expanded Disability Score Change from Baseline at Week 36	0.9757	0.9084	0.6729	
EDSS01-Expanded Disability Score Change from Baseline at Week 48	0.2356	0.7812	0.1190	
EDSS01-Expanded Disability Score Change from Baseline at Week 60	0.2364	IFN B-1a in 13-14=9 IFN B-1a in 15-17=38 DMF in 13-14=16 DMF in 15-17=46	0.0218	
EDSS01-Expanded Disability Score Change from Baseline at Week 72	0.1733	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=45	0.7274	
EDSS01-Expanded Disability Score Change from Baseline at Week 96	0.6222	0.8241	0.5676	
Participant's Assessment General Fatigue Total Score at Week 24	0.4708	0.7371	0.8866	
Participant's Assessment General Fatigue Total Score at Week 48	0.9106	0.3929	0.6879	
Participant's Assessment General Fatigue Total Score at Week 72	0.6959	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=14 DMF in 15-17=45	0.5263	
Participant's Assessment General Fatigue Total Score at Week 96	0.6917	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=16 DMF in 15-17=38	0.3913	
Participant's Assessment Sleep/Rest Fatigue Total Score at Week 24	0.5442	0.3424	0.6591	
Participant's Assessment Sleep/Rest Fatigue Total Score at Week 48	0.7753	0.7984	0.0875	
Participant's Assessment Sleep/Rest Fatigue Total Score at Week 72	0.8343	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=14 DMF in 15-17=45	0.5190	

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS (0/>0)	Baseline
Participant's Assessment Sleep/Rest Fatigue Total Score at Week 96	0.8160	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=16 DMF in 15-17=38	0.6136	
Participant's Assessment Cognitive Fatigue Total Score at Week 24	0.9500	0.1844	0.3819	
Participant's Assessment Cognitive Fatigue Total Score at Week 48	0.8944	0.5860	0.2024	
Participant's Assessment Cognitive Fatigue Total Score at Week 72	0.4866	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=14 DMF in 15-17=45	0.7272	
Participant's Assessment Cognitive Fatigue Total Score at Week 96	0.7710	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=16 DMF in 15-17=38	0.3763	
Participant's Assessment General Fatigue Total Score Change from Baseline at Week 24	0.9827	0.0916	0.6273	
Participant's Assessment General Fatigue Total Score Change from Baseline at Week 48	0.4152	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.2288	
Participant's Assessment General Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.0703	
Participant's Assessment General Fatigue Total Score Change from Baseline at Week 96	0.1369	0.7525	0.6271	
Participant's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 24	0.2237	0.2514	0.5510	
Participant's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 48	0.7413	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.8639	
Participant's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.6340	
Participant's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 96	0.8583	0.8649	0.6895	
Participant's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 24	0.6434	0.2887	0.3262	
Participant's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 48	0.9783	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.3344	
Participant's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.1240	
Participant's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 96	0.4252	0.8693	0.2350	
Participant's Assessment General Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=7 Events in DMF in 0=0	
Participant's Assessment General Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=5	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=9 Events in DMF in 0=1	
Participant's Assessment General Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=5	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=0	

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment General Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=4	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=2 Events in DMF in 15-17=5	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=6 Events in DMF in 0=1
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=1 Events in DMF in >0=4 Events in DMF in 0=3
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=2
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=0 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=5 Events in DMF in 0=2
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=1
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=3 Events in DMF in F=8 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=9	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=9 Events in DMF in 0=1
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=3 Events in IFN B-1a in M=3 Events in DMF in F=7 Events in DMF in M=4	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=9	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=5 Events in DMF in >0=9 Events in DMF in 0=2
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=2 Events in IFN B-1a in M=4 Events in DMF in F=8 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=9	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=9 Events in DMF in 0=2
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=2 Events in DMF in F=7 Events in DMF in M=4	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=4 Events in DMF in 15-17=7	0.1449
Participant's Assessment General Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=3 Events in DMF in F=9 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=3 Events in DMF in 15-17=7	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=4 Events in DMF in >0=7 Events in DMF in 0=3
Participant's Assessment General Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=3 Events in DMF in F=8 Events in DMF in M=2	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=3 Events in DMF in >0=7 Events in DMF in 0=3
Participant's Assessment General Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=3	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=4 Events in DMF in >0=5 Events in DMF in 0=6
Participant's Assessment General Fatigue Total Score MCID Decrease 15% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	IFN B-1a in 13-14=7 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=32	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=5 Events in DMF in >0=9 Events in DMF in 0=4
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=4 Events in DMF in F=6 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=3 Events in DMF in 15-17=5	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=4 Events in DMF in >0=4 Events in DMF in 0=4
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=5	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=2
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=2	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=7 Events in DMF in 0=3
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=8 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=7	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=7 Events in DMF in 0=2
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=3 Events in DMF in >0=4 Events in DMF in 0=0

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=3 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=5 Events in DMF in >0=2 Events in DMF in 0=1
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=3
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=2 Events in DMF in 15-17=9	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=3 Events in DMF in >0=7 Events in DMF in 0=4
Participant's Assessment General Fatigue Total Score MCID Increase 4.4% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=4 Events in DMF in F=9 Events in DMF in M=5	0.2650	0.3777
Participant's Assessment General Fatigue Total Score MCID Increase 4.4% Week 48	0.2086	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.4102
Participant's Assessment General Fatigue Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.2668
Participant's Assessment General Fatigue Total Score MCID Increase 4.4% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=4 Events in DMF in M=7	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=3 Events in DMF in 15-17=8	0.3049
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.4% Week 24	0.1567	0.1707	0.1005
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.4% Week 48	0.5023	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.9351
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.2500
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.4% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	IFN B-1a in 13-14=7 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=32	0.8327
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 4.4% Week 24	0.8742	0.8958	0.5434
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 4.4% Week 48	0.6335	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.1111
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.1145
Participant's Assessment Cognitive Fatigue Total Score MCID Increase 4.4% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=4 Events in DMF in F=8 Events in DMF in M=5	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=5 Events in DMF in 15-17=8	0.0255
Participant's Assessment General Fatigue Total Score MCID Decrease 4.4% Week 24	0.8271	0.2937	0.5654
Participant's Assessment General Fatigue Total Score MCID Decrease 4.4% Week 48	0.7141	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.9094
Participant's Assessment General Fatigue Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=7 Events in DMF in >0=9 Events in DMF in 0=9

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment General Fatigue Total Score MCID Decrease 4.4% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	IFN B-1a in 13-14=7 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=32	0.2161
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.4% Week 24	0.0721	0.3909	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=6 Events in DMF in >0=8 Events in DMF in 0=7
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.4% Week 48	0.3747	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.1657
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.8569
Participant's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.4% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	IFN B-1a in 13-14=7 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=32	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=4 Events in DMF in >0=9 Events in DMF in 0=4
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 4.4% Week 24	0.6971	0.5714	0.8773
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 4.4% Week 48	0.9682	IFN B-1a in 13-14=10 IFN B-1a in 15-17=33 DMF in 13-14=8 DMF in 15-17=41	0.7008
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=26 IFN B-1a in M=9 DMF in F=33 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=38	0.4118
Participant's Assessment Cognitive Fatigue Total Score MCID Decrease 4.4% Week 96	IFN B-1a in F=25 IFN B-1a in M=9 DMF in F=29 DMF in M=13	IFN B-1a in 13-14=7 IFN B-1a in 15-17=27 DMF in 13-14=10 DMF in 15-17=32	0.3637
Parent's Assessment General Fatigue Total Score at Week 24	0.4927	0.8551	0.7248
Parent's Assessment General Fatigue Total Score at Week 48	0.5438	0.4312	0.4488
Parent's Assessment General Fatigue Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=29 DMF in M=14	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=14 DMF in 15-17=29	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=30 DMF in 0=13
Parent's Assessment General Fatigue Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=9	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=13 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=17 DMF in 0=11
Parent's Assessment Sleep/Rest Fatigue Total Score at Week 24	0.9202	0.9661	0.8232
Parent's Assessment Sleep/Rest Fatigue Total Score at Week 48	0.9016	0.2458	0.2438
Parent's Assessment Sleep/Rest Fatigue Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=28 DMF in M=14	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=14 DMF in 15-17=28	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=30 DMF in 0=12
Parent's Assessment Sleep/Rest Fatigue Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=9	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=13 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=17 DMF in 0=11
Parent's Assessment Cognitive Fatigue Total Score at Week 24	0.6415	0.5942	0.9483
Parent's Assessment Cognitive Fatigue Total Score at Week 48	0.9278	0.5792	0.7100
Parent's Assessment Cognitive Fatigue Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=29 DMF in M=14	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=14 DMF in 15-17=29	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=30 DMF in 0=13
Parent's Assessment Cognitive Fatigue Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=9	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=13 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=17 DMF in 0=11

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment General Fatigue Total Score Change from Baseline at Week 24	0.6546	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.1799
Parent's Assessment General Fatigue Total Score Change from Baseline at Week 48	IFN B-1a in F=27 IFN B-1a in M=9 DMF in F=23 DMF in M=12	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment General Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=21 IFN B-1a in M=4 DMF in F=19 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	IFN B-1a in >0=17 IFN B-1a in 0=8 DMF in >0=23 DMF in 0=8
Parent's Assessment General Fatigue Total Score Change from Baseline at Week 96	0.4016	IFN B-1a in 13-14=6 IFN B-1a in 15-17=13 DMF in 13-14=8 DMF in 15-17=12	0.7458
Parent's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 24	0.4995	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.7583
Parent's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 48	IFN B-1a in F=27 IFN B-1a in M=9 DMF in F=23 DMF in M=12	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=21 IFN B-1a in M=4 DMF in F=19 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	IFN B-1a in >0=17 IFN B-1a in 0=8 DMF in >0=23 DMF in 0=8
Parent's Assessment Sleep/Rest Fatigue Total Score Change from Baseline at Week 96	0.0690	IFN B-1a in 13-14=6 IFN B-1a in 15-17=13 DMF in 13-14=8 DMF in 15-17=12	0.6591
Parent's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 24	0.7976	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.5571
Parent's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 48	IFN B-1a in F=27 IFN B-1a in M=9 DMF in F=23 DMF in M=12	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 72	IFN B-1a in F=21 IFN B-1a in M=4 DMF in F=19 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	IFN B-1a in >0=17 IFN B-1a in 0=8 DMF in >0=23 DMF in 0=8
Parent's Assessment Cognitive Fatigue Total Score Change from Baseline at Week 96	0.0578	IFN B-1a in 13-14=6 IFN B-1a in 15-17=13 DMF in 13-14=8 DMF in 15-17=12	0.2197
Parent's Assessment General Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=6	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=8	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=0 Events in DMF in >0=6 Events in DMF in 0=3
Parent's Assessment General Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=6	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=8	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=1 Events in DMF in >0=6 Events in DMF in 0=3
Parent's Assessment General Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=3 Events in IFN B-1a in M=0 Events in DMF in F=5 Events in DMF in M=5	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=1 Events in DMF in 15-17=9	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=1 Events in DMF in >0=8 Events in DMF in 0=2
Parent's Assessment General Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=2 Events in DMF in M=0	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=1	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=1 Events in DMF in >0=2 Events in DMF in 0=0
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=5 Events in IFN B-1a in M=4 Events in DMF in F=4 Events in DMF in M=4	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=4 Events in DMF in >0=6 Events in DMF in 0=2
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=4	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=1 Events in DMF in >0=5 Events in DMF in 0=2

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=2 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=1
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=3 Events in IFN B-1a in M=4 Events in DMF in F=4 Events in DMF in M=6	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=8	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=7 Events in DMF in 0=3
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=4 Events in DMF in M=4	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=3
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=3	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=2
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=1 Events in IFN B-1a in M=2 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=3 Events in DMF in >0=1 Events in DMF in 0=0
Parent's Assessment General Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=9 Events in IFN B-1a in M=2 Events in DMF in F=7 Events in DMF in M=2	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=3 Events in DMF in 15-17=6	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=5 Events in DMF in >0=8 Events in DMF in 0=1
Parent's Assessment General Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=9 Events in IFN B-1a in M=2 Events in DMF in F=4 Events in DMF in M=0	Events in IFN B-1a in 13-14=5 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=4 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment General Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=8 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=4 Events in DMF in >0=4 Events in DMF in 0=1
Parent's Assessment General Fatigue Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=0 Events in DMF in F=2 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=3 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=8	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=4 Events in DMF in >0=8 Events in DMF in 0=1
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=3 Events in DMF in F=3 Events in DMF in M=3	Events in IFN B-1a in 13-14=5 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=6 Events in DMF in 0=0
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=5	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=6 Events in DMF in 0=0
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=1
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=3 Events in DMF in F=4 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=3 Events in DMF in >0=4 Events in DMF in 0=0
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=2	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=0
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=6 Events in IFN B-1a in M=0 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=0
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=0 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=1 Events in DMF in 0=0

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment General Fatigue Total Score MCID Increase 4.5% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=3 Events in DMF in F=4 Events in DMF in M=6	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=5 Events in DMF in >0=7 Events in DMF in 0=3
Parent's Assessment General Fatigue Total Score MCID Increase 4.5% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=8 Events in DMF in M=7	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment General Fatigue Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=0 Events in DMF in F=5 Events in DMF in M=6	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=2 Events in DMF in 15-17=9	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=1 Events in DMF in >0=9 Events in DMF in 0=2
Parent's Assessment General Fatigue Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=1	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=0
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.5% Week 24	0.1625	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=9 Events in DMF in >0=8 Events in DMF in 0=2
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.5% Week 48	Events in IFN B-1a in F=9 Events in IFN B-1a in M=4 Events in DMF in F=7 Events in DMF in M=4	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=6 Events in DMF in >0=8 Events in DMF in 0=3
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=7 Events in DMF in M=4	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=9 Events in DMF in 0=2
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=3 Events in DMF in F=3 Events in DMF in M=2	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=4 Events in DMF in >0=3 Events in DMF in 0=2
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 4.5% Week 24	Events in IFN B-1a in F=6 Events in IFN B-1a in M=4 Events in DMF in F=6 Events in DMF in M=6	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=3 Events in DMF in 15-17=9	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=2 Events in DMF in >0=9 Events in DMF in 0=3
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 4.5% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=4 Events in DMF in F=9 Events in DMF in M=4	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=4	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=2 Events in DMF in 15-17=5	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=2
Parent's Assessment Cognitive Fatigue Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=2 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=3 Events in DMF in >0=5 Events in DMF in 0=0
Parent's Assessment General Fatigue Total Score MCID Decrease 4.5% Week 24	0.5924	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.1533
Parent's Assessment General Fatigue Total Score MCID Decrease 4.5% Week 48	IFN B-1a in F=27 IFN B-1a in M=9 DMF in F=23 DMF in M=12	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	IFN B-1a in >0=22 IFN B-1a in 0=14 DMF in >0=26 DMF in 0=9
Parent's Assessment General Fatigue Total Score MCID Decrease 4.5% Week 72	IFN B-1a in F=21 IFN B-1a in M=4 DMF in F=19 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=4 Events in DMF in >0=9 Events in DMF in 0=3
Parent's Assessment General Fatigue Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=8 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=6 Events in DMF in 0=2
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.5% Week 24	0.4114	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.5755
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.5% Week 48	Events in IFN B-1a in F=9 Events in IFN B-1a in M=3 Events in DMF in F=5 Events in DMF in M=6	IFN B-1a in 13-14=9 IFN B-1a in 15-17=27 DMF in 13-14=6 DMF in 15-17=29	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=4 Events in DMF in >0=8 Events in DMF in 0=3

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.5% Week 72	Events in IFN B-1a in F=8 Events in IFN B-1a in M=1 Events in DMF in F=8 Events in DMF in M=5	IFN B-1a in 13-14=7 IFN B-1a in 15-17=18 DMF in 13-14=8 DMF in 15-17=23	IFN B-1a in >0=17 IFN B-1a in 0=8 DMF in >0=23 DMF in 0=8
Parent's Assessment Sleep/Rest Fatigue Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=8 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=6 Events in DMF in 0=2
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 4.5% Week 24	0.6334	IFN B-1a in 13-14=11 IFN B-1a in 15-17=38 DMF in 13-14=8 DMF in 15-17=32	0.4594
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 4.5% Week 48	IFN B-1a in F=27 IFN B-1a in M=9 DMF in F=23 DMF in M=12	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=1
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 4.5% Week 72	Events in IFN B-1a in F=9 Events in IFN B-1a in M=0 Events in DMF in F=5 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=7 Events in DMF in 0=0
Parent's Assessment Cognitive Fatigue Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=8 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=0
Participant's Assessment Feelings Total Score at Week 24	0.3347	0.4407	0.5747
Participant's Assessment Feelings Total Score at Week 48	0.7567	0.6629	0.8100
Participant's Assessment Feelings Total Score at Week 72	0.9774	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=44	0.2498
Participant's Assessment Feelings Total Score at Week 96	0.3742	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=15 DMF in 15-17=39	0.6919
Participant's Assessment Get Along With Others Total Score at Week 24	0.4850	0.9377	0.5146
Participant's Assessment Get Along With Others Total Score at Week 48	0.2204	0.1842	0.5010
Participant's Assessment Get Along With Others Total Score at Week 72	0.2637	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=44	0.6283
Participant's Assessment Get Along With Others Total Score at Week 96	0.6496	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=15 DMF in 15-17=39	0.6777
Participant's Assessment Health and Activities Total Score at Week 24	0.8282	0.8583	0.5954
Participant's Assessment Health and Activities Total Score at Week 48	0.8629	0.3221	0.8688
Participant's Assessment Health and Activities Total Score at Week 72	0.9783	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=44	0.3180
Participant's Assessment Health and Activities Total Score at Week 96	0.4171	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=15 DMF in 15-17=39	0.7518
Participant's Assessment School Total Score at Week 24	0.7425	0.1142	0.3841
Participant's Assessment School Total Score at Week 48	0.7972	0.9498	0.2939

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS (0/>0) Baseline
Participant's Assessment School Total Score at Week 72	0.4185	IFN B-1a in 13-14=8 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=44	0.9717
Participant's Assessment School Total Score at Week 96	0.9848	IFN B-1a in 13-14=7 IFN B-1a in 15-17=31 DMF in 13-14=15 DMF in 15-17=39	0.2860
Participant's Assessment Feelings Total Score Change from Baseline at Week 24	0.1057	0.2254	0.2411
Participant's Assessment Feelings Total Score Change from Baseline at Week 48	0.9001	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.8815
Participant's Assessment Feelings Total Score Change from Baseline at Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.2167
Participant's Assessment Feelings Total Score Change from Baseline at Week 96	0.2510	0.8390	0.3412
Participant's Assessment Get Along With Others Total Score Change from Baseline at Week 24	0.9688	0.7036	0.2155
Participant's Assessment Get Along With Others Total Score Change from Baseline at Week 48	0.9126	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.0684
Participant's Assessment Get Along With Others Total Score Change from Baseline at Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.0380
Participant's Assessment Get Along With Others Total Score Change from Baseline at Week 96	0.7756	0.9791	0.1206
Participant's Assessment Health and Activities Total Score Change from Baseline at Week 24	0.5025	0.2828	0.0349
Participant's Assessment Health and Activities Total Score Change from Baseline at Week 48	0.9597	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	2e-04
Participant's Assessment Health and Activities Total Score Change from Baseline at Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.0042
Participant's Assessment Health and Activities Total Score Change from Baseline at Week 96	0.7050	0.3515	0.0467
Participant's Assessment School Total Score Change from Baseline at Week 24	0.2646	0.1292	0.4966
Participant's Assessment School Total Score Change from Baseline at Week 48	0.3371	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.7533
Participant's Assessment School Total Score Change from Baseline at Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.2492
Participant's Assessment School Total Score Change from Baseline at Week 96	0.9843	0.9874	0.2081
Participant's Assessment Feelings Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=4 Events in DMF in F=7 Events in DMF in M=2	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=0 Events in DMF in 15-17=9	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=4 Events in DMF in >0=8 Events in DMF in 0=1

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment Feelings Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=4	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.8897
Participant's Assessment Feelings Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=6 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=9	0.1296
Participant's Assessment Feelings Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=4 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=3 Events in DMF in 15-17=3	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=4 Events in DMF in >0=5 Events in DMF in 0=1
Participant's Assessment Get Along With Others Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=4 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=1
Participant's Assessment Get Along With Others Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=1 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=0
Participant's Assessment Get Along With Others Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=1 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=0
Participant's Assessment Get Along With Others Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=1 Events in DMF in 0=0
Participant's Assessment Health and Activities Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=9	0.0180
Participant's Assessment Health and Activities Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=4 Events in IFN B-1a in M=3 Events in DMF in F=2 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=5	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=7 Events in DMF in >0=5 Events in DMF in 0=0
Participant's Assessment Health and Activities Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=5 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=5	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=5 Events in DMF in >0=6 Events in DMF in 0=0
Participant's Assessment Health and Activities Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=1	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=3 Events in DMF in >0=2 Events in DMF in 0=0
Participant's Assessment School Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=8	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=7 Events in DMF in 0=2
Participant's Assessment School Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=6 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=8	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=0
Participant's Assessment School Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=1 Events in DMF in >0=8 Events in DMF in 0=0
Participant's Assessment School Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=0 Events in DMF in F=5 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=3 Events in DMF in 15-17=4	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=7 Events in DMF in 0=0
Participant's Assessment Feelings Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=7 Events in IFN B-1a in M=6 Events in DMF in F=4 Events in DMF in M=0	0.9936	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=7 Events in DMF in >0=1 Events in DMF in 0=3
Participant's Assessment Feelings Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=9 Events in IFN B-1a in M=3 Events in DMF in F=5 Events in DMF in M=2	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=6 Events in DMF in >0=5 Events in DMF in 0=2
Participant's Assessment Feelings Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=6	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=1 Events in DMF in >0=5 Events in DMF in 0=3

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment Feelings Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=4	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=2 Events in DMF in 15-17=6	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=1 Events in DMF in >0=5 Events in DMF in 0=3
Participant's Assessment Get Along With Others Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=2 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=1 Events in DMF in >0=3 Events in DMF in 0=3
Participant's Assessment Get Along With Others Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=5	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=1 Events in DMF in >0=3 Events in DMF in 0=2
Participant's Assessment Get Along With Others Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=0 Events in DMF in >0=2 Events in DMF in 0=1
Participant's Assessment Get Along With Others Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=1 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=0 Events in DMF in >0=2 Events in DMF in 0=3
Participant's Assessment Health and Activities Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=5 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=1 Events in DMF in >0=2 Events in DMF in 0=4
Participant's Assessment Health and Activities Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=4 Events in DMF in 0=2
Participant's Assessment Health and Activities Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=0	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=4
Participant's Assessment Health and Activities Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=0 Events in DMF in F=8 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=3 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=0 Events in DMF in >0=5 Events in DMF in 0=4
Participant's Assessment School Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=7 Events in IFN B-1a in M=3 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=7 Events in DMF in >0=4 Events in DMF in 0=2
Participant's Assessment School Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=3 Events in DMF in F=4 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=3 Events in DMF in 15-17=1	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=5 Events in DMF in >0=3 Events in DMF in 0=1
Participant's Assessment School Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=7	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=3 Events in DMF in >0=4 Events in DMF in 0=4
Participant's Assessment School Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=7 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=3 Events in DMF in 15-17=5	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=3
Participant's Assessment Feelings Total Score MCID Increase 4.4% Week 24	0.2882	0.4803	0.8933
Participant's Assessment Feelings Total Score MCID Increase 4.4% Week 48	0.4908	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.3010
Participant's Assessment Feelings Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.6902
Participant's Assessment Feelings Total Score MCID Increase 4.4% Week 96	Events in IFN B-1a in F=8 Events in IFN B-1a in M=4 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=5 Events in DMF in 15-17=4	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=4 Events in DMF in >0=7 Events in DMF in 0=2
Participant's Assessment Get Along With Others Total Score MCID Increase 4.4% Week 24	0.6641	0.1359	0.1010

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment Get Along With Others Total Score MCID Increase 4.4% Week 48	Events in IFN B-1a in F=9 Events in IFN B-1a in M=4 Events in DMF in F=9 Events in DMF in M=3	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.1878
Participant's Assessment Get Along With Others Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=6 Events in DMF in >0=8 Events in DMF in 0=1
Participant's Assessment Get Along With Others Total Score MCID Increase 4.4% Week 96	IFN B-1a in F=16 IFN B-1a in M=6 DMF in F=16 DMF in M=8	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=6 Events in DMF in >0=4 Events in DMF in 0=0
Participant's Assessment Health and Activities Total Score MCID Increase 4.4% Week 24	0.8845	0.2279	0.0348
Participant's Assessment Health and Activities Total Score MCID Increase 4.4% Week 48	0.9179	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	4e-04
Participant's Assessment Health and Activities Total Score MCID Increase 4.4% Week 72	Events in IFN B-1a in F=6 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=4	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=3 Events in DMF in 15-17=9	0.0081
Participant's Assessment Health and Activities Total Score MCID Increase 4.4% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=4 Events in DMF in 15-17=2	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=5 Events in DMF in >0=5 Events in DMF in 0=1
Participant's Assessment School Total Score MCID Increase 4.4% Week 24	0.2488	0.2307	0.3967
Participant's Assessment School Total Score MCID Increase 4.4% Week 48	0.0912	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.2390
Participant's Assessment School Total Score MCID Increase 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.1121
Participant's Assessment School Total Score MCID Increase 4.4% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=4 Events in DMF in F=7 Events in DMF in M=5	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=5 Events in DMF in 15-17=7	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=4 Events in DMF in >0=9 Events in DMF in 0=3
Participant's Assessment Feelings Total Score MCID Decrease 4.4% Week 24	0.0132	0.8234	0.6127
Participant's Assessment Feelings Total Score MCID Decrease 4.4% Week 48	0.1789	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	0.6049
Participant's Assessment Feelings Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	0.2271
Participant's Assessment Feelings Total Score MCID Decrease 4.4% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=9 Events in DMF in M=5	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=5 Events in DMF in 15-17=9	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=6
Participant's Assessment Get Along With Others Total Score MCID Decrease 4.4% Week 24	0.9269	0.8286	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=7 Events in DMF in >0=5 Events in DMF in 0=6
Participant's Assessment Get Along With Others Total Score MCID Decrease 4.4% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=4 Events in DMF in 15-17=6	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=3 Events in DMF in >0=6 Events in DMF in 0=4
Participant's Assessment Get Along With Others Total Score MCID Decrease 4.4% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=2 Events in DMF in F=8 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=9	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=5

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Participant's Assessment Get Along With Others Total Score MCID Decrease 4.4% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=3 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=0 Events in DMF in >0=6 Events in DMF in 0=3
Participant's Assessment Health and Activities Total Score MCID Decrease 4.4% Week 24	0.3307	0.1534	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=6 Events in DMF in >0=7 Events in DMF in 0=6
Participant's Assessment Health and Activities Total Score MCID Decrease 4.4% Week 48	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=8 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=3 Events in DMF in 15-17=7	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=5
Participant's Assessment Health and Activities Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=2 Events in DMF in >0=9 Events in DMF in 0=6
Participant's Assessment Health and Activities Total Score MCID Decrease 4.4% Week 96	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=9 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=4 Events in DMF in 15-17=8	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=7 Events in DMF in 0=5
Participant's Assessment School Total Score MCID Decrease 4.4% Week 24	0.2792	0.2868	0.7856
Participant's Assessment School Total Score MCID Decrease 4.4% Week 48	0.1242	IFN B-1a in 13-14=9 IFN B-1a in 15-17=32 DMF in 13-14=9 DMF in 15-17=31	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=8 Events in DMF in >0=9 Events in DMF in 0=5
Participant's Assessment School Total Score MCID Decrease 4.4% Week 72	IFN B-1a in F=22 IFN B-1a in M=8 DMF in F=24 DMF in M=12	IFN B-1a in 13-14=7 IFN B-1a in 15-17=23 DMF in 13-14=10 DMF in 15-17=26	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=8 Events in DMF in 0=9
Participant's Assessment School Total Score MCID Decrease 4.4% Week 96	Events in IFN B-1a in F=8 Events in IFN B-1a in M=2 Events in DMF in F=9 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=5 Events in DMF in 15-17=7	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=4 Events in DMF in >0=6 Events in DMF in 0=6
Parent's Assessment Emotional Functioning Total Score at Week 24	0.1844	0.9772	0.8771
Parent's Assessment Emotional Functioning Total Score at Week 48	0.9688	0.7809	0.5836
Parent's Assessment Emotional Functioning Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=31 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=15 DMF in 15-17=31	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=32 DMF in 0=14
Parent's Assessment Emotional Functioning Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=14 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=18 DMF in 0=11
Parent's Assessment Physical Functioning Total Score at Week 24	0.2909	0.6975	0.7639
Parent's Assessment Physical Functioning Total Score at Week 48	0.7740	0.9193	0.8552
Parent's Assessment Physical Functioning Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=31 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=15 DMF in 15-17=31	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=32 DMF in 0=14
Parent's Assessment Physical Functioning Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=14 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=18 DMF in 0=11
Parent's Assessment Social Functioning Total Score at Week 24	0.9801	0.6290	0.7709
Parent's Assessment Social Functioning Total Score at Week 48	0.5256	0.9496	0.3488
Parent's Assessment Social Functioning Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=31 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=15 DMF in 15-17=31	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=32 DMF in 0=14

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Social Functioning Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=14 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=18 DMF in 0=11
Parent's Assessment Work/Study/School Functioning Total Score at Week 24	0.4547	0.0919	0.9067
Parent's Assessment Work/Study/School Functioning Total Score at Week 48	0.5671	0.3959	0.9076
Parent's Assessment Work/Study/School Functioning Total Score at Week 72	IFN B-1a in F=22 IFN B-1a in M=7 DMF in F=31 DMF in M=15	IFN B-1a in 13-14=8 IFN B-1a in 15-17=21 DMF in 13-14=15 DMF in 15-17=31	IFN B-1a in >0=20 IFN B-1a in 0=9 DMF in >0=32 DMF in 0=14
Parent's Assessment Work/Study/School Functioning Total Score at Week 96	IFN B-1a in F=17 IFN B-1a in M=5 DMF in F=19 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=15 DMF in 13-14=14 DMF in 15-17=15	IFN B-1a in >0=14 IFN B-1a in 0=8 DMF in >0=18 DMF in 0=11
Parent's Assessment Emotional Functioning Total Score Change from Baseline at Week 24	0.4020	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Emotional Functioning Total Score Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Emotional Functioning Total Score Change from Baseline at Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Emotional Functioning Total Score Change from Baseline at Week 96	0.0235	0.7824	0.5041
Parent's Assessment Physical Functioning Total Score Change from Baseline at Week 24	0.0136	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Physical Functioning Total Score Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Physical Functioning Total Score Change from Baseline at Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Physical Functioning Total Score Change from Baseline at Week 96	0.8196	0.6229	0.3497
Parent's Assessment Social Functioning Total Score Change from Baseline at Week 24	0.5470	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Social Functioning Total Score Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Social Functioning Total Score Change from Baseline at Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Social Functioning Total Score Change from Baseline at Week 96	0.3744	0.9897	0.6568
Parent's Assessment Work/Study/School Functioning Total Score Change from Baseline at Week 24	0.4161	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Work/Study/School Functioning Total Score Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Work/Study/School Functioning Total Score Change from Baseline at Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Work/Study/School Functioning Total Score Change from Baseline at Week 96	0.1975	0.8318	0.2397
Parent's Assessment Emotional Functioning Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=6 Events in IFN B-1a in M=3 Events in DMF in F=3 Events in DMF in M=5	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=0 Events in DMF in 15-17=8	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=4 Events in DMF in >0=6 Events in DMF in 0=2
Parent's Assessment Emotional Functioning Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=2 Events in IFN B-1a in M=3 Events in DMF in F=7 Events in DMF in M=4	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=9 Events in DMF in 0=2
Parent's Assessment Emotional Functioning Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=2 Events in IFN B-1a in M=2 Events in DMF in F=5 Events in DMF in M=4	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=2 Events in DMF in 15-17=7	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=1 Events in DMF in >0=6 Events in DMF in 0=3
Parent's Assessment Emotional Functioning Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=3 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=3 Events in DMF in >0=1 Events in DMF in 0=0
Parent's Assessment Physical Functioning Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=1
Parent's Assessment Physical Functioning Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=4 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=0 Events in DMF in 15-17=6	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=6 Events in DMF in 0=0
Parent's Assessment Physical Functioning Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=0 Events in DMF in 15-17=2	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=3 Events in DMF in >0=2 Events in DMF in 0=0
Parent's Assessment Physical Functioning Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=1 Events in DMF in 0=0
Parent's Assessment Social Functioning Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=3 Events in IFN B-1a in M=3 Events in DMF in F=5 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=7 Events in DMF in 0=0
Parent's Assessment Social Functioning Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=1 Events in IFN B-1a in M=3 Events in DMF in F=5 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=6 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=1 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=1 Events in DMF in 15-17=5	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=1 Events in DMF in >0=5 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=1 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=2 Events in DMF in >0=3 Events in DMF in 0=0
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 15% Week 24	Events in IFN B-1a in F=3 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=4	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=2
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 15% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=2 Events in DMF in F=7 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=8	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=9 Events in DMF in 0=1
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 15% Week 72	Events in IFN B-1a in F=2 Events in IFN B-1a in M=1 Events in DMF in F=7 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=1 Events in DMF in 15-17=8	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=1
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 15% Week 96	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=4 Events in DMF in 0=0

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Emotional Functioning Total Score MCID Decrease 15% Week 24	0.3719	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=7 Events in DMF in >0=6 Events in DMF in 0=2
Parent's Assessment Emotional Functioning Total Score MCID Decrease 15% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	Events in IFN B-1a in 13-14=5 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=5 Events in DMF in >0=4 Events in DMF in 0=1
Parent's Assessment Emotional Functioning Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=5 Events in DMF in 0=0
Parent's Assessment Emotional Functioning Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=0 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=4 Events in DMF in >0=3 Events in DMF in 0=0
Parent's Assessment Physical Functioning Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=4 Events in IFN B-1a in M=4 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=1
Parent's Assessment Physical Functioning Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=6 Events in IFN B-1a in M=5 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=2
Parent's Assessment Physical Functioning Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=1 Events in DMF in 15-17=6	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=5 Events in DMF in 0=2
Parent's Assessment Physical Functioning Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=1 Events in DMF in >0=2 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Decrease 15% Week 24	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=2
Parent's Assessment Social Functioning Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=4 Events in IFN B-1a in M=3 Events in DMF in F=2 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=2 Events in DMF in 0=2
Parent's Assessment Social Functioning Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=8 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=2 Events in DMF in >0=1 Events in DMF in 0=0
Parent's Assessment Social Functioning Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=1
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 15% Week 24	0.4032	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=5 Events in DMF in >0=4 Events in DMF in 0=3
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=3 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=3 Events in DMF in >0=4 Events in DMF in 0=0
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 15% Week 72	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=3 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=5 Events in DMF in 0=2
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=0 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=0	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=0 Events in DMF in 0=0
Parent's Assessment Emotional Functioning Total Score MCID Increase 4.5% Week 24	0.8526	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Emotional Functioning Total Score MCID Increase 4.5% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Emotional Functioning Total Score MCID Increase 4.5% Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Emotional Functioning Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=4 Events in DMF in F=4 Events in DMF in M=0	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=0 Events in DMF in 15-17=4	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment Physical Functioning Total Score MCID Increase 4.5% Week 24	Events in IFN B-1a in F=9 Events in IFN B-1a in M=2 Events in DMF in F=7 Events in DMF in M=5	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=3 Events in DMF in 15-17=9	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Physical Functioning Total Score MCID Increase 4.5% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=2 Events in DMF in F=9 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=3 Events in DMF in 15-17=9	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Physical Functioning Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=8 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=3 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment Physical Functioning Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=1	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=3 Events in DMF in >0=2 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Increase 4.5% Week 24	Events in IFN B-1a in F=8 Events in IFN B-1a in M=5 Events in DMF in F=7 Events in DMF in M=3	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Social Functioning Total Score MCID Increase 4.5% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=3 Events in DMF in F=7 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=2 Events in DMF in 15-17=8	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=7 Events in DMF in >0=9 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=4 Events in IFN B-1a in M=2 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=3 Events in DMF in 15-17=6	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=3 Events in DMF in >0=8 Events in DMF in 0=1
Parent's Assessment Social Functioning Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=5 Events in IFN B-1a in M=2 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=5 Events in DMF in >0=3 Events in DMF in 0=1
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 4.5% Week 24	0.4951	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 4.5% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 4.5% Week 72	Events in IFN B-1a in F=5 Events in IFN B-1a in M=3 Events in DMF in F=9 Events in DMF in M=3	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Work/Study/School Functioning Total Score MCID Increase 4.5% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=3 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=5 Events in DMF in 15-17=4	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=4 Events in DMF in >0=7 Events in DMF in 0=2
Parent's Assessment Emotional Functioning Total Score MCID Decrease 4.5% Week 24	0.2352	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Emotional Functioning Total Score MCID Decrease 4.5% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Emotional Functioning Total Score MCID Decrease 4.5% Week 72	Events in IFN B-1a in F=7 Events in IFN B-1a in M=4 Events in DMF in F=8 Events in DMF in M=3	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=3 Events in DMF in 15-17=8	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=5 Events in DMF in >0=9 Events in DMF in 0=2
Parent's Assessment Emotional Functioning Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=9 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=3	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=3 Events in DMF in 15-17=4	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=4 Events in DMF in >0=6 Events in DMF in 0=1

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Parent's Assessment Physical Functioning Total Score MCID Decrease 4.5% Week 24	0.9918	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Physical Functioning Total Score MCID Decrease 4.5% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Physical Functioning Total Score MCID Decrease 4.5% Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	IFN B-1a in 13-14=7 IFN B-1a in 15-17=19 DMF in 13-14=8 DMF in 15-17=20	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Physical Functioning Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=7 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=5	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=4 Events in DMF in 0=3
Parent's Assessment Social Functioning Total Score MCID Decrease 4.5% Week 24	0.5204	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=5 Events in DMF in >0=9 Events in DMF in 0=3
Parent's Assessment Social Functioning Total Score MCID Decrease 4.5% Week 48	IFN B-1a in F=25 IFN B-1a in M=10 DMF in F=21 DMF in M=9	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Social Functioning Total Score MCID Decrease 4.5% Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	Events in IFN B-1a in 13-14=5 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=1 Events in DMF in 15-17=7	IFN B-1a in >0=18 IFN B-1a in 0=8 DMF in >0=21 DMF in 0=7
Parent's Assessment Social Functioning Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=1
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 4.5% Week 24	0.4385	IFN B-1a in 13-14=10 IFN B-1a in 15-17=35 DMF in 13-14=8 DMF in 15-17=28	IFN B-1a in >0=29 IFN B-1a in 0=16 DMF in >0=27 DMF in 0=9
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 4.5% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=6 Events in DMF in F=6 Events in DMF in M=2	IFN B-1a in 13-14=9 IFN B-1a in 15-17=26 DMF in 13-14=6 DMF in 15-17=24	IFN B-1a in >0=22 IFN B-1a in 0=13 DMF in >0=23 DMF in 0=7
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 4.5% Week 72	IFN B-1a in F=20 IFN B-1a in M=6 DMF in F=18 DMF in M=10	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=5 Events in DMF in 15-17=7	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=3 Events in DMF in >0=7 Events in DMF in 0=5
Parent's Assessment Work/Study/School Functioning Total Score MCID Decrease 4.5% Week 96	Events in IFN B-1a in F=6 Events in IFN B-1a in M=1 Events in DMF in F=4 Events in DMF in M=1	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=3 Events in DMF in >0=2 Events in DMF in 0=3
BVMT1-Trial 1 at Baseline	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=32 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=10 DMF in 15-17=31	0.8321
BVMT1-Trial 1 at Week 48	0.3148	0.1374	0.8573
BVMT1-Trial 1 at Week 96	0.3066	IFN B-1a in 13-14=7 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=36	0.9184
BVMT1-Trial 1 Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=28 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	0.6978
BVMT1-Trial 1 Change from Baseline at Week 96	IFN B-1a in F=16 IFN B-1a in M=9 DMF in F=25 DMF in M=6	IFN B-1a in 13-14=4 IFN B-1a in 15-17=21 DMF in 13-14=9 DMF in 15-17=22	0.1156
BVMT1-Trial 1 MCID Increase 15% Week 48	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=28 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	Events in IFN B-1a in >0=6 Events in IFN B-1a in 0=6 Events in DMF in >0=9 Events in DMF in 0=3

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
BVMT1-Trial 1 MCID Increase 15% Week 96	IFN B-1a in F=16 IFN B-1a in M=9 DMF in F=25 DMF in M=6	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=9	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=3
BVMT1-Trial 1 MCID Decrease 15% Week 48	Events in IFN B-1a in F=5 Events in IFN B-1a in M=1 Events in DMF in F=6 Events in DMF in M=4	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=2 Events in DMF in 15-17=8	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=1 Events in DMF in >0=9 Events in DMF in 0=1
BVMT1-Trial 1 MCID Decrease 15% Week 96	Events in IFN B-1a in F=3 Events in IFN B-1a in M=2 Events in DMF in F=2 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=5 Events in DMF in 13-14=4 Events in DMF in 15-17=1	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=1 Events in DMF in 0=4
BVMT1-Trial 2 at Baseline	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=32 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=10 DMF in 15-17=31	0.1390
BVMT1-Trial 2 at Week 48	0.2969	0.2265	0.7024
BVMT1-Trial 2 at Week 96	0.5172	IFN B-1a in 13-14=7 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=36	0.4103
BVMT1-Trial 2 Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=28 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	0.3732
BVMT1-Trial 2 Change from Baseline at Week 96	IFN B-1a in F=16 IFN B-1a in M=9 DMF in F=25 DMF in M=6	IFN B-1a in 13-14=4 IFN B-1a in 15-17=21 DMF in 13-14=9 DMF in 15-17=22	0.5620
BVMT1-Trial 2 MCID Increase 15% Week 48	Events in IFN B-1a in F=8 Events in IFN B-1a in M=7 Events in DMF in F=8 Events in DMF in M=4	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	0.2243
BVMT1-Trial 2 MCID Increase 15% Week 96	IFN B-1a in F=16 IFN B-1a in M=9 DMF in F=25 DMF in M=6	IFN B-1a in 13-14=4 IFN B-1a in 15-17=21 DMF in 13-14=9 DMF in 15-17=22	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=3 Events in DMF in >0=8 Events in DMF in 0=3
BVMT1-Trial 2 MCID Decrease 15% Week 48	Events in IFN B-1a in F=3 Events in IFN B-1a in M=0 Events in DMF in F=4 Events in DMF in M=2	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=5	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=1 Events in DMF in >0=4 Events in DMF in 0=2
BVMT1-Trial 2 MCID Decrease 15% Week 96	Events in IFN B-1a in F=1 Events in IFN B-1a in M=1 Events in DMF in F=0 Events in DMF in M=2	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=2 Events in DMF in 15-17=0	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=2 Events in DMF in >0=0 Events in DMF in 0=2
BVMT1-Trial 3 at Baseline	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=32 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=10 DMF in 15-17=31	0.7481
BVMT1-Trial 3 at Week 48	0.4671	0.1126	0.3951
BVMT1-Trial 3 at Week 96	0.4192	IFN B-1a in 13-14=7 IFN B-1a in 15-17=33 DMF in 13-14=15 DMF in 15-17=36	0.1213
BVMT1-Trial 3 Change from Baseline at Week 48	IFN B-1a in F=25 IFN B-1a in M=12 DMF in F=28 DMF in M=9	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	0.5122
BVMT1-Trial 3 Change from Baseline at Week 96	IFN B-1a in F=16 IFN B-1a in M=9 DMF in F=25 DMF in M=6	IFN B-1a in 13-14=4 IFN B-1a in 15-17=21 DMF in 13-14=9 DMF in 15-17=22	0.8037
BVMT1-Trial 3 MCID Increase 15% Week 48	Events in IFN B-1a in F=7 Events in IFN B-1a in M=9 Events in DMF in F=5 Events in DMF in M=2	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=9 DMF in 15-17=28	0.2547
BVMT1-Trial 3 MCID Increase 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=3 Events in DMF in F=8 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=2 Events in DMF in 15-17=7	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=1 Events in DMF in >0=8 Events in DMF in 0=1

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
BVMT1-Trial 3 MCID Decrease 15% Week 48	Events in IFN B-1a in F=2 Events in IFN B-1a in M=1 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=1
BVMT1-Trial 3 MCID Decrease 15% Week 96	Events in IFN B-1a in F=1 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=1 Events in DMF in 15-17=3	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=2 Events in DMF in >0=2 Events in DMF in 0=2
SDMT Score at Baseline	0.4904	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=10 DMF in 15-17=32	0.3541
SDMT Score at Week 48	0.2780	0.1577	0.2933
SDMT Score at Week 96	0.5281	IFN B-1a in 13-14=7 IFN B-1a in 15-17=33 DMF in 13-14=14 DMF in 15-17=38	0.7379
SDMT Score Change from Baseline at Week 48	0.3168	IFN B-1a in 13-14=8 IFN B-1a in 15-17=29 DMF in 13-14=10 DMF in 15-17=29	0.3554
SDMT Score Change from Baseline at Week 96	0.4634	IFN B-1a in 13-14=4 IFN B-1a in 15-17=22 DMF in 13-14=9 DMF in 15-17=24	0.6369
SDMT Score MCID Increase 15% Week 48	Events in IFN B-1a in F=0 Events in IFN B-1a in M=1 Events in DMF in F=1 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=0 Events in DMF in 15-17=2	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=2 Events in DMF in 0=0
SDMT Score MCID Increase 15% Week 96	Events in IFN B-1a in F=0 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=1	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=0 Events in DMF in 13-14=2 Events in DMF in 15-17=2	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=0 Events in DMF in >0=2 Events in DMF in 0=2
SDMT Score MCID Decrease 15% Week 48	Events in IFN B-1a in F=3 Events in IFN B-1a in M=0 Events in DMF in F=0 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=0	Events in IFN B-1a in >0=3 Events in IFN B-1a in 0=0 Events in DMF in >0=0 Events in DMF in 0=0
SDMT Score MCID Decrease 15% Week 96	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=0 Events in DMF in >0=1 Events in DMF in 0=0
Any AE	0.9946	1.0000	1.0000
Any MILD AE	0.4456	0.5752	0.8680
Any Moderate AE	0.4978	0.6976	0.6025
Any Severe AE	0.9994	Events in IFN B-1a in 13-14=4 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=1 Events in DMF in >0=1 Events in DMF in 0=0
Any AE Serious	0.7521	0.1158	0.9257
Any AE Leading to Drug Withdrawal	Events in IFN B-1a in F=7 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=1 Events in DMF in >0=3 Events in DMF in 0=2
Any AE Leading to Discontinuation	Events in IFN B-1a in F=7 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=1 Events in DMF in 15-17=4	Events in IFN B-1a in >0=7 Events in IFN B-1a in 0=1 Events in DMF in >0=3 Events in DMF in 0=2
Abdominal pain	0.9920	0.8605	0.5465
Abdominal pain, MILD	0.9919	0.9082	0.5027
Vomiting	0.8451	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=7 Events in DMF in 15-17=9	0.6106

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Vomiting, MILD	0.9928	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=5 Events in DMF in 15-17=9	0.8666
Diarrhoea	0.0975	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=4 Events in DMF in 13-14=5 Events in DMF in 15-17=9	0.9914
Abdominal pain upper	Events in IFN B-1a in F=1 Events in IFN B-1a in M=0 Events in DMF in F=9 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=5 Events in DMF in 15-17=7	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=7 Events in DMF in 0=5
Abdominal pain upper, MILD	Events in IFN B-1a in F=1 Events in IFN B-1a in M=0 Events in DMF in F=8 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=4 Events in DMF in 15-17=7	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=6 Events in DMF in 0=5
Multiple sclerosis relapse	0.8383	0.9846	0.9872
Flushing	0.9922	0.9934	0.9917
Flushing, MILD	0.9921	0.9934	0.9917
Cough	Events in IFN B-1a in F=1 Events in IFN B-1a in M=1 Events in DMF in F=7 Events in DMF in M=3	Events in IFN B-1a in 13-14=0 Events in IFN B-1a in 15-17=2 Events in DMF in 13-14=7 Events in DMF in 15-17=3	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=2 Events in DMF in >0=7 Events in DMF in 0=3
Rash	Events in IFN B-1a in F=1 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=0 Events in DMF in 13-14=2 Events in DMF in 15-17=7	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=5 Events in DMF in 0=4
Rash, MILD	Events in IFN B-1a in F=1 Events in IFN B-1a in M=0 Events in DMF in F=6 Events in DMF in M=3	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=0 Events in DMF in 13-14=2 Events in DMF in 15-17=7	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=5 Events in DMF in 0=4
Pyrexia	0.4253	0.3263	Events in IFN B-1a in >0=9 Events in IFN B-1a in 0=5 Events in DMF in >0=5 Events in DMF in 0=0
Pyrexia, MILD	0.4164	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=8 Events in DMF in 13-14=3 Events in DMF in 15-17=1	Events in IFN B-1a in >0=8 Events in IFN B-1a in 0=3 Events in DMF in >0=4 Events in DMF in 0=0
Influenza like illness	0.5239	0.9921	0.9911
Influenza like illness, MILD	0.4827	0.9918	0.9909
Influenza like illness, MODERATE	Events in IFN B-1a in F=5 Events in IFN B-1a in M=3 Events in DMF in F=0 Events in DMF in M=0	Events in IFN B-1a in 13-14=2 Events in IFN B-1a in 15-17=6 Events in DMF in 13-14=0 Events in DMF in 15-17=0	Events in IFN B-1a in >0=4 Events in IFN B-1a in 0=4 Events in DMF in >0=0 Events in DMF in 0=0
Myalgia	Events in IFN B-1a in F=8 Events in IFN B-1a in M=0 Events in DMF in F=1 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=7 Events in DMF in 13-14=0 Events in DMF in 15-17=1	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=3 Events in DMF in >0=1 Events in DMF in 0=0
Dysmenorrhoea, MILD	0.9996	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=4 Events in DMF in 15-17=6	Events in IFN B-1a in >0=0 Events in IFN B-1a in 0=2 Events in DMF in >0=8 Events in DMF in 0=2
Gastrointestinal disorders	0.3931	0.6338	0.1750
Gastrointestinal disorders, MILD	0.9463	0.6792	0.0916
Vascular disorders	0.7236	0.9886	0.9481
Vascular disorders, MILD	0.6043	0.9885	0.9889
Respiratory, thoracic and mediastinal disorders	0.4423	0.2439	0.3185
Respiratory, thoracic and mediastinal disorders, MILD	0.5636	0.2919	0.2625

Description	Sex (Male/Female)	Age group (13-14/15-17)	EDSS Baseline (0/>0)
Skin and subcutaneous tissue disorders	0.9918	0.1003	0.9914
Skin and subcutaneous tissue disorders, MILD	0.9919	0.0407	0.9915
General disorders and administration site conditions	0.8139	0.4998	0.1552
General disorders and administration site conditions, MILD	0.7826	0.4711	0.8758
General disorders and administration site conditions, MODERATE	Events in IFN B-1a in F=7 Events in IFN B-1a in M=5 Events in DMF in F=1 Events in DMF in M=2	Events in IFN B-1a in 13-14=3 Events in IFN B-1a in 15-17=9 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=5 Events in IFN B-1a in 0=7 Events in DMF in >0=2 Events in DMF in 0=1
Injury, poisoning and procedural complications	0.6305	0.9926	0.3184
Any AESI	0.1733	0.9918	0.9918
Any Serious AESI	Events in IFN B-1a in F=2 Events in IFN B-1a in M=0 Events in DMF in F=3 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=1 Events in DMF in 13-14=1 Events in DMF in 15-17=2	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=0 Events in DMF in >0=2 Events in DMF in 0=1
Any Non-Serious AESI	0.1733	0.9918	0.9918
Any Severe AESI	Events in IFN B-1a in F=1 Events in IFN B-1a in M=0 Events in DMF in F=0 Events in DMF in M=0	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=0 Events in DMF in 13-14=0 Events in DMF in 15-17=0	Events in IFN B-1a in >0=1 Events in IFN B-1a in 0=0 Events in DMF in >0=0 Events in DMF in 0=0
Any Non-Severe AESI	0.1733	0.9918	0.9918
Time to First Relapse	0.8696	0.9952	0.3832
Time to First EDSS 12 weeks Improvement	0.3129	0.9335	0.9999
Time to First EDSS 24 weeks Improvement	0.9978	0.1508	0.9999
Time to First EDSS 12 weeks Progression	Events in IFN B-1a in F=3 Events in IFN B-1a in M=1 Events in DMF in F=5 Events in DMF in M=1	Events in IFN B-1a in 13-14=1 Events in IFN B-1a in 15-17=3 Events in DMF in 13-14=2 Events in DMF in 15-17=4	Events in IFN B-1a in >0=2 Events in IFN B-1a in 0=2 Events in DMF in >0=5 Events in DMF in 0=1
Time to First EDSS 24 weeks Progression	No. Event=7	No. Event=7	No. Event=7