

Table of contents

Supplementary Table 1. Patient disposition[1]	2
Supplementary Table 2. Mean change in PedsQL subscales per the self- and parent-reporting scores presented by (a) occurrence of confirmed relapses during the study, (b) number of relapses in the last 2 years prior to the start of the study and (c) EDSS status at EOS.....	4
References	7

Supplementary Table 1. Patient disposition[1]

Disposition categories	n (%)	
Screened	348	
Excluded	133 (38.2%)	
Did not meet inclusion criterion	13 (3.7%)	
Met exclusion criterion	105 (30.2%)	
Withdrew consent	7 (2.0%)	
Had intercurrent medical event	1 (0.3%)	
Had other reasons	7 (2.0%)	
Randomized	215	
	Fingolimod	Interferon beta-1a
	107	108
Were included in the full analysis set	107 (100%)	107 (99.1%)
Were included in the safety	107 (100%)	107 (99.1%)
Discontinuations		
Discontinued trial	7 (6.5%)	20 (18.5%)
Withdrew consent	3 (2.8%)	5 (4.6%)
Had adverse event	3 (2.8%)	2 (1.9%)
Were withdrawn by physician	1 (0.9%)	2 (1.9%)
Had unsatisfactory therapeutic effect	-	7 (6.5%)
Withdrew or were withdrawn by guardian	-	2 (1.9%)

Had administrative problem	-	1 (0.9%)
Had protocol violation	-	1 (0.9%)
Completed trial	100 (93.5%)	88 (81.5%)
Were receiving trial regimen	99 (92.5%)	81 (75.0%)
Were not receiving trial regimen	1 (0.9%)	7 (6.5%)

Supplementary Table 2. Mean change in PedsQL subscales per the self- and parent-reporting scores presented by (a) occurrence of confirmed relapses during the study, (b) number of relapses in the last 2 years prior to the start of the study and (c) EDSS status at EOS

(a)

Occurrence of confirmed relapses during the study								
Subgroups	Free of relapse				At least 1 relapse			
Treatment	Fingolimod		IFN β -1a		Fingolimod		IFN β -1a	
Time point	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS
Self-reported	(n=85)		(n=43)		(n=14)		(n=52)	
Physical Health Summary Score	81.73	4.37**	85.54	-2.18	73.88	3.13	80.59	-4.09
Psychosocial Health Summary Score	77.10	4.88**	79.11	-0.58	74.29	3.93	78.56	-2.44
Emotional Functioning	71.65	5.59*	75.12	-0.23	67.86	6.79	76.06	-4.81
Social Functioning	90.59	2.00	91.16	0.35	91.07	-2.50	88.75	-2.31
School Functioning	69.06	6.94*	71.05	-1.86	63.93	7.50	70.87	-0.19
Parent reported	(n=83)		(n=46)		(n=15)		(n=47)	
Physical Health Summary Score	80.99	2.97	83.55	-1.55	62.92	-1.67	78.86	-5.87
Psychosocial Health Summary Score	74.86	3.64	78.46	1.54	68.00	4.22	75.50	-2.49
Emotional Functioning	68.86	5.54	74.67	1.20	67.33	-1.00	70.96	-2.55
Social Functioning	87.65	2.77	89.28	2.03	78.00	5.00	85.00	-2.69
School Functioning	68.07	2.62	71.47	1.36	58.67	8.67	70.53	-2.23

* p \leq 0.1; **p \leq 0.05
p-value is from the Wilcoxon rank sum test and represent significant effect of fingolimod versus IFN β -1a
EOS, end of study; IFN, interferon; n, number of subjects with a value at both baseline and end of study; PedsQL, Pediatric Quality of Life

(b)

Number of relapses in the last 2 years prior to the start of the study												
Subgroups	≤1 relapse				2–3 relapses				>3 relapses			
Treatment	Fingolimod		IFN β-1a		Fingolimod		IFN β-1a		Fingolimod		IFN β-1a	
Time point	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS
Self-reported	(n=26)		(n=18)		(n=54)		(n=59)		(n=19)		(n=18)	
Physical Health Summary Score	85.70	2.28	84.72	-2.26	78.65	3.35*	83.42	-2.54	79.28	9.21**	78.99	-6.42
Psychosocial Health Summary Score	79.29	2.69	80.93	0.00	74.88	5.83***	79.46	-2.29	78.33	4.47	74.54	-0.93
Emotional Functioning	73.65	4.62	77.50	-2.78	69.72	6.94***	75.93	-3.22	71.58	3.95	72.78	-1.11
Social Functioning	93.65	-1.35	95.00	-0.56	88.43	3.98**	90.00	-1.78	92.89	-2.37	84.17	0.56
School Functioning	70.58	4.81	70.28	3.33	66.48	6.39**	72.46	-1.86	70.53	11.84	66.67	-2.22
Parent reported	(n=26)		(n=20)		(n=55)		(n=58)		(n=17)		(n=15)	
Physical Health Summary Score	85.46	-2.16	84.06	-6.72	78.30	1.19	81.46	-2.16	66.91	12.50**	76.25	-5.83
Psychosocial Health Summary Score	76.86	1.28	77.83	-0.33	73.12	4.16	77.11	0.70	71.37	6.08*	75.22	-5.33
Emotional Functioning	72.69	0.77	74.25	-3.00	66.27	7.82	72.84	1.47	70.00	-0.29	70.67	-6.00
Social Functioning	89.04	3.27	91.25	-0.75	85.18	2.45	86.84	0.64	85.00	5.00	82.67	-3.67
School Functioning	68.85	-0.19	68.00	2.75	67.91	2.23	71.68	-0.04	59.12	13.53**	72.33	-6.33

* p≤0.1; **p≤0.05; ***p≤0.01
p-values are from the Wilcoxon rank sum test and represent significant effect of fingolimod versus IFN β-1a
EOS, end of study; IFN, interferon; n, number of subjects with a value at both baseline and end of study; PedsQL, Pediatric Quality of Life

(c)

EDSS status at EOS												
Subgroups	Improved				Stable				Deteriorated			
Treatment	Fingolimod		IFN β -1a		Fingolimod		IFN β -1a		Fingolimod		IFN β -1a	
Time point	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS	Baseline	Mean change at EOS
Self-reported	(n=22)		(n=10)		(n=67)		(n=66)		(n=8)		(n=19)	
Physical Health Summary Score	76.42	13.07*	80.00	0.63	84.10	1.25	85.65	-0.95	67.19	1.17	74.51	-13.16
Psychosocial Health Summary Score	74.47	10.68	72.33	5.83	78.13	3.40*	79.95	-1.62	72.08	0.00	78.25	-5.44
Emotional Functioning	67.50	11.59	68.00	6.00	72.16	4.70*	77.12	-2.88	71.25	0.00	74.47	-6.84
Social Functioning	92.27	2.95	86.50	2.50	91.42	0.82	91.59	-1.36	80.00	0.63	85.53	-2.11
School Functioning	63.64	17.50	62.50	9.00	70.82	4.55	71.14	-0.61	65.00	-0.63	74.74	-7.37
Parent reported	(n=21)		(n=11)		(n=66)		(n=63)		(n=10)		(n=19)	
Physical Health Summary Score	77.23	8.93	77.56	0.85	79.69	1.52	83.62	-2.64	73.13	-8.13	75.16	-10.03
Psychosocial Health Summary Score	71.19	10.17	70.61	11.67	74.27	2.65	77.79	0.24	78.83	-4.00	77.89	-10.00
Emotional Functioning	63.10	13.57	64.55	13.64	69.32	3.94	73.49	1.51	78.00	-10.00	75.26	-16.32
Social Functioning	88.33	5.71	85.00	8.64	85.61	2.42	88.44	0.19	88.00	-0.50	83.95	-7.37
School Functioning	62.14	11.31	62.27	12.73	67.88	1.59	71.47	-0.99	70.50	-1.50	74.47	-6.32

*p \leq 0.05
p-value is from the Wilcoxon rank sum test and represent significant effect of fingolimod vs. IFN β -1a
For patients with a baseline EDSS score of \leq 5.0, a decrease of \leq 1 point is defined as improvement, a change from -0.5 to 0.5 is defined as stable and an increase of \geq 1 point is defined as deterioration; for patients with a baseline EDSS score of $>$ 5.0, a decrease of \leq 0.5 point is defined as improvement, zero change is defined as stable and an increase of \geq 0.5 point is defined as deterioration
EDSS, Expanded Disability Status Scale; EOS, end of study; IFN, interferon; n, number of subjects with a value at both baseline and end of study; PedsQL, Pediatric Quality of Life

References

1. Chitnis T, Arnold DL, Banwell B, Bruck W, Ghezzi A, Giovannoni G, et al. Trial of fingolimod versus interferon beta-1a in pediatric multiple sclerosis. *N Engl J Med*. 2018;379(11):1017-27.