

Online Supplementary Data

Table S1 Baseline demographics and disease characteristics of patients who did and did not return for PRISMS-15

	Patients attending PRISMS-15 (n=290)	Patients not attending PRISMS-15 (n=270)	Overall (N=560)
Median (range) age, years	35.1 (19.7–50.5)	34.7 (18.1–53.4)	34.9 (18.1–53.4)
Female, n (%)	204 (70.3)	185 (68.5)	389 (69.5)
White, n (%)	287 (99.0)	267 (98.9)	554 (98.9)
Median (range) time since MS onset, years	5.6 (0.6–34.4)	5.0 (0.8–26.4)	5.3 (0.6–34.4)
Mean (SD) number of relapses in prior 2 years	3.0 (1.2)	3.0 (1.1)	3.0 (1.2)
Mean (SD) EDSS score	2.4 (1.2)	2.6 (1.3)	2.5 (1.2)
Original randomisation group, n (%)			
IFN β -1a, 44 μ g sc tiw	95/184 (51.6)	89/184 (48.4)	–
IFN β -1a, 22 μ g sc tiw	95/189 (50.3)	94/189 (49.7)	–
Placebo	100/187 (53.5)	87/187 (46.5)	–

EDSS, Expanded Disability Status Scale; IFN, interferon; MS, multiple sclerosis; sc, subcutaneously; tiw, three times weekly.

Table S2 Univariate regression analysis: regression coefficients and p values for significant ($p \leq 0.10$) prognostic factors

Variable	Clinical outcomes at 15 years		
	SPMS conversion	Change in EDSS	EDSS 3-month confirmed progression
Age at baseline	+0.0358; $p=0.0343$	–	–
Female sex	-0.4879; $p=0.0620$	-0.4516; $p=0.0759$	–
Time since MS onset	-	–	–
Number of prior relapses	+0.2407; $p=0.0206$	–	–
Baseline EDSS score	+0.6643; $p<0.0001$	–	–
Baseline log(T2 BOD)	+0.3416; $p=0.0011$	+0.2099; $p=0.0226$	–
Change in EDSS score at 24 months	+0.6342; $p<0.0001$	+0.7303; $p<0.0001$	+1.3607; $p<0.0001$
Annualised relapse rate at 24 months	–	+0.2368; $p=0.0617$	–
Change in log(T2 BOD) at 24 months	–	+0.8412; $p=0.0438$	–
T2 active lesions per scan at 24 months	-	+0.1163; $p=0.0025$	–
Early IFN β -1a treatment	-	–	–
Medication Possession Ratio	-0.0136; $p=0.0004$	-0.0137; $p=0.0002$	-0.0078; $p=0.0445$

BOD, burden of disease; EDSS, Expanded Disability Status Scale; IFN, interferon; MS, multiple sclerosis.

Table S3 Regression coefficients for prognostic factors in the final predictive multivariate regression models for selected clinical outcomes at 15 years in patients initially randomised to placebo (n=100)

Variable	Clinical outcomes at 15 years*		
	SPMS conversion	Change in EDSS	EDSS 3-month confirmed progression
Baseline EDSS score	+0.9160; p=0.0022	–	–
Baseline log(T2 BOD)	+0.5669; p=0.0304	–	–
Change in EDSS score at 24 months	+0.4622; p=0.1091	+0.66306; p<0.0001	+1.2155; p<0.0001
Change in log(T2 BOD) at 24 months	+3.0747; p=0.0017	+1.26599; p=0.0152	–
Medication Possession Ratio	–0.0151; p=0.0816	–0.00913; p=0.0816	–

*Data calculated using forward selection, stepwise multivariate analysis.

BOD, burden of disease; EDSS, Expanded Disability Status Scale; SPMS, secondary progressive multiple sclerosis.

Table S4

Disease characteristics at 2 years in the lowest (MIN) and highest (MAX) quartiles of cumulative total dose of sc IFN β -1a

Characteristic	Statistics	Cumulative dose of sc IFN β-1a	
		MIN (N=73)	MAX (N=72)
Confirmed EDSS progression up to Year 2, N (%)	N (missing)	73 (0)	72 (0)
	Yes	29 (39.7)	18 (25.0)
	No	44 (60.3)	54 (75.0)
Exacerbation Count up to Year 2	N (missing)	73 (0)	72 (0)
	Mean \pm SD	2.5 \pm 1.9	1.9 \pm 1.7
Mean Number of T2 Active Lesions per Scan	N (missing)	72 (1)	72 (0)
	Mean \pm SD	2.88 \pm 3.65	1.88 \pm 3.00
MRI Scans with T2 Activity (%)	N (missing)	72 (1)	72 (0)
	Mean \pm SD	58.91 \pm 38.36	48.96 \pm 37.16
Changes BOD from Baseline to Year 2 (%)	N (missing)	63 (10)	72 (0)
	Mean \pm SD	11.80 \pm 34.11	7.50 \pm 37.50

BOD, burden of disease; EDSS, expanded disability status scale; MRI, magnetic resonance imaging

Table S5Disease characteristics at 4 years in the lowest (MIN) and highest (MAX) quartiles of cumulative total dose of sc IFN β -1a

Characteristic	Statistics	Cumulative dose of sc IFN β-1a	
		MIN (N=73)	MAX (N=72)
Confirmed EDSS progression up to Year 4, N (%)	N (missing)	73 (0)	72 (0)
	Yes	33 (45.2)	26 (36.1)
	No	40 (54.8)	46 (63.9)
Exacerbation Count up to Year 4	N (missing)	73 (0)	72 (0)
	Mean \pm SD	3.5 \pm 2.7	3.2 \pm 2.7

EDSS, Expanded Disability Status Scale