Supplementary table S1   Conversion to multiple sclerosis (intent-to-treat population)

	Cumulative probability at 2 years (%)[*]			p Value[†]		
	sc IFN β-1a tiw	sc IFN β-1a qw	Placebo	tiw versus placebo	qw versus placebo	tiw versus qw
McDonald 2005 MS	62.5	75.5	85.8	<0.001	0.008	0.009
CDMS	20.6	21.6	37.5	<0.001	0.002	0.774

[*]Kaplan–Meier estimates.

[†]Two-sided log-rank test, stratified by randomisation stratification factors.

CDMS, clinically definite multiple sclerosis; IFN, interferon; MS, multiple sclerosis; qw, once weekly; sc, subcutaneous; tiw, three times weekly.

Supplementary table S2 Point estimates of CUA lesions per patient per scan during the double-blind period and treatment effect of sc IFN

β-1a

	LSM CUA lesions per patient per scan				sc IFN β-1a tiw versus placebo[*]				sc IFN β-1a qw versus placebo[*]				sc IFN β-1a tiw versus sc IFN β-1a qw[*]	
	sc IFN β-1a tiw (n=171)	sc IFN β-1a qw (n=175)	Placebo (n=171)		LSM ratio (95% CI)	p Value			LSM ratio (95% CI)	p Value			LSM ratio (95% CI)	p Value
Age														
<30 years (n=259)	0.71	1.76	3.13		0.23 (0.14 to 0.36)	<0.001			0.56 (0.36 to 0.88)	0.006			0.40 (0.26 to 0.64)	0.015
≥30 years (n=258)	0.47	0.60	2.14		0.22 (0.14 to 0.34)	<0.001			0.28 (0.18 to 0.43)	<0.001			0.79 (0.50 to 1.23)	0.048
Sex														
Male (n=185)	0.67	1.16	1.50		0.45 (0.26 to 0.76)	0.012			0.77 (0.45 to 1.31)	0.119			0.58 (0.34 to 1.01)	0.276
Female	0.39	0.71	3.07		0.13 (0.09 to 0.19)	<0.001			0.23 (0.16 to 0.33)	<0.001			0.56 (0.38 to 0.82)	0.002

		LSM CUA lesions per patient per scan				sc IFN β-1a tiw versus placebo[*]				sc IFN β-1a qw versus placebo[*]				sc IFN β-1a tiw versus sc IFN β-1a qw[*]	
	(n=332)																
Steroid use during first attack																
	Yes (n=366)	0.67	0.95	2.89		0.23 (0.16 to 0.34)	<0.001		0.33 (0.23 to 0.48)	<0.001		0.71 (0.48 to 1.04)	0.015
	No (n=151)	0.39	1.65	2.06		0.19 (0.10 to 0.35)	<0.001		0.80 (0.44 to 1.46)	0.005		0.23 (0.12 to 0.44)	0.105
Presentation of first event																
	Monofocal (n=277)	0.66	1.23	1.94		0.34 (0.21 to 0.56)	<0.001		0.64 (0.39 to 1.04)	0.013		0.54 (0.33 to 0.88)	0.173
	Multi-focal (n=240)	0.50	1.05	3.43		0.15 (0.09 to 0.22)	<0.001		0.30 (0.20 to 0.46)	<0.001		0.48 (0.31 to 0.74)	<0.001
Gd+ lesions at baseline																
	0 (n=304)	0.27	0.58	1.69		0.16 (0.11 to 0.25)	<0.001		0.35 (0.23 to 0.52)	<0.001		0.47 (0.31 to 0.72)	0.007

		LSM CUA lesions per patient per scan			sc IFN β-1a tiw versus placebo[*]			sc IFN β-1a qw versus placebo[*]			sc IFN β-1a tiw versus sc IFN β-1a qw[*]	
	≥1 (n=213)	1.06	1.93	3.97	0.27 (0.17 to 0.42)	<0.001		0.49 (0.31 to 0.76)	0.001		0.55 (0.35 to 0.88)	0.173
T2 lesions at baseline												
	<9 (n=140)	0.24	0.29	0.72	0.33 (0.17 to 0.65)	0.006		0.40 (0.22 to 0.75)	0.035		0.83 (0.41 to 1.67)	0.440
	≥9 (n=377)	0.56	1.18	3.37	0.17 (0.12 to 0.23)	<0.001		0.35 (0.25 to 0.49)	<0.001		0.47 (0.34 to 0.66)	<0.001

[*]Treatment effects were estimated using a negative binomial model, with treatment as covariate and log number of scans as an offset variable; p values were calculated using a 2-sided stratified non-parametric analysis of variance model on ranked data, with effects for treatment group.

CUA, combined unique active; Gd+, gadolinium-enhancing; IFN, interferon; LSM, least squares mean; qw, once weekly; sc, subcutaneous; tiw, three times weekly.

Supplementary figure S1   Last observed value of median changes from baseline in (A) T2, (B) T1 hypointense, and (C) T1-Gd+ lesion volume during the double-blind period (intent-to-treat population). Red lines represent the median, boxes represent the interquartile range. In all cases, the range extended beyond the limits of the axis. Gd+, gadolinium-enhancing; qw, once weekly; tiw, three times weekly