Supplemental Material Table 1 Univariate and multivariate analyses: T2 lesions on MRI at 4 years

Variable label	Level	Univariate analysis		Multivariate analysis	
		Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
Intercept				1.9386 (1.2975, 2.5797)	<0.0001
sNfL at baseline (log-transformed)		0.8870 (0.6659, 1.1082)	<0.0001	0.7341 (0.5063, 0.9620)	<0.0001
Treatment arm	Peginterferon beta-1a 125 µg every 2 or 4 weeks	–0.3761 (–0.6035, –0.1488)	0.0012	–0.5490 (–0.7912, –0.3068)	<0.0001
	Placebo	Reference		Reference	
Age at reference start date, years		–0.0491 (–0.0589, –0.0393)	<0.0001	–0.0370 (–0.0502, –0.0239)	<0.0001
Sex	Female	0.0772 (–0.1628, 0.3172)	0.5284		
	Male	Reference			
EDSS score at baseline		–0.2417 (–0.3348, –0.1487)	<0.0001		
MSFC score at baseline		0.2009 (0.0366, 0.3652)	0.0165	0.5360 (0.3224, 0.7496)	<0.0001
Number of relapses 3 years prior to study		0.1106 (–0.0191, 0.2402)	0.0948		
Onset year of symptoms		–0.0553 (–0.0714, –0.0393)	<0.0001	–0.0365 (–0.0559, –0.0171)	0.0002
Gd+ lesions at baseline		0.1487 (0.1084, 0.1890)	<0.0001		
Volume of T2 lesions at baseline (log-transformed)		0.3837 (0.3038, 0.4636)	<0.0001	0.3904 (0.2788, 0.5020)	<0.0001
Dispersion				1.7189 (1.5036, 1.9651)	

CI: confidence interval; EDSS: Expanded Disability Status Scale; Gd+: gadolinium enhancing; MSFC: Multiple Sclerosis Functional Composite;

sNfL: serum neurofilament light chain.

Supplemental Material Table 2 Univariate and multivariate analyses: Percent brain volume change at 4 years
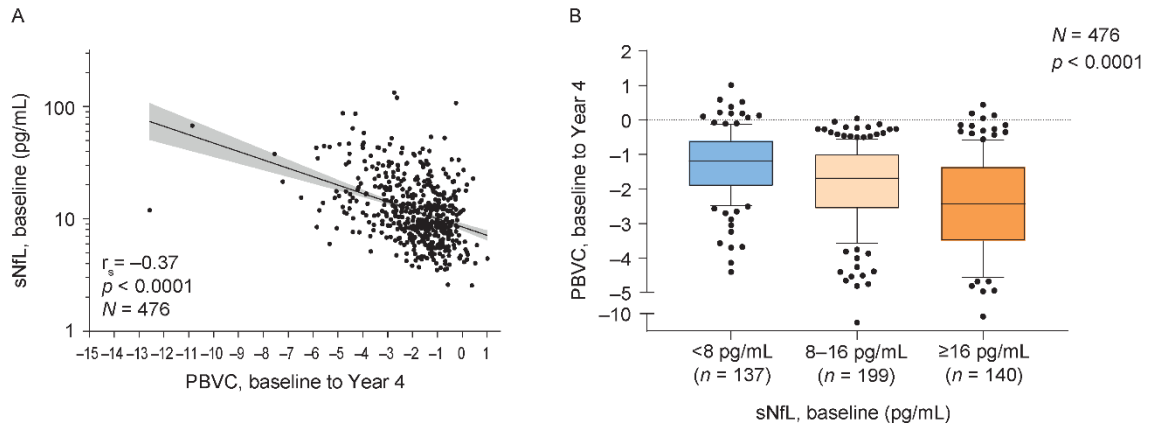
Variable label	Level	Univariate analysis		Multivariate analysis	
		Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
Intercept				0.5943 (–0.0943, 1.2828)	0.0905
sNfL at baseline (log-transformed)		–0.8757 (–1.0632, –0.6882)	<0.0001	–0.5785 (–0.7820, –0.3750)	<0.0001
Treatment arm	Peginterferon beta-1a 125 µg every 2 or 4 weeks	0.0268 (–0.1972, 0.2509)	0.8	–0.0767 (–0.3176, 0.1642)	0.5319
	Placebo	Reference		Reference	
Age at reference start date, years		–0.0002 (–0.0111, 0.0107)	0.9755	–0.0149 (–0.0285, –0.0014)	0.0304
Sex	Female	0.0766 (–0.1592, 0.3124)	0.5237		
	Male	Reference			
EDSS score at baseline		–0.1685 (–0.2578, –0.0792)	0.0002	–0.1194 (–0.2314, –0.0074)	0.0367
MSFC score at baseline		0.2902 (0.1416, 0.4388)	0.0001		
Number of relapses 3 years prior to study		–0.1222 (–0.2446, 0.0003)	0.0506		
Onset year of symptoms		0.0149 (–0.0023, 0.0321)	0.0898	0.0338 (0.0128, 0.0548)	0.0017
Gd+ lesions at Baseline		–0.0859 (–0.1077, –0.0641)	<0.0001		
Volume of T2 lesions at baseline (log-transformed)		–0.3641 (–0.4327, –0.2955)	<0.0001	–0.2929 (–0.3946, –0.1913)	<0.0001

CI: confidence interval; EDSS: Expanded Disability Status Scale; Gd+: gadolinium enhancing; MSFC: Multiple Sclerosis Functional Composite;
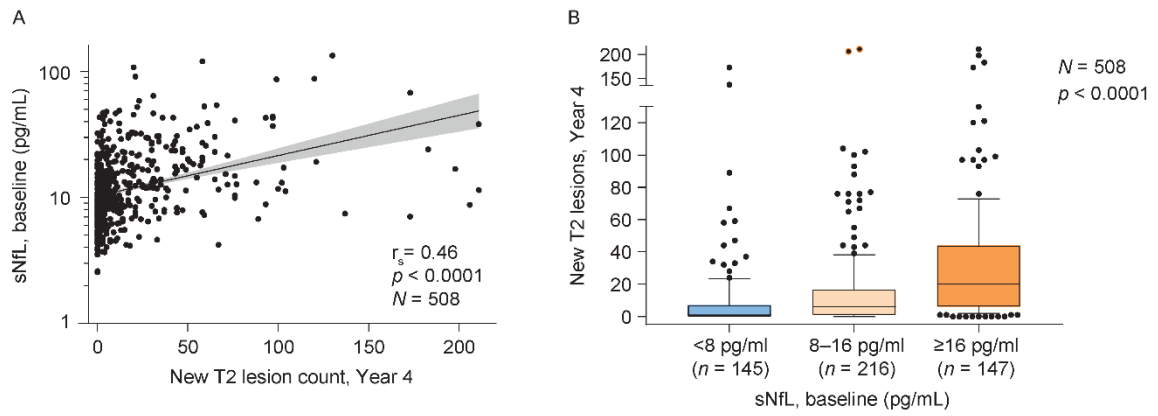
sNfL: serum neurofilament light chain.

Supplemental Material Table 3 Univariate and multivariate analyses: EDSS score at 4 years

Variable label	Level	Univariate analysis		Multivariate analysis	
		Estimate (95% CI)	*p*	Estimate (95% CI)	*p*
Intercept				–0.3828 (–0.7824, 0.0167)	0.0603
sNfL at baseline (log-transformed)		0.1479 (0.0404, 0.2555)	0.0071	0.1137 (–0.0036, 0.2310)	0.0574
Treatment arm	Peginterferon beta-1a 125 µg every 2 or 4 weeks	–0.0503 (–0.1673, 0.0667)	0.399	–0.0692 (–0.2083, 0.0699)	0.3290
	Placebo	Reference		Reference	
Age at reference start date, years		0.0050 (–0.0007, 0.0106)	0.0843	0.0121 (0.0048, 0.0195)	0.0012
Sex	Female	0.0734 (–0.0483, 0.1952)	0.2369		
	Male	Reference			
EDSS score at baseline		–0.0890 (–0.1347, –0.0433)	0.0001	–0.1300 (–0.1926, –0.0674)	<0.0001
MSFC score at baseline		–0.0612 (–0.1405, 0.0181)	0.1301		
Number of relapses 3 years prior to study		0.0461 (–0.0193, 0.1115)	0.1666		
Onset year of symptoms		0.0037 (–0.0049, 0.0124)	0.3982		
Gd+ lesions at baseline		0.0202 (0.0077, 0.0327)	0.0016		
Volume of T2 lesions at baseline (log-transformed)		0.0592 (0.0210, 0.0975)	0.0025	0.0618 (0.0049, 0.1188)	0.0334

CI: confidence interval; EDSS: Expanded Disability Status Scale; Gd+: gadolinium enhancing; MSFC: Multiple Sclerosis Functional Composite; sNfL: serum neurofilament light chain.

Supplemental Material Figure 1. Spearman correlation between sNfL level at baseline and PBVC over 4 years. (a) Correlation shown as a scatterplot with the 95% confidence interval represented with gray shading. (b) Correlation shown as a box plot with whiskers and outliers based on sNfL tertiles. PBVC: percent brain volume change; sNfL: serum neurofilament light chain.

Supplemental Material Figure 2. Spearman correlation between sNfL level at baseline and new T2 lesion count at Year 4. (a) Correlation shown as a scatterplot with the 95% confidence interval represented with gray shading. (b) Correlation shown as a box plot with whiskers and outliers based on sNfL tertiles. sNfL: serum neurofilament light chain.