Table S1. **Clinical and MRI outcomes from double-blind, randomized, placebo-controlled trials of IFNβ therapies in patients with RRMS**

Reference	Population and study design	Interferon	Clinical outcomes				MRI outcomes[a]
			ARR	Median time to first relapse	Other	Progression of disability	
IFNB Multiple Sclerosis Study Group et al[27,28] Goodin et al [33]	N = 372 Two pooled 5-y trials; 21-y follow-up survival analysis	IFNβ-1b	Placebo: 1.12 (95% CI, 1.02-1.23) 1.6 MIU: 0.96 (95% CI, 0.87-1.06)[b] 8 MIU: 0.78 (95% CI, 0.7-0.88) • ~30% reduction in ARR with 8 MIU vs placebo during all 5 y, but $P < .05$ only during years 1-2	<u>Year 2</u> Placebo: 153 d 1.6 MIU: 180 d 8 MIU: 295 d[d,e] <u>Year 3</u> Placebo: 147 d 1.6 MIU: 199 d 8 MIU: 264 d[e]	Reduction in 21-y all-cause mortality vs placebo: 50 µg: 46.0%[e] 250 µg:46.8%[e]	No statistically significant difference between groups	Outcome: median change in lesion area <u>Year 1</u> Placebo: ↑6.7% 1.6 MIU: ↑5.7% 8 MIU: ↓4.9%[b] <u>Year 3</u> Placebo: ↑21.0% 1.6 MIU: ↑6.1% 8 MIU: ↓3.8%[c] <u>Year 5</u> Placebo: ↑30.2% 1.6 MIU: ↑10.6% 8 MIU: ↑3.6%[e]
Jacobs et al[29]	MSCRG N = 301 104 wk	IFNβ-1a IM	Placebo: 0.90 IFNβ-1a: 0.61[b]	Placebo: 36.1 wk IFNβ-1a: 47.3 wk	Probability of sustained progression: Placebo: 34.9% IFNβ-1a: 21.9%	Delayed time to sustained progression vs placebo ($P = .02$)	Outcome: median change in T2 lesion volume <u>Year 1</u> Placebo: ↓3.3% IFNβ-1a: ↓13.1%[d] <u>Year 2</u> Placebo: ↓6.5% IFNβ-1a: ↓13.2%

PRISMS Study Group[3]	PRISMS N = 560 2 y	IFNβ-1a SC	Mean relapses over 2 y: Placebo: 2.56 22 μg: 1.82[b] 44 μg: 1.73[b]	Placebo: NR 22 μg: delayed 3 mo[b] 44 μg: delayed 5 mo[b]	Percentage reduction in relapses vs placebo: 22 μg: 27% (95% CI, 14%-39%)[b] 44 μg: 33% (95% CI, 21%-44%)[b] • Significant reduction in severity of relapse vs placebo for both doses (P < .005)		Number of T2 active lesions vs placebo: 22 mg: ↓67%[c] 44 mg: ↓78%[c,f]
Calabresi et al[26] Arnold et al[34]	ADVANCE N = 1512 48-wk trial; 96-wk MRI follow-up	Peginterferon beta-1a	Placebo: 0.397 2-wk dosing: 0.256[c] 4-wk dosing: 0.288[e]	NR	Risk of relapse vs placebo (HR [95% CI]): 2-wk dosing: 0.61 (0.47-0.80)[c] 4-wk dosing: 0.74 (0.57-0.95)[e]	Risk of progression vs placebo (HR [95% CI]): 2-wk dosing: 0.62 (0.40-0.97)[e] 4-wk dosing: 0.62 (0.40-0.97)[f]	Change in T1 lesion formation vs delayed treatment[g]: 2-wk dosing: ↓58%[c] Every-4-wk dosing: ↓52%[h] • Active lesion formation ↓65% with 2-wk dosing vs delayed treatment; ↓55% vs 4-wk dosing (P < .001 for both) Outcome: mean change in T2 lesion volume Delayed treatment: ↑0.62 cm^3 2-wk dosing: ↓0.23 cm^3 [h,i] 4-wk dosing: ↑0.36 cm^3

Note: See main text for full reference information.

Abbreviations: ARR, annualized relapse rate; HR, hazard ratio; IFN, interferon; IM, intramuscular; MIU, million international units; MRI, magnetic resonance imaging; MSCRG, Multiple Sclerosis Collaborative Research Group; NR, not reported; PRISMS, Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis; RRMS, relapsing-remitting multiple sclerosis; SC, subcutaneous.

[a]Increase and decrease in MRI outcomes indicated by ↑ and ↓, respectively.

[b]$P < .01$ vs placebo.

[c]$P < .001$ vs placebo.

[d]$P < .05$ vs 1.6 MIU.

[e]$P < .05$ vs placebo.

[f]$P < .001$ vs 22 μg.

[g]Placebo in year 1, followed by peginterferon beta-1a every 2 weeks or every 4 weeks in year 2.

[h]$P < .001$ vs delayed treatment.

[i]$P < .05$ vs every-4-weeks dosing.