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

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population and study design</th>
<th>Interferon</th>
<th>Clinical outcomes</th>
<th>MRI outcomesa</th>
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<tbody>
<tr>
<td>IFNB Multiple Sclerosis Study Group et al27,28 Goodin et al33</td>
<td>N = 372 Two pooled 5-y trials; 21-y follow-up survival analysis</td>
<td>IFNβ-1b</td>
<td>ARR</td>
<td>Outcome: median change in lesion area</td>
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<td></td>
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<td></td>
<td>Median time to first relapse</td>
<td>Year 1 Placebo: ( \downarrow )6.7% 1.6 MIU: ( \uparrow )5.7% 8 MIU: ( \downarrow )4.9%b</td>
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<td></td>
<td>Other</td>
<td>Year 5 Placebo: ( \uparrow )30.2% 1.6 MIU: ( \uparrow )10.6% 8 MIU: ( \uparrow )3.6%c</td>
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<td>Probability of sustained progression: Placebo: 34.9% IFNβ-1a: 21.9%</td>
<td>Year 2 Placebo: ( \downarrow )3.3% IFNβ-1a: ( \downarrow )13.1%d</td>
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<td>Delayed time to sustained progression vs placebo (( P = .02 ))</td>
<td></td>
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<tr>
<td>Jacobs et al50</td>
<td>MSCRG N = 301 104 wk</td>
<td>IFNβ-1a IM</td>
<td>Placebo: 0.90 wk IFNβ-1a: 0.61b</td>
<td>Year 1 Placebo: ( \downarrow )6.5% IFNβ-1a: ( \downarrow )13.2%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Placebo: 36.1 wk IFNβ-1a: 47.3 wk</td>
<td>Year 2 Placebo: ( \downarrow )6.5% IFNβ-1a: ( \downarrow )13.2%</td>
</tr>
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<td>Probability of sustained progression: Placebo: 34.9% IFNβ-1a: 21.9%</td>
<td>Year 3 Placebo: ( \uparrow )21.0% 1.6 MIU: ( \uparrow )6.1% 8 MIU: ( \downarrow )3.8%e</td>
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<td>Delayed time to sustained progression vs placebo (( P = .02 ))</td>
<td>Year 4 Placebo: ( \uparrow )24.6% 1.6 MIU: ( \uparrow )8.7% 8 MIU: ( \downarrow )5.3%e</td>
</tr>
</tbody>
</table>

**Notes:**
- ARR: Annualized Relapse Rate
- CI: Confidence Interval
- MIU: MilliInternational Units
- wk: Week
- Year: Year

**References:**
- IFNB Multiple Sclerosis Study Group et al27,28
- Goodin et al33
- Jacobs et al50
- MSCRG
- Placebo: 0.90 wk IFNβ-1a: 0.61b
- 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

<table>
<thead>
<tr>
<th>Study Group</th>
<th>PRISMS N</th>
<th>IFNβ-1a SC</th>
<th>Mean relapses over 2 y:</th>
<th>Placebo: NR</th>
<th>Percentage reduction in relapses vs placebo:</th>
<th>Number of T2 active lesions vs placebo:</th>
</tr>
</thead>
</table>
| PRISMS Study Group<sup>3</sup> | 560 | 2 y | Placebo: 2.56  
22 µg: 1.82<sup>b</sup>  
44 µg: 1.73<sup>b</sup> | 22 µg: delayed 3 mo<sup>b</sup>  
44 µg: delayed 5 mo<sup>b</sup> | 22 µg: 27% (95% CI, 14%-39%)<sup>b</sup>  
44 µg: 33% (95% CI, 21%-44%)<sup>b</sup> | 22 mg: ↓67%<sup>c</sup>  
44 mg: ↓78%<sup>c,f</sup> |
| Calabresi et al<sup>26</sup> | 1512 | 48-wk trial; 96-wk MRI follow-up | Peginterferon beta-1a | Placebo: 0.397  
2-wk dosing: 0.256<sup>e</sup>  
4-wk dosing: 0.288<sup>e</sup> | 0.61 (0.47-0.80)<sup>c</sup>  
0.74 (0.57-0.95)<sup>e</sup> | |
| Arnold et al<sup>34</sup> | 1512 | 48-wk trial; 96-wk MRI follow-up | Peginterferon beta-1a | Placebo: 0.397  
2-wk dosing: 0.256<sup>e</sup>  
4-wk dosing: 0.288<sup>e</sup> | 0.61 (0.47-0.80)<sup>c</sup>  
0.74 (0.57-0.95)<sup>e</sup> | |

Note: See main text for full reference information.

- Risk of relapse vs placebo (HR [95% CI]): 2-wk dosing: 0.61 (0.47-0.80)<sup>c</sup>  
4-wk dosing: 0.74 (0.57-0.95)<sup>e</sup>  
Risk of progression vs placebo (HR [95% CI]): 2-wk dosing: 0.62 (0.40-0.97)<sup>e</sup>  
4-wk dosing: 0.62 (0.40-0.97)<sup>f</sup>  
Change in T1 lesion formation vs delayed treatment<sup>c</sup>: 2-wk dosing: ↓58%<sup>c</sup>  
Every-4-wk dosing: ↓52%<sup>b</sup>  
- Active lesion formation ↓65% with 2-wk dosing vs delayed treatment; ↓55% vs 4-wk dosing (<i>P</i> < .001 for both)  
Outcome: mean change in T2 lesion volume  
Delayed treatment: ↑0.62 cm<sup>3</sup>  
2-wk dosing: ↓0.23 cm<sup>3</sup><sup>h,j</sup>  
4-wk dosing: ↑0.36 cm<sup>3</sup>
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.

*Increase and decrease in MRI outcomes indicated by ▲ and ▼, respectively.

*bP < .01 vs placebo.

cP < .001 vs placebo.

dP < .05 vs 1.6 MIU.

eP < .05 vs placebo.

fP < .05 vs 22 μg.

gPlacebo in year 1, followed by peginterferon beta-1a every 2 weeks or every 4 weeks in year 2.

hP < .001 vs delayed treatment.

iP < .05 vs every-4-weeks dosing.