

Interferon β -1a SC tiw reduces cumulative MRI lesions over 24 months in patients with relapsing multiple sclerosis: *post hoc* analyses of PRISMS data

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Introduction

- Magnetic resonance imaging (MRI) is increasingly being used in patients with multiple sclerosis (MS), not only to aid diagnosis but also to detect clinically silent disease activity and to monitor the response to disease-modifying drug therapy.¹
- PRISMS-2 (Prevention of Relapses and disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) was a 2-year, multicenter, double-blind, placebo-controlled trial in patients with relapsing MS (RMS), which showed that interferon beta-1a (IFN β -1a) 44 and 22 μ g subcutaneously (SC) three times weekly (tiw) significantly reduced numbers of relapses, risk of 3-month confirmed disability progression, and numbers of active T2 lesions compared with placebo.²
- In the PRISMS trial, monthly MRI scans over the entire 2 years were obtained in a subgroup of patients.

Objective

- To evaluate cumulative lesion activity up to specified time points (Months 1–9, 12, 18, and 24) in patients receiving placebo, IFN β -1a 44 μ g SC tiw, or IFN β -1a 22 μ g SC tiw and undergoing monthly MRI scans over 2 years.

Methods

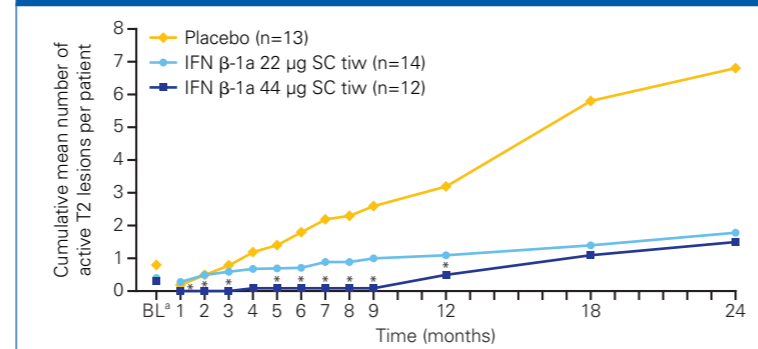
- In the PRISMS trial, patients with RMS were randomized to receive IFN β -1a 44 μ g SC tiw (n=184) or 22 μ g SC tiw (n=189) or placebo (n=187) for 2 years.²
- Eligible patients were 18–50 years of age, had a history of \geq 2 relapses in the previous 2 years, and had an Expanded Disability Status Scale score of 0–5.0. Diagnosis of clinically definite or laboratory-supported definite MS was based on the Poser criteria.³ All patients had T2 MRI brain scans every 6 months.⁴
- Post hoc* analyses were conducted on data from a single-center cohort (n=39; monthly MRI cohort) who had monthly T2 and T1 gadolinium (Gd)-enhanced MRI brain scans over the entire 2 years, including at screening (up to 42 days before Study Day 1) and baseline (Study Day 1).
- In the monthly MRI cohort, between-group differences in the cumulative numbers of active T2, T1 Gd-enhancing (Gd+), and combined unique active (CUA) lesions at Months 1–9, 12, 18, and 24 after starting treatment were compared using negative binomial regression adjusting for the number of corresponding lesions at baseline.
 - Active T2 lesions were defined as the sum of new, newly enlarging, and recurrent T2 lesions.
 - CUA lesions were defined as the sum of active T2 lesions and T1 Gd+ lesions, avoiding double counting.

Results

Active T2 lesions

- At baseline, the mean (standard deviation [SD]) number of active T2 lesions was 0.8 (1.17) in the placebo group (n=13), 0.3 (0.65) in the IFN β -1a 44 μ g SC tiw group (n=12), and 0.4 (0.76) in the IFN β -1a 22 μ g SC tiw group (n=14; **Figure 1**).
- The cumulative mean number of active T2 lesions was significantly (p<0.05) lower with IFN β -1a 44 μ g SC tiw than with placebo as early as Month 1 and remained so at the majority of subsequent time points evaluated (Months 2, 3, 5–9, and 12; **Figure 1**).
- Cumulative mean numbers of active T2 lesions were numerically lower with IFN β -1a 22 μ g SC tiw than with placebo from Month 3 onwards, but the differences between the IFN β -1a 22 μ g SC tiw and placebo groups were not statistically significant (**Figure 1**).
- Over 24 months, the cumulative mean (SD) number of active T2 lesions was 6.8 (10.30) in the placebo group, 1.5 (4.27) in the IFN β -1a 44 μ g SC tiw group, and 1.8 (2.99) in the IFN β -1a 22 μ g SC tiw group (**Figure 1**).

Figure 1. Cumulative mean number of active T2 lesions per patient in the monthly MRI cohort.



Cumulative mean numbers of lesions at Months 1–9, 12, 18, and 24 do not include the numbers of lesions recorded in the pre-treatment baseline scans.

BL, baseline; IFN β -1a, interferon beta-1a; MRI, magnetic resonance imaging; SC, subcutaneously; tiw, three times weekly.

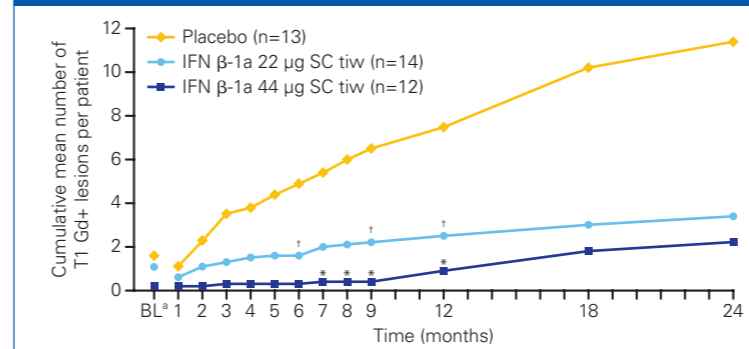
*The baseline data points show the mean number of active T2 lesions per patient recorded pre-treatment on Study Day 1 (or, if missing, at screening).

*p<0.05 for IFN β -1a 44 μ g SC tiw versus placebo. Post-baseline cumulative numbers of lesions were compared using negative binomial regression adjusting for the number of corresponding lesions at baseline.

T1 Gd+ lesions

- At baseline, the mean (SD) number of T1 Gd+ lesions was 1.6 (2.06) in the placebo group, 0.2 (0.39) in the IFN β -1a 44 μ g SC tiw group, and 1.1 (1.46) in the IFN β -1a 22 μ g SC tiw group (**Figure 2**).
- The cumulative mean number of T1 Gd+ lesions was numerically or statistically significantly lower with IFN β -1a 44 and 22 μ g SC tiw than with placebo at all time points evaluated after starting treatment; the difference between IFN β -1a 44 μ g SC tiw and placebo was statistically significant at Months 7–9 and 12, while the difference between IFN β -1a 22 μ g SC tiw and placebo was statistically significant at Months 6, 9, and 12 (**Figure 2**).
- Over 24 months, the cumulative mean (SD) number of T1 Gd+ lesions was 11.4 (17.92) in the placebo group, 2.2 (6.58) in the IFN β -1a 44 μ g SC tiw group, and 3.4 (5.49) in the IFN β -1a 22 μ g SC tiw group (**Figure 2**).

Figure 2. Cumulative mean number of T1 Gd+ lesions per patient in the monthly MRI cohort.



Cumulative mean numbers of lesions at Months 1–9, 12, 18, and 24 do not include the numbers of lesions recorded in the pre-treatment baseline scans.

BL, baseline; Gd+, gadolinium-enhancing; IFN β -1a, interferon beta 1-a; MRI, magnetic resonance imaging; SC, subcutaneously; tiw, three times weekly.

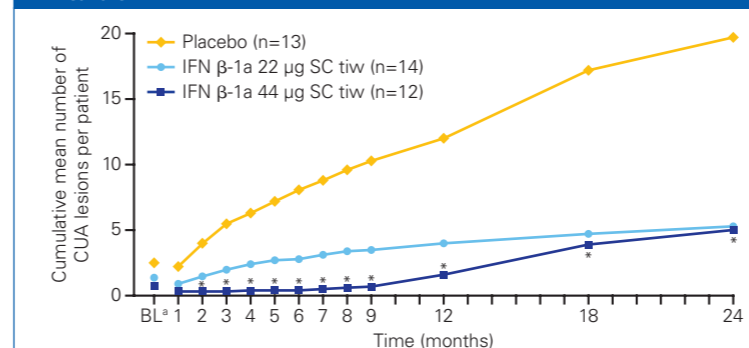
*The baseline data points show the mean number of T1 Gd+ lesions per patient recorded pre-treatment on Study Day 1 (or, if missing, at screening).

*p<0.05 for IFN β -1a 44 μ g SC tiw versus placebo. *p<0.05 for IFN β -1a 22 μ g SC tiw versus placebo. Post-baseline cumulative numbers of lesions were compared using negative binomial regression adjusting for the number of corresponding lesions at baseline.

CUA lesions

- At baseline, the mean (SD) number of CUA lesions was 2.5 (3.36) in the placebo group, 0.7 (0.98) in the IFN β -1a 44 μ g SC tiw group, and 1.4 (1.79) in the IFN β -1a 22 μ g SC tiw group (**Figure 3**).
- The cumulative mean number of CUA lesions was significantly lower with IFN β -1a 44 μ g SC tiw than with placebo as early as Month 2 and remained so at all subsequent time points evaluated (Months 3–9, 12, 18, and 24; **Figure 3**).
- The cumulative mean number of CUA lesions was numerically but not statistically significantly lower with IFN β -1a 22 μ g SC tiw than with placebo at all evaluated time points after starting treatment (**Figure 3**).

Figure 3. Cumulative mean number of CUA lesions per patient in the monthly MRI cohort.



Cumulative mean numbers of lesions at Months 1–9, 12, 18, and 24 do not include the numbers of lesions recorded in the pre-treatment baseline scans. CUA lesions are the sum of active T2 lesions and T1 Gd+ lesions, avoiding double counting.

BL, baseline; CUA, combined unique active; IFN β -1a, interferon beta 1-a; MRI, magnetic resonance imaging; SC, subcutaneously; tiw, three times weekly.

*The baseline data points show the mean number of CUA lesions per patient recorded pre-treatment on Study Day 1 (or, if missing, at screening).

*p<0.05 for IFN β -1a 44 μ g SC tiw versus placebo. Post-baseline cumulative numbers of lesions were compared using negative binomial regression adjusting for the number of corresponding lesions at baseline.

- Over 24 months, the cumulative mean (SD) number of CUA lesions was 19.7 (29.10) in the placebo group, 5.0 (15.44) in the IFN β -1a 44 μ g SC tiw group, and 5.3 (7.35) in the IFN β -1a 22 μ g SC tiw group (p<0.05 for IFN β -1a 44 μ g SC tiw vs placebo; **Figure 3**).

Conclusions

- In this cohort of 39 patients who underwent monthly MRI scans for 24 months, a significant reduction in the cumulative mean number of active T2 lesions with IFN β -1a 44 μ g SC tiw versus placebo was seen as early as 1 month after starting treatment and continued to be seen at Months 2, 3, 5–9, and 12.
- Cumulative mean numbers of T1 Gd+ lesions were significantly lower with IFN β -1a 44 μ g SC tiw than with placebo at Months 7–9 and 12 and significantly lower with IFN β -1a 22 μ g SC tiw than with placebo at Months 6, 9, and 12.
- A significant reduction in the cumulative mean number of CUA lesions with IFN β -1a 44 μ g SC tiw versus placebo was seen as early as 2 months after the start of treatment and continued to be seen at all subsequent time points evaluated up to and including Month 24.
- In patients receiving placebo, numbers of active lesions accumulated rapidly over 2 years. These findings highlight the importance of disease-modifying drug therapy in patients with RMS to reduce disease activity, which may be clinically silent.

References

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Disclosures

DL is the director of the UBC MS/MRI Research Group, which has been contracted to perform central analysis of MRI scans for therapeutic trials with Genzyme, Hoffmann-La Roche, Merck Serono, Nuron, Perspectives, and Sanofi-Aventis. He has acted as a consultant to Vertex Pharmaceuticals; has served on scientific advisory boards for Novartis, Nuron, and Roche; has served on a data and safety advisory board for Opexa; and has received research funding from the Canadian Institute of Health Research and Multiple Sclerosis Society of Canada. AT has acted as a consultant for Biogen, Genzyme, Roche, and Teva, and is Principal Investigator on clinical trials with Biogen, Chugai, Genzyme, and Roche. EW has acted as a consultant for EMD Serono, Inc.,* and Teva, and is Principal Investigator on a clinical trial sponsored by Alexion Pharmaceuticals. HZ is an employee of EMD Serono, Inc.,* Rockland, MA, USA. FD is an employee of EMD Serono, Inc.,* Billerica, MA, USA.

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