Predictive value of early MRI measures in patients with RRMS receiving interferon β-1a SC tiw or placebo: post hoc analysis of PRISMS data

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Introduction

• Magnetic resonance imaging (MRI) is an important component of diagnosis and monitoring the course of disease, as well as assessing the efficacy of treatment of patients with relapsing forms of multiple sclerosis (RRMS). However, databases containing a wide range of MRI measures are only available in a post hoc manner.

• Early on-treatment prediction of which patients will show long-lasting clinical response to therapy would offer considerable advantage in clinical practice. Previous research has included MRI measure monitoring groups of patients with RRMS treated with interferon beta (IFN) β-1a.

• PRISMS (Prognosis and Relapse-ability by Interferon β-1a Subcutaneously in Multiple Sclerosis) was a double-blind, placebo-controlled three times weekly trial that significantly reduced relapses and active T2 lesions, while significantly delaying disability progression in patients with RRMS. Monthly MRI scans in the primary MRI cohort showed the rapid onset of radiologically measured treatment effect compared with placebo. The 2-year extension of the PRISMS trials provide the opportunity to evaluate treatment effects over a longer follow-up period.

Objective

• To examine the predictive value of early clinical and MRI measures in patients with RRMS receiving interferon beta-1a SC tiw or placebo.

• Patients receiving IFN β-1a 44 µg SC tiw had relapsed, were compared using a similar model.

• In an analysis of the primary MRI cohort data, patients with SC tiw 22 µg group versus placebo trended toward statistically significant differences in future confirmed EDSS progression. However, patients with SC tiw 44 µg group versus placebo had no statistically significant differences in future confirmed EDSS progression (Figure 1A). No statistically significant differences were observed in any treatment group, with or without active T2 lesions at 6 months, in the presence or absence of active T2 lesions at 6 months, or in comparison of patients with or without active T2 lesions at 6 months in the placebo/delayed treatment group.

Methods

• Exploratory analyses were conducted on data from the PRISMS trial, in which patients with RRMS were randomly assigned to IFN β-1a 44 µg SC tiw or placebo for 2 years.

• In the 2-year extension phase, patients originally receiving placebo for 2 years in PRISMS were randomized to IFN β-1a 44 µg SC tiw or placebo for an additional 2 years. Patients receiving IFN β-1a 44 µg SC tiw group versus placebo for 2 years had no statistically significant differences in confirmed EDSS progression at 2, 3, or 4 years of follow-up, or in the delayed treatment group.

• In the overall PRISMS cohort, 146/187 (78%) patients in the placebo/delayed treatment group had ≥1 active T2 lesion at 6 months versus 168/197 (85%) in the IFN β-1a 44 µg SC tiw group, respectively.

• In comparisons between patients with or without active T2 lesions at 6 months, or those with or without confirmed EDSS progression at 2, 3, or 4 years, or those with or without active T2 lesions at 6 months, or patients with or without active T2 lesions at 6 months in the placebo/delayed treatment group.

Results

• S6 patients were recruted from 22 centers in 4 countries. Demographic and baseline patient characteristics are shown in Table 1.

• Patients with >1 active T2 lesion at 6 months had relapsed, were compared using a similar model.

Table 1. Demographic and baseline patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo/delayed n=188</th>
<th>IFN β-1a 44 µg SC tiw n=184</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.9 ± 11.7</td>
<td>41.5 ± 11.1</td>
</tr>
<tr>
<td>Female (%)</td>
<td>67.4</td>
<td>66.3</td>
</tr>
<tr>
<td>Race, white (%)</td>
<td>99.0</td>
<td>97.9</td>
</tr>
<tr>
<td>Mean (SD) EDSS score</td>
<td>2.0 (1.2)</td>
<td>1.8 (1.2)</td>
</tr>
<tr>
<td>Mean (SD) baseline EDSS</td>
<td>1.7 (1.4)</td>
<td>1.7 (1.4)</td>
</tr>
<tr>
<td>Baseline EDSS score</td>
<td>1.7 (1.4)</td>
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</tr>
</tbody>
</table>

• In a subanalysis of PRISMS data, patients with SC tiw 22 µg group versus placebo had no statistically significant differences in future confirmed EDSS progression (Figure 1B). However, patients with SC tiw 44 µg group versus placebo had no statistically significant differences in future confirmed EDSS progression at 2, 3, or 4 years of follow-up, or in the delayed treatment group. No statistically significant differences were observed in any treatment group, with or without active T2 lesions at 6 months, or in comparison of patients with or without active T2 lesions at 6 months, or in the placebo/delayed treatment group.

• No significant differences in percentages of patients who relapsed were statistically significant at 1 year (p=0.048) and 2 years (p=0.015) when comparing those with or without confirmed EDSS progression at 1 or 2 years, respectively. However, patients with SC tiw 44 µg group versus placebo/delayed treatment group at 1, 2, 3, and 4 years showed significantly greater disability progression than those with 0–1 lesion.

• In an analysis of the primary MRI cohort data, patients with SC tiw 22 µg group versus placebo had no statistically significant differences in confirmed EDSS progression at 2, 3, or 4 years of follow-up, or in the delayed treatment group.

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Discussion

• Patients receiving IFN β-1a 44 µg SC tiw protected from treatment regardless of presence/absence of active T2 lesions at 6 months. These patients relapsed at rates similar to patients in the placebo/delayed treatment group without Xeloda T2 lesions, who may be considered to have a relatively benign level of disease activity.

• Presence versus absence of active T2 lesions at 6 months showed no meaningful differences in future confirmed EDSS progression in either the placebo/delayed treatment or IFN β-1a 44 µg SC tiw group, although there was a clear trend towards difference between patients with versus presence versus absence of active T2 lesions in the placebo/delayed treatment group only.

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Conclusions

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