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Predictive Value of MRI Measures in Patients with Relapsing Multiple Sclerosis receiving IFN-β-1a SC tiw or IFN-β-1a IM qw: post hoc analyses of EVIDENCE data

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Introduction

In the placebo-controlled trials of interferon beta-1a (IFN-β-1a) administered subcutaneously (SC) three times weekly (tiw) and IFN-β-1a administered intramuscularly (IM) once weekly (qw) for treatment of relapsing forms of multiple sclerosis (MS), both arms were effective on clinical and magnetic resonance imaging (MRI) endpoints. 1,2 The randomized, head-to-head study demonstrated the superior efficacy and safety of IFN-β-1a SC tiw versus IFN-β-1a IM qw in reducing relapse and MRI disease activity over 24 and 48 weeks compared with IFN-β-1a IM qw in patients with MS.3

Post hoc analyses from the EVIDENCE study,3,4 demonstrated that mean numbers of combined unique active (CUA) MRI lesions were significantly reduced with IFN-β-1a SC tiw versus IFN-β-1a IM qw as early as 8 weeks after treatment initiation (14 ± 18 vs. 20 ± 29), based on a non-parametric analysis of variance (ANOVA) model.5

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Objective

To examine the predictive value of early MRI measures for achieving endpoints including NEDA at Week 48 in patients treated with IFN-β-1a SC tiw.

Methods

In the EVIDENCE trial, patients with RMS whose MRI scores went beyond IFN-β-1a 44 SC tiw (n=320) or IFN-β-1a 30 µg IM qw (n=138), with efficacy assessed at 24 and 48 weeks and with follow-up until all patients had completed at least 48 weeks of treatment, for an average of 64 weeks on study.2

Patients with RMS clinically defined or laboratory-supported, according to Poser's criteria, and Expanded Disability Status Scale (EDSS) scores of 0–5.5 had to have experienced at least 36 relapses in the 2 years prior to study entry.

The primary endpoint was the proportion of patients remaining free of relapses during the study.2

Screening, including MRI scanning with proton density/T2-weighted and T1-weighted post gadolinium T1-weighted sequences, took place 4 weeks prior to randomization and initiation of therapy.6

The dosage of IFN-β-1a SC tiw was up-titrated 8 µg per week in the first 2 weeks, 22 µg per week in the third and fourth weeks, and the full 44 µg per week was given for the remainder of treatment.7,8 The 30 µg IM qw was not up-titrated.

MRIs scores (t1)enth and without Gd enhancement and T2) were performed on Study Day 1 and every 4 weeks thereafter up to Week 24.2

– An ATR tiw was defined as a new or enlarging lesion.

– Gd-enhancing lesions (Gd+ lesions) were the sum of new enhancing lesions and T1 persistently enhancing lesions.

– A CUA (combined active lesion score was defined as an active lesion on the T1 Gd+ T2 scan, or both, avoiding double counting.

Table 1. Baseline demographic and disease characteristics

Patient Group Sensitivity Analysis *t Alpha β Gd+ baseline N (n=320) N (n=138) N (n=320) N (n=138) N (n=320) N (n=138)
Mechl (≥10) 10 (3.1) 30 (21.6) 13 (4.1) 28 (20.2) 11 (3.4) 24 (17.3)
Mechl (≥5) 9 (2.8) 10 (7.3) 8 (2.4) 12 (8.7) 7 (2.2) 12 (8.7)
Mechl (≥1) 10 (3.1) 30 (21.6) 10 (3.1) 30 (21.6) 10 (3.1) 30 (21.6)
Mechl (≥0) 10 (3.1) 30 (21.6) 10 (3.1) 30 (21.6) 10 (3.1) 30 (21.6)
Race, %
White 85 (25.1) 85 (25.1) 85 (25.1) 85 (25.1) 85 (25.1) 85 (25.1)
Black 15 (4.7) 15 (4.7) 15 (4.7) 15 (4.7) 15 (4.7) 15 (4.7)
Other 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)
**Sex, n (%)
Female 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3)
Female 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3) 180 (56.3)
Male 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5)
Male 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5) 120 (37.5)
**Other, n (%)
**Other, n (%)
**Value not applicable

Conclusions

In this active relapsing population, patients treated with IFN-β-1a SC tiw had fewer MRI lesions compared with IFN-β-1a IM qw, beginning shortly after treatment initiation. Despite the fact that IFN-β-1a SC tiw was gradually up-titrated to the full dose over 4 weeks, by Week 4, these lesions already significantly differed from those of MRI in patients receiving IFN-β-1a SC tiw versus those patients treated with IFN-β-1a IM qw.

These findings are supported by a post hoc post-hoc analysis of EVIDENCE, which demonstrated that the mean numbers of Gd+ lesions in patients receiving IFN-β-1a SC tiw versus those patients receiving IFN-β-1a IM qw at or beyond Week 4 weeks were more likely to achieve NEDA status at Week 48 versus treatment with IFN-β-1a IM qw, whether or not early lesions were present.

References


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Disclosures

ATH is an inventor and holds a pending patent application for NEDA as a MRI biomarker. BF: owns stock in Biogen, BI. PM: has potential personal financial relationships that could be perceived as constituting potential conflicts of interest (COIs): has received research support and travel support from Biogen, Boston, MA, and holds stock in Biogen, Boston, MA, and holds stock in Genzyme/Sanofi, New York, NY, USA.

EM: has potential personal financial relationships that could be perceived as constituting potential conflicts of interest (COIs): has received research support and travel support from Biogen, Boston, MA, and holds stock in Biogen, Boston, MA, and holds stock in Genzyme/Sanofi, New York, NY, USA.

PJM has potential personal financial relationships that could be perceived as constituting potential conflicts of interest (COIs): has received research support and travel support from Biogen, Boston, MA, and holds stock in Biogen, Boston, MA, and holds stock in Genzyme/Sanofi, New York, NY, USA.

AP is an inventor and holds a pending patent application for NEDA as a MRI biomarker. D. Magill, G. Burger, B. Dungan, SR: have nothing to disclose.

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