DX35

Evaluation of Peginterferon Beta-1a Tolerability Profile From the ADVANCE Study: Gaining Consensus Using the Delphi Technique

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INTRODUCTION

• The safety/tolerability profile of multiple sclerosis (MS) therapies may impact patient adherence to treatment and affect outcome.1,2

• ADVANCE was a 2-year, double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of peginterferon beta-1a 125 mcg subcutaneous administration every 2 or 4 weeks in patients with relapsing-remitting MS.3

• The study demonstrated that peginterferon beta-1a significantly reduced annualized relapse rate, magnetic resonance imaging lesion activity, and risk of relapse and disability progression vs. placebo.

• Flu-like symptoms (FLS) and injection site reactions (ISR) were reported with peginterferon beta-1a treatment.

• A better understanding of the characteristics and impact of FLS and ISR in MS patients based on experiences in the ADVANCE study using a consensus-generating Delphi technique.4

METHODS

• ADVANCE investigators with a predefined number of enrolled patients qualified the opportunity to participate in a consensus-generating process using modified Delphi methodology to identify areas that merit iterative rounds of questionnaires to build consensus.4

• Predefined patient number criteria: ≥ 2 enrolled patients in the United States and Western Europe (Germany, Spain, France, and United Kingdom) or ≥ 2 patients in the rest of the world.

• An independent steering committee of expert clinicians (n=4) convened to oversee the development of 2 Web-based (SurveyMonkey, www.surveymonkey.com) questionnaires with access provided through an e-mail link.

• Questionnaire 1 consisted of 150 questions designed to better understand the frequency, duration, impact, and management of FLS and ISR in MS patients treated with peginterferon beta-1a in ADVANCE.4

• Four question formats were used: Yes/no, multiple choice, ranking, and open-ended; both qualitative and quantitative techniques were used to analyze the results.

• For relevant questions, responders were asked to provide a response for 2 separate time periods: 0–3 months of treatment (within the first 3 months of treatment) and > 3 months of treatment.

• After completion and analysis of the first questionnaire, questionnaire 2 (15 questions) was designed to generate consensus on management as well as characteristics and impact of this side effect.

• Average rating (AR) of ≥ 2.7 based on the 4-point Likert scale was defined as a priori as the response level for consensus by the steering committee (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree).

• Here we report results on the characteristics and impact of FLS and ISR. Recommendations for the management of these side effects are presented in poster DX57.5

RESULTS

• A total of 30 ADVANCE investigators (i.e., Delphi responders) completed questionnaire 1, and 29 also completed questionnaire 2 (Figure 1).

• Responders came from academic (50%) and community (50%) settings, 83% were physicians, and the average time in practice was 20.4 years.

• Of 30 ADVANCE investigators, 20.4% were nurses, 30.0% were clinical research associates, 20.4% were research coordinators, and 19.4% were research assistants.

• In questionnaire 1, the majority (> 71%) of responders reported that the onset of FLS was 1–8 hours after dosing (Figure 2A).

• Eighty percent of responders (AR = 2.90) agreed that FLS may last up to 3 days following peginterferon beta-1a administration.

Onset and Duration of FLS

• In questionnaire 1, the majority (> 71%) of responders reported that the onset of FLS was 1–8 hours after dosing (Figure 2A).

• When asked about the duration of individual FLS episodes, 61% (0–3 months) and 79% (> 3 months) reported the duration to be ≤ 24 hours (Figure 2A).

• In questionnaire 2, a consensus was reached (AR = 3.72) that FLS generally last ≤ 24 hours (Figure 2A).

• Responders also agreed that for most patients, FLS have a mild to moderate impact on activities of daily living after the first 3 months of treatment (Figure 2B).

Onset and Duration of ISR

• Because the responses regarding onset and duration of ISR varied in questionnaire 1 (Figure 3), no additional questions on the characteristics of ISR were included in questionnaire 2.

• The impact of ISR on activities of daily living was reported to be minimal (AR = 3.48; Figure 4).

CONCLUSIONS

• Delphi responders agreed that FLS begin within 24 hours of peginterferon beta-1a administration and generally last ≤ 24 hours, although symptoms may last up to 3 days for some patients.

• Responders also agreed that for most patients, FLS have only mild to moderate impact on activities of daily living during the first 3 months of treatment followed by minimal impact after 3 months of treatment.

• The impact of ISR was reported to be minimal (AR = 3.48) throughout treatment.

• Delphi responders were a small subset of investigators who participated in this study and their observations were based only on the number of patients enrolled at their sites in a clinical study. Thus, these results should be confirmed after gaining more experience with peginterferon beta-1a in clinical practice.

• Recommendations for the management of FLS and ISR are reported in poster DX57.5

Impact of FLS and ISR on Patients’ Lives

• In questionnaire 2, agreement was reached (AR = 3.54) that for most patients, FLS have only mild to moderate impact on activities of daily living during the first 3 months of treatment followed by minimal impact (AR = 3.00) after 3 months of treatment (Figure 4).

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References


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