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 administered 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 would assist clinicians with improving patient adherence and could potentially improve treatment outcome for peginterferon beta-1a, which is approved for the treatment of relapsing MS.
- Here we report the characteristics and impact of peginterferon beta-1a treatment-related FLS and ISR in patients with MS based on experiences in the ADVANCE study using a consensus-generating Delphi technique.[4]

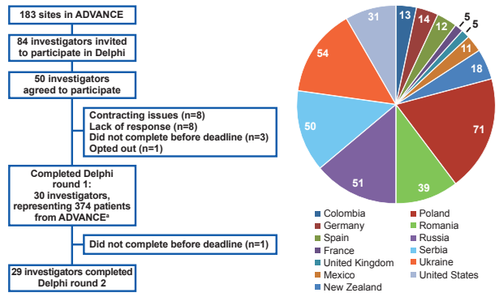
METHODS

- ADVANCE investigators with a predefined number of enrolled patients qualified for the opportunity to participate in a consensus-generating process using modified Delphi methodology that utilizes 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 ≥ 10 patients in the rest of the world.
- An independent steering committee of expert clinicians (n=4) was 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.
  - 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 these side effects.
  - An average rating (AR) of ≥ 2.7 based on the 4-point Likert scale was defined 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.

Figure 1. Survey responder distribution

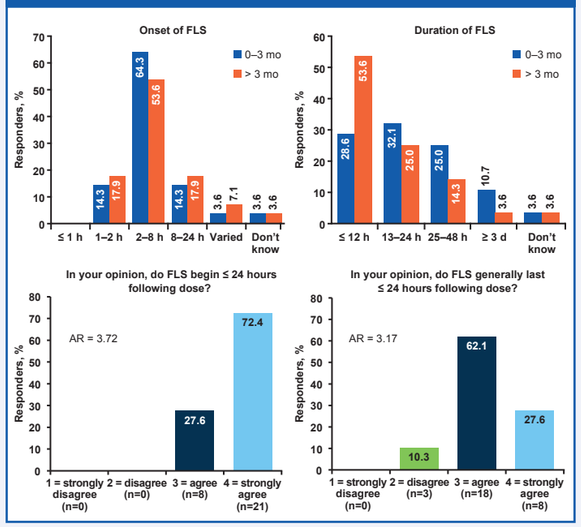


[a]Number of patients in each country.

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 begin within 24 hours and generally last ≤ 24 hours (AR = 3.17) following peginterferon beta-1a administration (Figure 2B).
  - Eighty percent of responders (AR = 2.90) agreed that FLS may last up to 3 days following peginterferon beta-1a administration.

Figure 2. Onset and duration of FLS



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.

Figure 3. Onset and duration of ISR

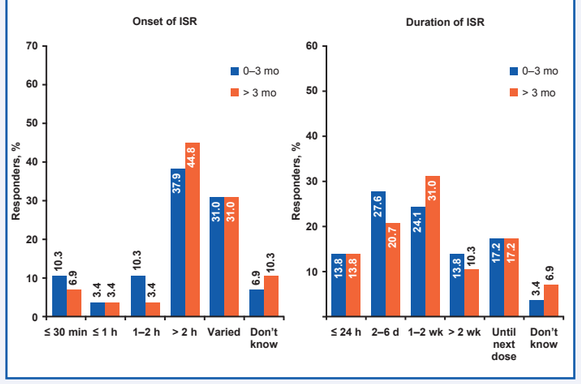
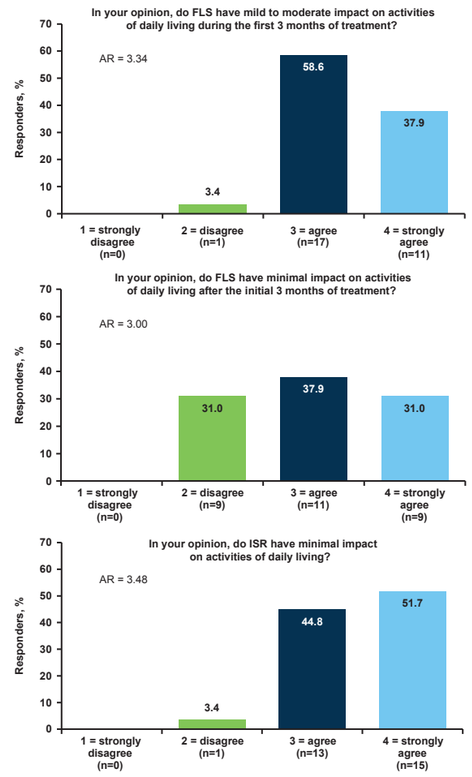


Figure 4. Impact of FLS and ISR on patients' lives



Impact of FLS and ISR on Patients' Lives

- In questionnaire 2, agreement was reached (AR = 3.34) 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).
- 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 the study and their observations were based only on the number of patients enrolled at their site 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]

References

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Disclosures

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