DX23

Application of the Delphi Technique for Evaluation of the Tolerability Profile of Peginterferon Beta-1a

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INTRODUCTION

- Adherence to interferon treatment for multiple sclerosis (MS) has been linked to improved treatment outcomes.[1]
- Reasons for poor patient adherence to prescribed MS therapy include frequency of administration and adverse events (AEs) such as flu-like symptoms (FLS) and injection site reactions (ISR) associated with interferon treatment.[2,3]
- Peginterferon beta-1a is a pegylated form of interferon beta-1a in development for the treatment of relapsing-remitting MS (RRMS).
- ADVANCE is a 2-year randomized controlled study. Results from Year 1 demonstrated that use of peginterferon beta-1a 125 mcg every 2 weeks (Q2W) or every 4 weeks (Q4W) in patients with RRMS significantly reduced relapse rate, risk of relapse, disability progression, and magnetic resonance imaging lesions compared with placebo.[4]
- The most common AEs in ADVANCE were FLS and ISR.[4]
- A better understanding of the impact and management of FLS and ISR associated with peginterferon beta-1a therapy would assist prescribers with improving patient adherence and potentially impact patient outcomes.

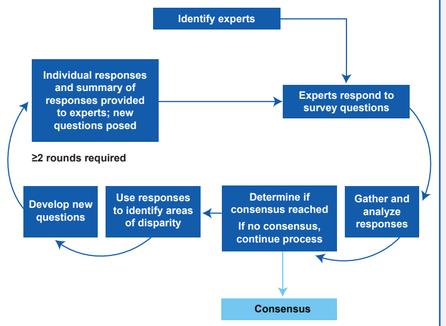
OBJECTIVE

- The objective of this study was to better characterize the FLS and ISR reported during ADVANCE and identify management strategies for these AEs.

METHODS

- The Delphi technique, a widely accepted methodology for obtaining consensus,[5] was selected to elicit the impact of peginterferon beta-1a–related FLS and ISR and determine effective management strategies from practitioners that participated in the ADVANCE trial.
  - The Delphi technique utilizes iterative rounds of questionnaires to build consensus (Figure 1).

Figure 1: The Delphi technique



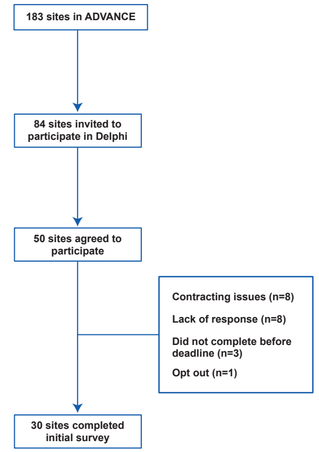
  - Data are obtained through expert responses. Questionnaires evolve as the process moves through the iterative rounds.
  - Ultimate goal is to reach consensus.
- A steering committee of practitioners (n=4) with substantial experience with peginterferon beta-1a oversaw the development of the initial survey questions.
  - Questions were designed to gain a better understanding of peginterferon beta-1a–associated FLS and ISR and their management.
  - This committee also provided input into the qualifications for investigator participation (experts).
- Inclusion criteria:
  - Involved in direct patient care at a site in the ADVANCE study.
  - Since the United States and Canada had fewer patients enrolled in ADVANCE, yet a good geographic representation was desired for this expert panel, the following inclusion criteria were applied:
    - Sites enrolled ≥ 2 patients (United States, Canada, western Europe) or ≥10 patients (rest of world).

RESULTS

Study sites

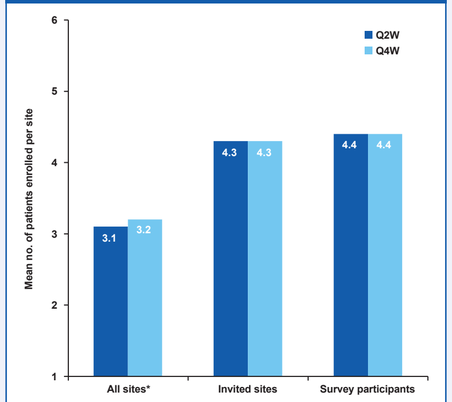
- Of the 183 sites that participated in ADVANCE, 84 sites met the inclusion criteria and were invited to participate (Figure 2).
  - 50 sites agreed to participate;
  - 30 sites completed the survey (participating sites)

Figure 2: Site participation



- In the 84 sites invited to participate, the mean number (standard deviation) of patients enrolled for Q2W and Q4W dosing were both 4.3 (3.8) (Figure 3).

Figure 3: Mean number of patients enrolled per study site



Q2W, every 2 weeks; Q4W, every 4 weeks.
*In Year 1 of ADVANCE.

- Based on date from Year 1 of ADVANCE, median time on peginterferon beta-1a was 337 days for both Q2W and Q4W dosing and was the same for invited and participating sites.

Demographics

- Patient demographics at Baseline were similar (Table 1).

FLS and ISR

- Table 2 provides an overview of the incidence of FLS and ISR among the Year 1 ADVANCE study participants, invited sites, and participating sites.

Survey response

- Study sites representing 374 patients in 13 countries (Figure 4).
  - Most of the patient population represented came from Poland, Ukraine, Russia, and Serbia.

Limitations

- Delphi study enrollment was complex due to individual country requirements and added time to the enrollment process.
- The first questionnaire closed in early May and sites that had not completed their enrollment activites were excluded from participation.

Next steps

- Initial survey responses will be analyzed.
- A second survey will be developed and disseminated to survey participants to try to create a consensus regarding best practices for management of FLS and ISR that can be shared with other clinicians.

Table 1: Patient demographics

Parameter	ADVANCE Q4W N=500	ADVANCE Q2W N=512	Invited sites Q4W N=344	Invited sites Q2W N=347	Participating sites Q4W N=122	Participating sites Q2W N=128
Mean (SD) age, y	36.4 (9.9)	36.9 (9.8)	36.4 (9.9)	37.4 (9.7)	35.3 (9.8)	35.9 (9.6)
Female, n (%)	352 (70)	361 (71)	249 (72)	250 (72)	85 (70)	87 (68)
White, n (%)	409 (82)	416 (81)	317 (93)	320 (92)	112 (92)	117 (91)
Asian, n (%)	56 (11)	59 (12)	0 (0)	1 (0.3)	0 (0)	1 (1)

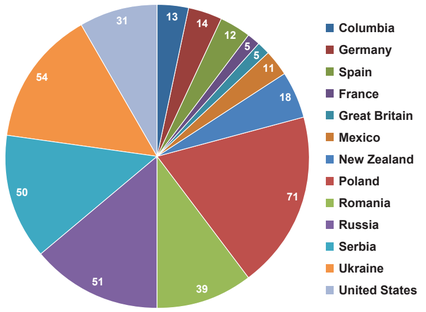
Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation.

Table 2: FLS and ISR

Parameter	ADVANCE Q4W N=500; n (%)	ADVANCE Q2W N=512; n (%)	Invited sites Q4W N=344; n (%)	Invited sites Q2W N=347; n (%)	Participating sites Q4W N=122; n (%)	Participating sites Q2W N=128; n (%)
FLS						
Patients with FLS	234 (46.8)	239 (46.7)	173 (50.3)	171 (49.3)	76 (62.3)	83 (64.8)
Use of symptomatic therapy for FLS	175/234 (74.8)	168/239 (70.3)	129/173 (74.6)	123/171 (71.9)	60/76 (79.0)	66/83 (79.5)
Discontinuation related to FLS	8 (1.6)	4 (0.8)	6 (1.7)	3 (0.9)	5 (4.1)	3 (2.3)
ISR						
Patients with ISR	298 (59.6)	336 (65.6)	222 (64.5)	240 (69.2)	86 (70.5)	99 (77.3)
Use of symptomatic therapy for ISR	24/298 (8.1)	35/336 (10.4)	18/222 (8.1)	20/240 (8.3)	3/86 (3.5)	7/99 (7.1)
Discontinuation related to ISR	3 (0.6)	5 (1.08)	3 (0.9)	4 (1.2)	2 (2)	1 (1)

FLS, flu-like symptoms; ISR, injection-site reactions; Q2W, every 2 weeks; Q4W, every 4 weeks.

Figure 4: Geographic distribution of participating sites* (patients/country)



*n=30 participating sites representing 374 patients from ADVANCE.

CONCLUSIONS

- Sites participating in this Delphi-based project to develop consensus regarding management of peginterferon beta-1a–associated FLS and ISR are representative of the ADVANCE study population.
- The recommendations of investigators from these sites will reflect substantive experience with peginterferon beta-1a and may have an impact on patient adherence to therapy and ultimately influence patient outcomes.

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Disclosures

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