DX15

Peginterferon Beta-1a via Autoinjector In Relapsing Multiple Sclerosis

Calabresi PA,[1] Hung S,[2] Deykin A,[2] Liu S,[2] Sperling B,[2] Seddighzadeh A[2]

[1]Johns Hopkins University, Baltimore, MD, USA; [2]Biogen Idec Inc., Cambridge, MA, USA

Fifth Cooperative Meeting of the Consortium of Multiple Sclerosis Centers and the Americas Committee for Treatment and Research in Multiple Sclerosis
May 29–June 1, 2013
Orlando, FL, USA

INTRODUCTION

- Despite recent approvals of new therapeutic agents for the treatment of multiple sclerosis (MS), there continues to be a high unmet medical need in this patient population for effective therapies that have an established long-term safety profile and are convenient; characteristics which may help to improve adherence to medication.[1]
- A single-use, disposable autoinjector is under development to simplify the process of subcutaneous (SC) self-injection of polyethylene glycol-modified (pegylated) interferon beta-1a (peginterferon beta-1a) from a pre-filled syringe (PFS).
- The pharmacokinetic and safety profiles of peginterferon beta-1a delivered by autoinjector or PFS have been shown to be similar in a Phase 1 healthy volunteer study.[2]
- Peginterferon beta-1a has also been tested in patients with relapsing MS in a recent pivotal Phase 3 trial – the ADVANCE study.[3]
  - After 1 year of treatment, compared with placebo, peginterferon beta-1a 125 µg (SC every 2 or 4 weeks) significantly reduced annualized relapse rate, new or newly enlarging T2 lesions, and the risk of relapse and disability progression, with a safety profile reflecting that of established interferon (IFN) beta-1a therapies.
- Here, we present data from a subset of patients participating in the ATTAIN study, an ongoing extension to the ADVANCE trial, that is examining the long-term efficacy and safety profile of peginterferon beta-1a.

OBJECTIVES

- The primary objective was to evaluate the safety and tolerability of the single-use autoinjector in a subset of patients with relapsing MS participating in the ATTAIN study.
- Additional objectives were to evaluate patient perceptions regarding ease-of-use of, and overall satisfaction with, the single-use autoinjector, along with a patient assessment of the clarity of the autoinjector training materials.

METHODS

Study Design

- ATTAIN is a multicenter, dose-frequency blinded extension study of the Phase 3, placebo-controlled, double-blind, multicenter ADVANCE study.[3]
- In this 8-week ATTAIN sub-study, a subset of patients self-administered peginterferon beta-1a (125 µg) or placebo SC every 2 weeks. For all patients, the first 2 injections used the manual PFS and the next 2 injections used the single-use autoinjector with peginterferon beta-1a or placebo.
  - Patients remained on the dose schedule to which they were assigned during the ADVANCE study (ie, active drug every 2 or 4 weeks) and continued to be blinded to dose frequency (each sub-study participant received 1 injection of peginterferon beta-1a or placebo every 2 weeks).
  - The autoinjector is a spring-powered injector, with an integrated, concealed needle and a medication window to visualize the PFS. It incorporates a needle guard that is deployed automatically when manually pushing down on the injector, and a visible indication of the initiation and end of each dosing administration step.

Patients

- Key inclusion criteria:
  - ADVANCE study participants who completed treatment up to Week 96
  - Key inclusion criteria for the ADVANCE study:
    - males and females aged 18–65 years
    - confirmed diagnosis of relapsing MS
    - baseline Expanded Disability Status Scale score ≤5.0
    - ≥2 relapses within the last 3 years and ≥1 relapse in the 12 months prior to randomization.
- Key exclusion criteria:
  - ADVANCE study participants who received their last dose of study treatment >2 weeks before entering the ATTAIN extension study
  - Key exclusion criteria for the ADVANCE study:
    - primary progressive, secondary progressive, or progressive MS
    - prior treatment with glatiramer acetate or IFN exceeding 4 weeks
    - discontinuation of IFN treatment <6 months prior to baseline.

Study Endpoints and Assessments

- Primary endpoints:
  - Incidence of adverse events (AEs) associated with the use of the single-use autoinjector
    - Safety and concomitant medication use were monitored throughout the study, with a follow-up assessment scheduled 8 weeks after the first injection
  - Patient assessment of injection pain score
    - Assessed using a Visual Analog Scale (where 0=no pain; 10=extremely painful) within 1 hour pre-injection, immediately post-injection, and at 30 and 60 minutes post-injection
  - Clinician assessment of injection site reactions
    - Clinicians at the study center assessed injection sites 1 hour pre-injection and within 1 hour post-injection. The injection site was examined for erythema, induration, temperature, and tenderness.
- Additional endpoints:
  - Ease-of-use profile of the single-use autoinjector
    - Patients completed an ease-of-use questionnaire following the final injection of the sub-study
  - Patient satisfaction with the single-use autoinjector
    - Patients completed an Autoinjector Satisfaction Questionnaire following the final injection of the sub-study
  - Patient assessment of the autoinjector training materials
    - Patients were trained in the proper use of the autoinjector prior to the first injection using the 'Instructions for Use' materials. Patients also undertook subsequent practice sessions using an injection pad
    - After completion of the first administration of treatment using the autoinjector, patients completed an Assessment of Training Materials questionnaire.

Patient Populations

- Data from all patients enrolled in the sub-study were included in the analysis of safety and questionnaire outcome measures.
- As data for patient assessment of injection pain and clinician assessment of injection-site reactions were summarized for each injection, only patients who received injections using the planned schedule of devices were included (ie, the first 2 injections used the manual PFS and the next 2 injections used the peginterferon beta-1a or placebo autoinjector).

Data Analysis

- Safety and tolerability data were summarized separately for PFS and autoinjector injection periods.
- Questionnaire data were summarized using basic statistics.
- This study was not powered for formal statistical analyses.

RESULTS

Patients

- In total, 39 patients were enrolled, all of whom completed the study treatment, and received 2 injections with the PFS and 2 injections with the autoinjector. Patient demographics are presented in Table 1.

Table 1: Patient demographics and baseline clinical characteristics

	Total (N=39)
Age, years, mean (SD)	40.92 (9.77)
Gender, female, n (%)	26 (67)
BMI, kg/m^2, mean (SD)	24.73 (4.66)
Race, Caucasian, n (%)	39 (100)
EDSS score, mean (SD)	2.68 (1.40)

BMI = body mass index; EDSS = Expanded Disability Status Scale; SD = standard deviation.

Safety and Tolerability

- The incidence of AEs was similar when peginterferon beta-1a was administered via PFS or autoinjector, with the majority of AEs being mild/moderate in severity (Table 2).

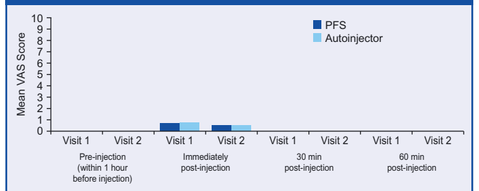
Table 2: Summary of AEs

AE incidence, n (%)	PFS (N=39)	Autoinjector (N=39)
Any AE(s)	27 (69)	23 (59)
AE severity		
Mild	10 (26)	8 (21)
Moderate	15 (38)	14 (36)
Severe	2 (5)	1 (3)
Any treatment-related event	24 (62)	22 (56)
Any AE leading to withdrawal	0 (0)	0 (0)
Any SAEs	2 (5)[a]	1 (3)[b]
Most common AEs[c]		
Pyrexia	13 (33)	13 (33)
Injection site erythema	11 (28)	9 (23)
Headache	5 (13)	7 (18)
Influenza-like illness	7 (18)	6 (15)
Injection site pain	9 (23)	6 (15)
Myalgia	7 (18)	6 (15)
Arthralgia	4 (10)	5 (13)
Chills	6 (15)	5 (13)

[a]MS relapses; [b]MS relapse and ureterolithiasis. [c]AEs occurring in ≥10% of patients (by preferred term).
AE = adverse event; PFS = pre-filled syringe; SAE = serious AE.

- A similar number of patients reported experiencing injection-site pain for injection via PFS and autoinjector (n=21 and n=19 vs n=23 and n=19, respectively, for injections 1 and 2).
  - The majority of these patients indicated that pain occurred at 'needle in' (for injections 1 and 2: PFS 36% and 31%; autoinjector 28% and 26%, respectively) and 'during injection' (for injections 1 and 2: PFS 26% and 23%; autoinjector 33% and 21%, respectively).
- Following injection with the autoinjector and the PFS, mean pain score was low, below 1.0 (out of 10) up to 60 minutes post-injection (Figure 1).
- Clinician injection-site assessments within 1 hour post-injection indicated no reports of erythema, induration, tenderness or local temperature increases following injection with the autoinjector; a single case of mild erythema was reported at first injection via the PFS.
- Given the low pain levels and absence of injection site reactions overall, treatment administered did not affect patient or clinician responses (approximately 25% of injections were placebo).

Figure 1: Mean pain scores following injection with the PFS and single-use autoinjector

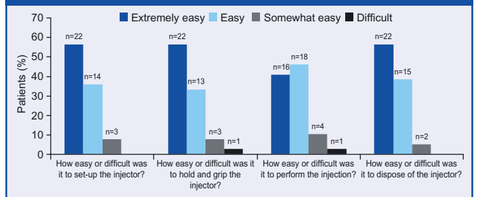


N=39 provided pain scores at each visit; PFS = pre-filled syringe; VAS = visual analogue scale.

Ease-of-use and patient satisfaction with the single-use autoinjector

- The majority of patients indicated that the single-use autoinjector was 'extremely easy' or 'easy' to set-up (92.3%), hold and grip (89.7%), perform injections with (87.2%), and dispose of (94.9%; Figure 2).

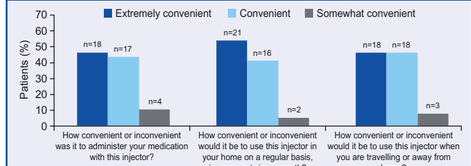
Figure 2: Patient responses to ease-of-use questions for the single-use autoinjector



N=39 completed the questionnaire; Frequency of patient response is shown above each bar; No patients indicated 'extremely difficult' in response to the questions.

- The majority of patients indicated that the single-use autoinjector was 'extremely convenient' or 'convenient'; none of the patients reported that the device was 'inconvenient' to use (Figure 3). Most patients (89.8%) rated their overall satisfaction with the autoinjector as 'extremely satisfied' or 'satisfied'; 87.2% of patients indicated that they would be 'extremely likely' or 'likely' to continue using the autoinjector to administer their medication.
- When reviewing the autoinjector training materials:
  - 95% of patients reported that they were 'very easy' (57.9%) or 'somewhat easy' (36.8%) to understand
  - 95% of patients reported that they were 'extremely satisfied' (47.4%) or 'somewhat satisfied' (47.4%) with the level of detail provided
  - 90% of patients reported that they were 'extremely satisfied' (57.9%) or 'somewhat satisfied' (31.6%) with the organization and presentation
  - overall, 92% of patients felt that the printed instructions were 'very effective' (63.2%) or 'somewhat effective' (28.9%) in educating patients on the use of the autoinjector.

Figure 3: Patient responses to convenience questions for the single-use autoinjector



N=39 completed the questionnaire; Frequency of patient response is shown above each bar; No patients indicated 'inconvenient' or 'extremely inconvenient' in response to the questions.

CONCLUSIONS

- In patients with relapsing MS, the safety profile of peginterferon beta-1a was similar when delivered using an autoinjector or a PFS; AEs were generally mild/moderate in severity.
- Clinicians and patients reported a similar tolerability profile when peginterferon beta-1a was administered using an autoinjector or a PFS; pain scores were low post-injection with the autoinjector, with no reports of clinician-assessed injection-site reactions.
- Patients perceived the single-use autoinjector to be easy to use and convenient; overall patient satisfaction with the autoinjector and accompanying training materials was high.
- Delivery of peginterferon beta-1a via a single-use, disposable autoinjector may simplify the injection process for MS patients who require long-term therapy.

REFERENCES

1. Devonshire V, Lapierre Y, Macdonell R, et al. *Eur J Neurol* 2011;18:69–77.
2. Hu X, Liu S, LaVallee N, et al. Poster presentation at AAN, March 16–23, 2013 San Diego, CA, USA (P01.163).
3. Calabresi PA, Kieseier B, Arnold DL, et al. Platform presentation at CMSC, May 29 - June 1, 2013 Orlando, FL, USA (DX05).

DISCLOSURES

PAC has provided consultation services to Abbott, and Vertex; received grant support from Novartis, Biogen Idec, Vertex, Abbott, and Bayer. SH, AD, SL, BS and AS: employees of Biogen Idec.

ACKNOWLEDGMENT

This study was sponsored by Biogen Idec (Cambridge, MA, USA). Writing and editorial support for the preparation of this poster was provided by Shelley Davies PhD, a professional medical writer contracted to CircleScience (Tytherington, UK); funding was provided by Biogen Idec.

For an electronic version of this poster, please scan code.

biogen idec