INTRODUCTION

• ALLOW was a Phase 3b, multi-center, randomized, parallel arm study to characterize flu-like symptoms (FLS) in patients transitioning from interferon (IFN) beta therapies to peginterferon beta-1a.

• Excluded 4-week key adverse event history, defined as either (1) overall FLS mean severity score over 48 weeks; (2) mean of FLS onset 12–13 hours after injection; (3) no clinically meaningful difference in Patient Determined Disease Steps (PDDS) for those patients completing the trial; (4) adverse event (AE) incidence consistent with the Phase 1 trial ADVANCE.

• Peginterferon beta-1a was well tolerated with an excellent safety profile in IFN-experienced patients.

OBJECTIVES

• To evaluate the incidence and severity of FLS in patients with RMS transitioning from non-pegylated IFN treatment to peginterferon beta-1a and the impact of prophylactic naproxen on FLS.

METHODS

Study inclusion/exclusion criteria were the following:

- Inclusion criteria: patients aged 18–65 with RMS who had been treated with a FL.
- Exclusion criteria: patients with progressive forms of multiple sclerosis, as well as certain pre-defined clinical and laboratory criteria.

- The primary endpoint was the proportion of patients experiencing new or worsening FLS over 48 weeks and impact of naproxen (500 mg twice daily) on FLS.
- Secondary endpoints included the following:
  - FLS severity over 48 weeks and impact of naproxen (500 mg twice daily) on FLS.
  - The onset and duration of FLS following injection with peginterferon beta-1a.
  - The incidence of AEs for the internal population over 48 weeks.
  - PDDS, a walking self-assessment scale that ranges from normal (0) to bedridden (+6), was evaluated at baseline, 12-weeks, and 48 weeks.

RESULTS

Patient Demographics

- Baseline patient characteristics were balanced between the two arms. Although demographics were representative of the RMS population, the average age was older than that enrolled in previous peginterferon beta-1a clinical trials, reflective of a treatment experienced population (Table 1).

- Of 261 patients who were randomized, 91.6% within each arm were completed the study.

Primary Endpoint

- A majority (88.6%) of patients did not experience new/worsening FLS events during the first 3 weeks of administering peginterferon beta-1a.
- New or worsening FLS was defined as ≥2 increase in FLS score from FLS score at screening prior to initiation of peginterferon beta-1a.

Secondary Endpoints

- FLS severity remained low across all study populations through Week 48, with a majority of FLS being mild to moderate (Figure 1).
- Prophylaxis regimen did not reduce FLS severity compared to current FLS regimen.
- Following injection, overall FLS onset occurred between 12.0 and 12.8 hours (mean), and lasted for a median of 12.3 hours (Figure 2).

- The most common AEs were injection-site-itch, injection-site reaction (IRR), and influenza-like illness (Table 3).

- In total, 13.5% of patients discontinued due to an AE, with 6% discontinuing due to IFN and 2.5% due to FLS (data not shown).
- PDDS scores from baseline to Week 48 was similar (0.53 to 0.34, respectively, with 0 = normal and 1 = mild disability; Figure 4).

CONCLUSIONS

• Peginterferon beta-1a demonstrated a similar safety and tolerability profile in the ALLOW study compared with ADVANCE in patients with RMS.
  - 98% of patients did not experience new or worsening FLS – primary endpoint.
  - Majority of FLS and IRR AEs were mild to moderate, with 2.5% of patients discontinuing for FLS and 6% of patients discontinuing for IRR.
  - FLS mean onset time after injection was 12–13 hours.
  - Median duration was 17 hours.

Naproxen 500 mg twice daily regimen did not significantly reduce FLS severity, onset time, nor duration compared to current FLS regimen (10.2% moderate and severe compared to 14.8% moderate and severe).

• Naproxen (500 mg twice daily) was not well tolerated for AE.

• Prophylaxis (500 mg twice daily) was not well tolerated for AE.

• No significant increase in mean walking disability (PDDS) was reported by any patient in the current study compared to baseline (PDDS baseline = 7.0, 95%CI 6.7, 7.2).

• Numbers of subjects who reported symptom: Table 2.

• PDDS = Patient Determined Disease Steps.

REFERENCES


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Disclosures

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