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Persistence, adherence, and quality of life in patients treated with an intramuscular interferon beta-1a autoinjector in a real-world clinical setting

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BACKGROUND

- Intramuscular interferon beta-1a (IM IFNβ-1a) was first approved in 1996 for treatment of relapsing forms of multiple sclerosis (MS) and is currently approved in more than 80 countries.
  - As of March 31, 2013, approximately 429,650 patients have been treated with IM IFNβ-1a, totaling 1,756,700 cumulative person-years of exposure.[1]
- MS affects the central nervous system and can cause impairment of motor functions.
  - Loss of motor coordination may limit a patient's ability to self-administer parenteral treatments such as IM IFNβ-1a.
- Simplifying the IM injection procedure may enable MS patients to self-administer IM IFNβ-1a more easily and may provide the following benefits:
  - Increased patient persistence and compliance with therapy.
  - More freedom to self-inject and a greater sense of control for patients.
  - Enhanced patient satisfaction and quality of life (QOL) for patients receiving chronic therapy.
- The AVONEX PEN® (once-weekly IM IFNβ-1a autoinjector) was approved for the treatment of MS in the European Union in 2011 and in the United States in 2012.[2,3]
  - In a phase 3b study of 74 patients with MS initially treated with manual injection and subsequently switched to autoinjection for 4 weeks, patients preferred the AVONEX PEN over manual injection.[4]
- The PERSIST study provides additional data from a broad range of patients initiating therapy with the AVONEX PEN to assist clinicians in selecting appropriate patients to receive this device as well as to identify factors that influence compliance.

OBJECTIVE

- Report 12-month final persistence, adherence, convenience, and tolerability data from the PERSIST study

METHODS

- PERSIST was a global, prospective, observational, open-label, 12-month phase 4 study of MS patients administering IM IFNβ-1a therapy (30 µg once weekly) by autoinjector.
- Patients enrolled in PERSIST were required to meet the following inclusion criteria:
  - Able to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information in accordance with national and local patient privacy regulations.
  - Satisfy the locally approved therapeutic indications for the AVONEX PEN.
  - Had the decision to initiate treatment with the AVONEX PEN reached by their physician prior to enrollment.
  - Have made no more than 2 injections with the AVONEX PEN prior to enrollment.
- Physician-reported persistence was assessed at 6 and 12 months; patient-reported compliance data were collected monthly.
- Outcomes evaluated at 3, 6, and 12 months include patient-reported tolerability, ease of use, satisfaction, fear of injection, and QOL. Patient-reported outcomes were measured with the following tools:
  - An injection site pain questionnaire.
  - An injection site reaction (ISR) questionnaire.
  - The AVONEX PEN instructions grading scale.
  - An ease-of-use grading scale.
  - A patient assessment of injection procedure.
  - A patient satisfaction questionnaire.
  - A fear-of-injection scale.
- Safety data were collected for all patients enrolled.

Statistical analysis

- To determine the sample size for this study, it was assumed that the persistence rate at the end of 12 months would be 68%; enrolling 250 patients would provide a 2-sided 95% confidence interval extending out 5.8% from the assumed persistence rate. Allowing for a 10% dropout rate, approximately 280 patients would be enrolled.
- The efficacy data presented are from a protocol-specified intent-to-treat (ITT) population, defined as those who were enrolled in the study and for whom data on the first AVONEX PEN injection were available.
- Data collected at each scheduled time point were tabulated using frequency distributions and/or basic summary statistics (mean and standard deviation [SD]).

RESULTS

Patients

- A total of 274 MS patients were enrolled in PERSIST; 234 (85.4%) had data from the first injection visit and were included in the ITT population.
  - At the final data cutoff on November 25, 2013, 184 of 234 patients in the ITT population (78.6%) had completed their 12-month visit.
  - Data analyzed and presented include complete 6-month data (n=190) and final 12-month data (n=184) from the ITT population; analyses of secondary endpoints are based on data collected from relevant patient-completed questionnaires.
- Baseline demographics and disease characteristics for patients in PERSIST were broadly comparable with contemporary MS trials (Table 1).

Table 1: Baseline demographics and disease characteristics

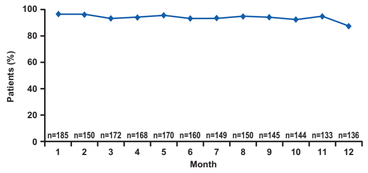
Enrolled	N=274
Age, mean (SD), years	43.0 (10.4)
Female, n (%)	208 (75.9)
White, n (%)	254 (92.7)
Disease duration, mean (SD), years	6.1 (6.2)
Patients with prior DMT use, n (%)	190 (69.3)
Duration of prior DMT use, mean (SD), months	45.8 (41.0)

DMT=disease-modifying therapy.

Persistence, compliance, and adherence

- At 6 months, 178 of 190 patients (93.7%) remained on the AVONEX PEN. Persistence at 12 months was similar (182 of 188 patients [96.8%]).
- Overall compliance, defined as not missing any injections, was 81.4% (171 of 210 patients) through month 6 and 74.6% (159 of 213 patients) through month 12.
  - The proportion of patients missing less than 20% of injections over both the first 6 and the first 12 months of PERSIST was 96.2% (202 of 210 and 205 of 213, respectively).
- Patient-reported adherence ranged from 87.5% to 96.2% over 12 months (Figure 1).
  - The 3 most common patient-reported reasons for missed injections were flu-like symptoms, not feeling like taking the injection, and forgetting to administer the injection.

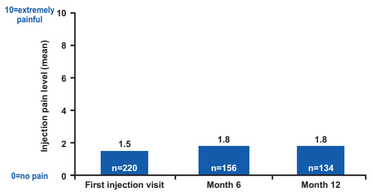
Figure 1: Patient-reported adherence in PERSIST



Tolerability

- Injection pain was measured on a scale of 0 (no pain) to 10 (extremely painful).
- The injection pain level at the first injection visit was low and remained low to month 12 (Figure 2).
- At 6 months, 116 of 160 patients (72.5%) reported injection-related pain levels ≤2. Similarly, at 12 months, 100 of 134 patients (74.6%) reported injection-related pain levels ≤2.

Figure 2: Patient-reported injection pain level



- Most patients (71.1% [108 of 152] at month 6 and 73.5% [100 of 136] at month 12) reported no ISRs; 0.9% (2 of 234) discontinued the study due to ISRs. Table 2 shows the incidence of ISRs experienced by patients in PERSIST.

Table 2: Incidence of ISRs in PERSIST at months 6 and 12

	No. (%) of patients	
ISR	Month 6 (n=152)	Month 12 (n=136)
Any ISR	44 (28.9)	36 (26.5)
Bruising	23 (15.1)	25 (18.4)
Pain	21 (13.8)	16 (11.8)
Redness	13 (8.6)	6 (4.4)
Swelling	4 (2.6)	5 (3.7)
Inflammation	1 (0.7)	1 (0.7)
Itching	3 (2.0)	4 (2.9)
Rash	2 (1.3)	0

Patient satisfaction

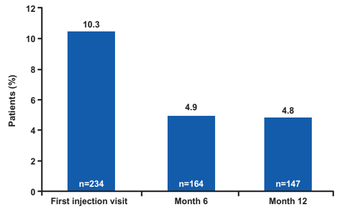
- The majority of patients (96.9% [157 of 162] at 6 months and 94.9% [129 of 136] at 12 months) reported being very satisfied or satisfied with the AVONEX PEN.
- Patient ratings of the reasons for satisfaction with the AVONEX PEN, assessed at 6 and 12 months, are listed in Table 3.

Table 3: Reasons for satisfaction with the AVONEX PEN

	No. (%) of patients	
Key feature of injection experience	Month 6 (n=162)	Month 12 (n=136)
Ease of use	136 (84.0)	111 (81.6)
Ease of preparation	128 (79.0)	111 (81.6)
Convenience	102 (63.0)	95 (69.9)
Injection comfort	98 (60.5)	78 (57.4)
Time required	94 (58.0)	83 (61.0)
Reduces fear about taking injections	89 (54.9)	81 (59.6)
Instructions for use	53 (32.7)	44 (32.4)

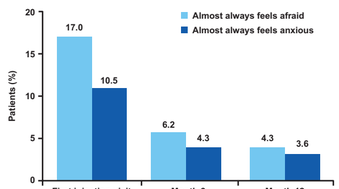
- Of the 5.1% of patients who were dissatisfied with the AVONEX PEN at 12 months, the reasons given most often included the device's being too difficult to use, the device's producing too forceful an injection, and bruising with the device.
- Autoinjection with the AVONEX PEN was reported to be easy or very easy by 154 of 188 patients (81.9%) at their first injection visit, 132 of 149 patients (88.6%) at month 6, and 112 of 127 patients (88.2%) at month 12.
  - At 6 and 12 months, of the patients who reported difficulty with the AVONEX PEN, most reported difficulty in injecting.
- The number of patients requiring injection assistance from a caregiver decreased from the first injection visit to month 12 (Figure 3).

Figure 3: PERSIST patients who required injection assistance by a caregiver



- The proportion of patients reporting fear of injection decreased over 12 months, as did the proportion of patients reporting anxiety about the injection (Figure 4).

Figure 4: Injection fear and anxiety reported by patients in PERSIST



- Of the patients who read the directions for use at their first injection visit (n=120), the majority reported that the directions were helpful or very helpful (84.2% [101 of 120]) and/or easy or very easy to understand (79.2% [95 of 120]); 86.7% (104 of 120) were satisfied or very satisfied with the level of detail provided.

CONCLUSIONS

- Final data for PERSIST patients at 6 and 12 months demonstrate a high level of compliance and persistence and thus adherence to therapy administered with the AVONEX PEN.
- Patients using the AVONEX PEN were less in need of injection assistance from a caregiver.
- The AVONEX PEN was well tolerated and was perceived by patients as easy to use.
- Patients reported being highly satisfied with the AVONEX PEN; fear and anxiety about injection decreased over time.
- These data support findings from previous studies evaluating the AVONEX PEN.[4]
- A potential study limitation was that several assessments were self-reported, resulting in incomplete data, under- or overestimation, and recall bias.

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