Subcutaneous interferon β-1a treatment of pediatric multiple sclerosis

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4th International Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) and the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS): 30 May–2 June 2012: San Diego, California, USA

Background

- Although patients with multiple sclerosis (MS) typically present with first symptoms when they are aged 20-40 years, disease onset occurs before the age of 16 years in 2-3% of patients, and before the age of 10 years in 1%.
- The risk of developing pediatric MS is estimated to be 1-2% in the general population and 3-6% in high-risk subpopulations.
- Results from cohort studies and isolated case reports have shown interferon β-1a (IFN β-1a) to be effective in pediatric MS populations, and interferon β-1a is being offered as a disease-modifying therapy for the treatment of pediatric MS. However, data from large pediatric controlled trials are lacking, and no placebo-controlled studies have been conducted.

Objective

- To review the safety, tolerability, and efficacy of subcutaneous (SC) IFN β-1a in children and adolescents with demyelinating events, using retrospective data from medical records.

Methods

Study design

- This was a single-center, retrospective, multinational study in patients who had received 1 injection of IFN β-1a for demyelinating events before the age of 16 years.
- Anonymized data were retrieved from medical health-care records collected between 1987 and 2009.
- The observation period for an individual patient began at the first medical record available on site and ended on the date of last follow-up at the site on December 31, 2009, whichever occurred first.
- Eligibility requirements were that patients must have started IFN β-1a therapy before 30 June 2009 and had at least 12 months of observation.
- To minimize the potential bias inherent in retrospective patient selection, every effort was made to assess all patients treated with SC IFN β-1a in participating centers.

Outcomes

- Safety and tolerability outcomes were:
  - Prescribed medical events (PMEs), defined as the known safety profile of SC IFN β-1a, which occurs after initiation of SC IFN β-1a treatment.
  - All serious MSAs that occurred after initiation of SC IFN β-1a treatment.
  - Non-serious MSAs considered by the investigator as related to SC IFN β-1a treatment.
  - Laboratory parameters (laboratory test results, thyrotropin, and hematology).
- Efficacy outcomes included changes in confirmed clinical activity, defined as the emergence of new neurological symptoms and signs in the 30 days after the previous event that persisted for >24 hours in the absence of an intercurrent illness.

Analyses

- Safety and tolerability outcomes were assessed for all patients in the study analysis set (TAS).
- Efficacy outcomes were evaluated only in patients with at least 12 months of follow-up.
- Two age categories were defined based on age at initiation of SC IFN β-1a:
  - Children: aged 2-12 years.
  - Adolescents: aged 12-18 years.
- All analyses were descriptive.

Results

- A total of 307 patients from 18 centers were included in the TAS: 65 (21.1%) from Russia, 98 (32.1%) from France, 23 (7.5%) from Canada, 23 (7.5%) from Tunisia and Vanuatu, and 131 (42.5%) from the USA. Two patients were collected but not included in the TAS at the age of 10 years at the time of IFN β-1a initiation could not be confirmed.
- Of the 305 patients, 289 had a final diagnosis of MS and were included in the MSA.
- Patient and disease characteristics at the first demyelinating event and MS disease history are presented in the Table 1.
- Median length of observation time for the TAS was 3.7 (0.4-16) years.

Table 1: Patient and disease characteristics at first demyelinating event and MS disease history (total analysis set).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age at MS diagnosis</td>
<td>11.8 (6.1, 15.4) years</td>
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<tr>
<td>Gender</td>
<td>Male: 36.0%, Female: 64.0%</td>
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<tr>
<td>Race</td>
<td>White: 67.0%, Non-white: 33.0%</td>
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<tr>
<td>MS course history</td>
<td>Relapsing-remitting: 73.4%, Primary progressive: 10.4%, Secondary progressive: 16.2%</td>
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<tr>
<td>MS disease history</td>
<td>Yes: 55.1%, No: 44.9%</td>
</tr>
<tr>
<td>Duration of MS disease history</td>
<td>1.8 (0.3, 4.1) years</td>
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Safety and tolerability of SC IFN β-1a

- During the observation period, the mean treatment duration was 2.2 (0.1-11.1) years, median length: 1.3 (0.1-11.1) years.
- 92% (275/300) of patients were treated for >6 months and 89.3% (263/295) for >12 months.
- A total of 199 patients permanently discontinued IFN β-1a therapy during the observation period:
  - Reasons for discontinuation were: clinical reasons (58.7%), parental decision (40.2%), other reasons (1.1%).
- Safety and tolerability outcomes were:
  - 18 (5.9%) patients had severe events: 16 (5.9%) events accounted for by 14 (4.6%) patients. A total of 6 (2.0%) patients showed persistent interferon β-1a treatment-related adverse events (Table 2).
  - 16 (5.2%) patients had serious MSAs: 16 (5.2%) events accounted for by 14 (4.6%) patients. A total of 6 (2.0%) patients showed persistent interferon β-1a treatment-related adverse events (Table 2).

Conclusions

- This is the first systematically described case series to provide real-world data on the safety and tolerability of SC IFN β-1a in pediatric patients with MS.

Efficacy of SC IFN β-1a

- The cumulative rate of medically confirmed attacks decreased after the initiation of SC IFN β-1a treatment (Figure 1).
- The median time to the first medically confirmed attack after starting SC IFN β-1a therapy was 19.5 months (Figure 2).

References