Oral Disease Modifying Therapies in Pediatric Multiple Sclerosis: A US Network Experience

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Background

- Disease modifying therapies (DMTs) are known to reduce relapses and delay disability in multiple sclerosis.
- DMTs have traditionally been administered parenterally.
- New oral DMTs have been recently FDA approved for the treatment of adults with MS.
- Little is known about the safety, tolerability and efficacy of this new therapy in the pediatric population.

Objectives

- To evaluate safety, tolerability and preliminary efficacy of the new FDA approved oral DMTs in pediatric MS patients.

Methods

- Retrospective longitudinal study design within the US Network of Pediatric MS Centers (USNPMSC).
- Pediatric MS patients who initiated one of the 3 new FDA approved oral DMTs: fingolimod, dimethyl fumarate and teriflunomide for at least one dose before 18 years of age were included in this study.
- Data compiled from a database at the Data Coordinating & Analysis Center for USNPMSC.

RESULTS

Oral DMT patients were identified in the USNPMSC Pediatric MS and Other Demyelinating Diseases database in April 2014. The data compiled below is abstracted as of August 18, 2014 (median of 9 months follow-up).

- 28 patients were identified across 7 participating sites. Eight patients received fingolimod, 17 received dimethyl fumarate, and 3 received both oral DMTs. Twenty-three patients were previously treated with other DMTs and 5 were treatment naive.
- Prior to oral DMTs, there were a total of 49 relapses. After starting oral DMTs, there were a total of 14 relapses.
- Follow-up time prior to oral DMT: 55.7 patient-years
- Follow-up time after oral DMT: 21.6 patient-years
- Overall relapse rate prior to oral DMT was 0.879 relapses per patient-year.
- Overall relapse rate after start of oral DMT was 0.653 relapses per patient-year.

Demographics

- Total number of patients in cohort: 28
- Male/Female ratio: 1:1.8
- Race:
  - Black: N=7
  - White: N=17
  - Mixed/Other: N=4
- Ethnicity:
  - Hispanic: N=6
  - Not Hispanic: N=21
  - Unknown: N=1
- Age:
  - Median: 14.3 years
  - Mean (SD): 13.8 years (3.4)
  - Min, Max: 3.32, 17.3

Side Effects of Previous DMTs

- Hair Loss n=1
- Anxiety n=2
- Injection Site Reaction n=2
- Headache n=2
- GI Symptoms n=4
- Flu-like Symptoms n=5
- Other n=5

Previous DMTs prior to switch

<table>
<thead>
<tr>
<th>DMT</th>
<th>n</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilantrir Acetate (Copaxone - Teva Neuroscience)</td>
<td>n=2</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Interferon B-1a (Avonex - Biogen Idec)</td>
<td>n=6</td>
<td>Side Effects</td>
</tr>
<tr>
<td>Interferon B-1a (Rebiplin - Merck Serono, Ziferlov)</td>
<td>n=6</td>
<td>Other</td>
</tr>
<tr>
<td>Interferon 1b (Betaseron - Bayer, Novartis)</td>
<td>n=3</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Natalizumab (Tyasri - Biogen Idec, Elan)</td>
<td>n=5</td>
<td>Side Effects</td>
</tr>
<tr>
<td>DMF</td>
<td>n=1</td>
<td>Not Effective</td>
</tr>
<tr>
<td>Treatment Naive</td>
<td>n=5</td>
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</table>

Side Effects on New DMTs

<table>
<thead>
<tr>
<th>DMT</th>
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<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMF</td>
<td>n=2</td>
<td>Ineffective</td>
</tr>
<tr>
<td>Interferon B-1a</td>
<td>n=2</td>
<td>Side Effects</td>
</tr>
<tr>
<td>Other</td>
<td>n=6</td>
<td>Other</td>
</tr>
</tbody>
</table>

Reason For Discontinuing Previous DMTs

- N=28
- N=23
- N=9
- N=0

Patients Receiving New Oral DMTs

- N=28
- N=23
- N=9
- N=0

Conclusions

- Within the first 9 months of oral DMTs medication onset, no safety concerns emerged in our cohort of pediatric MS patients.
- The number of relapses decreased from 49 relapses on previous DMTs to 14 on the new oral DMTs, thereby implying improved efficacy.
- The new oral DMTs are a good option for the management of pediatric-onset multiple sclerosis.

Limitations

- Limited data as related to a small cohort group.
- These are preliminary results and longer follow-up time would be needed to make accurate assessments of the true safety, tolerability and efficacy of the new oral DMTs in the pediatric population.

References


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