Lymphopenia in Patients With Multiple Sclerosis Treated With Delayed-Release Dimethyl Fumarate: Analysis of Two United States Electronic Health Record Databases

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INTRODUCTION

In clinical trials, delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) significantly reduced clinical and neuroanatomical disease activity and exhibited a favorable benefit-risk profile in patients with relapsing-remitting multiple sclerosis (RRMS).1 In clinical trials, the incidence of severe (Grade 3) lymphopenia (absolute lymphocyte count [ALC] <500 cells/µL) in DMF-treated patients was 7%. The incidence of severe lymphopenia persisting 26 months was 2.5% (please see poster P2.099). Further research, including data obtained in real-world settings, is needed to understand the effects of DMF on lymphocytes.

OBJECTIVE

Evaluate ALCs in patients with MS treated with DMF using data from 2 deidentified US electronic health record (EHR) databases.

METHODS

We identified patients with a diagnosis of MS (International Classification of Diseases, Ninth Revision, code 340) using 2 EHR databases.

- Geisinger Health System: patients identified from January 1, 2004 through March 31, 2015.
  - A health care delivery system serving the central, south central, and northeastern regions of the US state of Pennsylvania. It comprises 3 hospital campuses, 2 research centers, and the Geisinger Health Plan.
- Humedica: patients were identified from a deidentified EHR database from January 1, 2007 through December 31, 2014.
  - A compilation of medical records from ~55 million patients across the United States from various private health insurance plans.

Inclusion criteria:

- Patients who had Baseline and 6-month ALC values
- Patients with Baseline ALC ≥1000 cells/µL
- A health care delivery system serving the central, south central, and northeastern regions of the US state of Pennsylvania. It comprises 3 hospital campuses, 2 research centers, and the Geisinger Health Plan.
- Patients with Baseline and experienced ≥1 ALC <500 cells/µL at any time while on therapy

Total time on DMF was defined as:

- Geisinger Health System: time from DMF initiation to the earliest of the first disease-modifying therapy (DMT) switch or the last encounter in the database
- Humedica: time from DMF initiation to the earliest of the first DMT switch, the last encounter in the database, the end of database follow-up period, or, if no encounter, the end of database follow-up period
- ALCs were assessed at 6- and 12-month windows (1.5 months) post DMF initiation and categorized into the following:
  - <2000 cells/µL
  - 700–999 cells/µL
  - 500–699 cells/µL
  - <500 cells/µL (severe lymphopenia)

RESULTS

A total of 3187 patients with MS were identified to have received a prescription for DMF during the study period (Table 1). A total of 1014 patients (201 Geisinger and 813 Humedica) met the inclusion criteria.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Geisinger</th>
<th>Humedica</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>143 (71)</td>
</tr>
<tr>
<td>Time in database, mo*</td>
<td>56/69</td>
<td>70/71</td>
</tr>
<tr>
<td>Time from DMF initiation, mo*</td>
<td>13/14</td>
<td>11/11</td>
</tr>
<tr>
<td>Total time on DMF therapy, mo*</td>
<td>12/12</td>
<td>9/9</td>
</tr>
<tr>
<td>Age at DMF initiation, y</td>
<td>46/45</td>
<td>47/48</td>
</tr>
<tr>
<td>No. of ALC tests during DMF treatment</td>
<td>4/2</td>
<td>2/2</td>
</tr>
<tr>
<td>Time from DMF initiation to first ALC, d</td>
<td>136/111</td>
<td>105/78</td>
</tr>
</tbody>
</table>

Among patients who had both Baseline and 12-month ALC values:

- Mean ALCs decreased from 1490 to 1339 cells/µL for the Geisinger Health System and from 1858 to 1371 cells/µL for Humedica, representing a 25% decrease in both cohorts
- Few (Geisinger Health System, 4%; Humedica, 3%) developed severe lymphopenia (<500 cells/µL) at 12 months (Figure 1).

CONCLUSIONS

- Observed data are not systematically collected.
- Testing of lymphocytes is subject to physician discretion, health care delivery system protocols, and insurance reimbursement.
- Limited to the end of exposure.
- Limited follow-up was due to the relatively recent approval of DMF in the United States.
- May lead to an underestimate of identifying patients with severe lymphopenia.
- Does not allow for a rigorous assessment of lymphocyte recovery after DMF discontinuation.
- Prior DMTs, immunosuppressant therapies, and steroids, which may or may not predispose DMF patients to lower ALC values, were not accounted for in this analysis.

DISCLOSURES

- CONSORTIUM OF MULTIPLE SCLEROSIS CENTERS 2016 ANNUAL MEETING
- American Academy of Neurology
- June 1-4, 2016
- National Harbor, MD

REFERENCES

5. Acknowledgments

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