Comparative Effectiveness of Dimethyl Fumarate Versus Fingolimod and Teriflunomide on the Risk of Relapse in MS Patients Switching From First-Generation Platform Therapies in the US

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Conclusions
- As measured by risk of relapse, the effectiveness of DMF was greater than that of TERI and comparable to that of FTY in adults switching from platform therapy.
- These findings are largely consistent with previous comparative effectiveness studies and contribute to the aggregate of available real-world data to support decision-making in real-world clinical practice in order to achieve the maximum therapeutic benefit for patients.

Introduction
- Multiple sclerosis (MS) is a chronic progressive immune-mediated disease caused by the destruction of myelin, resulting in axonal injury and loss of neural function. It affects ~2.3 million people worldwide, and ~700,000 individuals in the United States.1,2
- The introduction of oral, first-generation DMTs such as dimethyl fumarate (DMF; also known as generic-name DMS, fingolimod (FTY), and teriflunomide (TERI)) has provided clinicians and patients with additional treatment options outside of the injectable-first generation (DMF) platform therapies.
- Based on previous real-world evidence comparing relapse outcomes among oral DMTs, there is demonstrated effectiveness that is greater than that of TERI and comparable to FTY.3
- Despite the types of therapeutic options available for the management of MS, there is limited comparative evidence in patients who may find it necessary to switch from an injectable platform to oral therapy.

Objective
- To compare the risk of relapses in patients with MS who have switched from a platform therapy to DMF, FTY, or TERI.

Methods
- Patients with MS 18–65 years of age initiating oral DMF from June 1, 2013–March 31, 2015 were identified through a retrospective claims analysis using the “Truven MarketScan® Commercial database.”
- The overall study period ran from June 1, 2013–March 31, 2016.
- Patients were grouped into 3 months based on the corresponding oral DMT received after switching from the initial injectable DMT – DMF (switched from injectable DMT to DMF, switched from injectable DMT to FTY, or switched from injectable DMT to TERI).
- The index date was the date of first oral DMT fill. Inclusion criteria were:
  - Continuous enrollment in the database for 12 months before and after the index date.
  - A diagnosis of multiple sclerosis (ICD-9 code 340) over the 12-month preindex period.
  - Continuous enrollment in the database for 12 months before and 12 months after the index date.
  - Discrimination of a platform DMT with no evidence of oral infusion DMT over the preindex period.
  - Reference to the index date for 180 days.
- DMF patients were propensity score matched (PSM) to FTY and TERI-based on age, sex, race, MS severity score based on MS-related comorbidities (visual impairment, gait, cerebral palsy, psychiatric, sensory, speech, bowel/bladder/cognitive, fatigue, or uses of walking device), Charlson Comorbidity Index (CCI) score, annualized relapse rate, and number of hospitalizations over the preindex period.
- Annualized relapse rate was defined as:
  - Hospitalization with a primary diagnosis of 340; or
  - An outpatient visit with diagnosis of 340 and one of the following claims within 30 days of the visit:
    - Intravenous steroid; or
    - Admission for hospitalization for neurologic disease; or
    - Dry eye exchange; or
    - All qualified claims dated within 30 days of each other were grouped into 1 relapse episode.

Results
- After applying the study inclusion and exclusion criteria, the overall study population included 3906 patients (Figure 1), of whom 3092 (79.2%) were switched to DMF, 1049 (27.0%) to FTY, and 96 (2.5%) to TERI.
- In total, 2032 of the 3112 (65.3%) patients within the matched DMF-TERI cohorts relapsed during the postindex period.
- Patients who switched to TERI had a higher risk of relapse (Figure 2) than those who switched to DMF (hazard ratio [HR], 1.472 [95% CI, 1.090–1.989]; P = .0113).
- Time to relapse among patients who switched to TERI (mean [SD], 241 [33.7] days) was earlier in comparison to those who switched to DMF (mean [SD], 279 [20.4] days). As measured by risk of relapse, the effectiveness of DMF was greater than that of TERI and comparable to that of FTY

Table: Characteristics of DMF and FTY patients before and after PSM

<table>
<thead>
<tr>
<th>DMF (n=1602)</th>
<th>FTY (n=1049)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>50.0 (19.6)</td>
<td>53.0 (17.3)</td>
</tr>
<tr>
<td>MS severity score</td>
<td>3.8 (1.1)</td>
<td>3.4 (1.0)</td>
</tr>
<tr>
<td>CCI score groups, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>593 (37)</td>
<td>303 (29)</td>
</tr>
<tr>
<td>1–2</td>
<td>630 (39)</td>
<td>342 (32)</td>
</tr>
<tr>
<td>3–4</td>
<td>317 (19)</td>
<td>204 (19)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>62 (4)</td>
<td>50 (5)</td>
</tr>
</tbody>
</table>

Figure: Differences in time to relapse between patients who switched to DMF and FTY.

DMF = delayed-release dimethyl fumarate; FTY = fingolimod; HR = hazard ratio; TERI = teriflunomide

Acknowledgments
- The authors wish to thank those who contributed to the success of this study: N. Johnson, J. Patel, K. Sargent, M. Wu, and S. Wang.

**References**

**Abbreviations**
ARR = annualized relapse rate; CCI = Charlson Comorbidity Index; DMF = delayed-release dimethyl fumarate; FTY = fingolimod; HR = hazard ratio; MS = multiple sclerosis; PSM = propensity score match; SD = standard deviation; TERI = teriflunomide.