Efficacy & Tolerance of Oral versus Injectable Disease Modifying Therapies in Multiple Sclerosis

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Abstract

Objective: To determine whether oral DMTs were better tolerated and/or more effective for controlling MS compared to injectable therapies (INJ) in clinical practice.

Methods: Patients were enrolled upon initiation of a new oral (fingolimod [FGD], teriflunomide [TER], or dimethyl fumarate [DMF]) or INJ therapy for MS. Both treatment-naive patients and those switching to a new DMT were included.

Main Outcomes: Outcomes included on-drug MS activity (defined as a clinical MS relapse or new MRI activity during treatment) and DMT discontinuation.

Results: Cox proportional hazards models were used to control for baseline differences among patients initiating oral versus injectable DMT. Subsequently, sensitivity analyses using propensity-weighted matching were performed. A higher proportion of TER-treated patients experienced MS activity, compared to those treated with INJ (p=0.0054) in the adjusted model. Breakthrough MS was equally prevalent among FGD and DMF-treated compared to INJ-treated patients. Sensitivity analyses using propensity matching to compare each oral DMT to INJ confirmed these findings. Overall, 32-46% of patients initiating DMT discontinued or switched treatments during the study. After controlling for baseline differences, discontinuation rates were comparable across treatment groups.

Conclusions & Relevance: In this cohort, oral and injectable DMTs were equally well tolerated, but TER appeared less effective for controlling MS activity than INJ DMTs. These findings will help inform the selection of the most appropriate DMT for MS patients, but should be validated in an independent patient cohort.

Key words: Oral DMTs; FGD; TER; DMF; INJ; Relapses; DMT discontinuation; Baseline differences; Comparative effectiveness; Cohort study; MS activity; Tolerability

Table 1: Descriptive Data for the Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FGD (n=92)</th>
<th>TER (n=83)</th>
<th>DMF (n=83)</th>
<th>INJ (n=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS activity at baseline, n (%)</td>
<td>29 (19.3)</td>
<td>25 (27.2)</td>
<td>31 (37.5)</td>
<td>18 (11.3)</td>
</tr>
<tr>
<td>Severe (EDSS ≥6.0)</td>
<td>12 (20.7)</td>
<td>11 (12.0)</td>
<td>8 (9.6)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Moderate (EDSS 3.5-5.5)</td>
<td>30 (32.6)</td>
<td>34 (37.0)</td>
<td>22 (26.5)</td>
<td>38 (24.0)</td>
</tr>
<tr>
<td>Mild (EDSS 0-3)</td>
<td>46 (50.0)</td>
<td>46 (50.7)</td>
<td>47 (56.3)</td>
<td>128 (81.7)</td>
</tr>
<tr>
<td>Follow-up duration, months, mean (SD)</td>
<td>18.2 (7.7)</td>
<td>20.4 (6.5)</td>
<td>20.3 (7.2)</td>
<td>17.2 (7.2)</td>
</tr>
</tbody>
</table>

Figure 1: Forest plots of hazard ratios (HR) for MS activity (A) and treatment discontinuation (B) after controlling for baseline variables. CI: confidence interval.

Figure 2: MS activity and persistence on therapy for oral (blue) versus injectable (red) disease modifying therapies after propensity matching. After propensity weighted matching, 88 DMF-treated patients, 46 TER-treated patients and 56 FGD-treated patients were matched with comparable INJ-treated patients. On-drug MS activity (A-C) and persistence on drug (D-F) were evaluated. Kaplan Meier time to event analyses are shown.

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Statistical Analysis

Chart reviews: Demographic and clinical data were extracted from the medical record including: age, sex, race, time since diagnosis, number of previous DMTs, estimated disability status score (EDSS), relapses within the last 12 months (0 vs. ≥1) and prescribing neurologist. EDSSs were categorized into mild (EDSS 0-3), moderate (EDSS 3.5-5.5) and severe (EDSS ≥6.0). All outcomes were on-treatment MS activity (including both clinical relapses and new MRI disease), treatment discontinuation, and reasons for discontinuation.

Conclusions

• After controlling for baseline differences, patients initiating teriflunomide were significantly more likely to experience on-drug MS activity compared to patients initiating injectable disease modifying therapy.
• Patients were equally likely to discontinue oral and injectable DMTs.
• Further study of the comparative effectiveness of MS DMTs is needed.