Clinical and Safety Outcomes From Patients Treated With Teriflunomide in the Phase 4 Teri-PRO Study

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OBJECTIVE

• To report clinical and safety outcomes for patients in the Teri-PRO (Teriflunomide Patient Reported Outcomes) study

INTRODUCTION

Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS in 70 countries, and approximately 71,000 patients are currently being treated with teriflunomide.

The phase 4 Teri-PRO study (NCT01895335) primarily evaluated patient-reported treatment satisfaction, disability, and quality of life with teriflunomide using patient-reported outcomes (PROs). The effectiveness, safety, and tolerability of teriflunomide in routine clinical practice were also assessed – High levels of treatment satisfaction with teriflunomide were observed over the course of the study – PROs in patients switching to teriflunomide from another disease-modifying therapy (DMT) and in treatment-naïve patients are described in posters P3-343 (Coyle et al) and P3-348 (Gold et al), respectively, at this congress

METHODS

Study Design and Patients

• Teri-PRO was a prospective, global, multicenter, single-arm, open-label study

• Patients were treated with teriflunomide 14 mg or 7 mg (US only) according to local labeling

• The full study design and eligibility criteria have been presented previously

• “Switchers” are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start

• All patients who received ≥1 dose of teriflunomide were included in the analysis

CONCLUSIONS

• In the Teri-PRO study, real-world effectiveness and safety of teriflunomide were consistent with the results of the clinical development program – Phase 4 (as measured by EDSS scoring) remained stable over the course of the study. In patients switching to teriflunomide from another DMT, EDSS remained stable regardless of prior DMT – Annualized treated relapse rates were low across the course of the study – Most AEs were mild to moderate in nature with no unexpected AEs reported

• In combination with other Teri-PRO outcomes, these observations support the use of teriflunomide as an effective treatment in patients with relapsing forms of MS, including in those patients switching from othr DMTs

RESULTS

• Of the overall Teri-PRO cohort (N=1000), 594 patients were switchers (defined as having received another DMT within 6 months prior to study start) – The majority of patients received teriflunomide 14 mg (total cohort: n=928, 92.8%; switchers: n=558, 93.6%) – Baseline EDSS scores remained stable over the entire study period for patients in both switcher and treatment-naïve cohorts – Annualized treated relapse rates were low across the course of the study – In patients switching to teriflunomide from another DMT, EDSS remained stable regardless of prior DMT – The majority of patients received teriflunomide 14 mg (total cohort: n=928, 92.8%; switchers: n=556, 93.6%)

• AEs leading to treatment discontinuation were reported in 109 (10.9%) and 481 (81.0%) patients in the total cohort and switcher cohort, respectively

• No deaths were considered related to teriflunomide treatment

• The real-world safety profile of teriflunomide was consistent with that seen in the clinical development program

Clinical Outcomes

Table 1. Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort</th>
<th>Switchers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>50 (15)</td>
<td>51 (15)</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>660:340</td>
<td>403:191</td>
</tr>
<tr>
<td>Race</td>
<td>311 (31.1%) White, 187 (18.7%) Black, 396 (39.6%) Other</td>
<td>235 (42.7%) White, 121 (21.7%) Black, 161 (29.6%) Other</td>
</tr>
<tr>
<td>Time since first symptoms of MS, mean (SD), y</td>
<td>13.2 (9.5)</td>
<td>13.8 (9.3)</td>
</tr>
<tr>
<td>Baseline EDSS score, mean (SD)</td>
<td>3.1 (2.0)g</td>
<td>3.1 (2.0)g</td>
</tr>
</tbody>
</table>

Table 2. Summary of Adverse Events

<table>
<thead>
<tr>
<th>AEs</th>
<th>All Patients (n=1000)</th>
<th>Switchers (n=948)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All events</td>
<td>1538 (153.8)</td>
<td>1253 (126.6)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>10 (1.0)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>AE leading to withdrawal of teriflunomide</td>
<td>47 (4.7)</td>
<td>36 (3.8)</td>
</tr>
<tr>
<td>Most common AEs with incidence ≥1% in any population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>280 (28.0)</td>
<td>230 (24.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>114 (11.4)</td>
<td>94 (9.9)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>213 (21.3)</td>
<td>180 (19.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>55 (5.5)</td>
<td>42 (4.5)</td>
</tr>
<tr>
<td>Mucosal disorder</td>
<td>44 (4.4)</td>
<td>34 (3.6)</td>
</tr>
</tbody>
</table>

Table 3. Baseline EDSS Scores

<table>
<thead>
<tr>
<th>Time</th>
<th>Total Cohort</th>
<th>Switchers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.1 (2.0)</td>
<td>3.1 (2.0)</td>
</tr>
<tr>
<td>Week 48</td>
<td>3.0 (2.0)</td>
<td>3.0 (2.0)</td>
</tr>
</tbody>
</table>

Figure 1. EDSS Scores at Baseline and Week 48

A. Patients

B. Patients Switching to Teriflunomide From Another DMT

Safety

• The safety profile of teriflunomide was similar in the total population and switcher cohort

• Most AEs were mild to moderate in severity

• Serious AEs were reported in 127 (12.7%) and 72 (12.1%) patients in the total population and the switcher cohort, respectively

• AEs leading to treatment discontinuation were reported in 109 (10.9%) and 56 (9.4%) patients in the total population and the switcher cohort, respectively

Acknowledgments and Disclosures

References


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Clinical Outcomes

• Expansion Disability Status Scale (EDSS) scores were measured at baseline and Week 48

• Annualized treated relapse rate and number of patients with ≥1 treated relapse were also assessed

• – Annualized treated relapse rate was calculated as the total number of treated relapses that occurred during the treatment period divided by the total number of treated patient-years in the study

• – A treated relapse was defined as a relapse treated by systemic corticosteroid therapy or by another DMT during the study period

• Most patients did not experience a relapse requiring treatment during the study period (all patients: 858 [85.8%]; switchers: 501 [84.3%])

• Safety and Tolerability Outcomes

• – Adverse events (AEs) and vital signs were assessed at baseline, Week 4, and Week 48 (or end of treatment, EOT)

• – AEs occurring between visits, including start date of the AE, were reported at the subsequent visit

• – AEs leading to withdrawal of teriflunomide were reported in 47 (4.7%) and 36 (3.8%) patients in the total cohort and switcher cohort, respectively

• – Headache and hypertension were the most common AEs with incidence ≥1% in any population

• – No deaths were considered related to teriflunomide treatment

• – The real-world safety profile of teriflunomide was consistent with that seen in the clinical development program

• Statistical Analysis

• – All patients who received ≥1 dose of teriflunomide were included in the analysis

• – In a post hoc analysis, P values for post-baseline change were assessed using an analysis of covariance model of change from baseline with values adjusted for baseline EDSS score. Analysis based on prior DMT in switcher patients was also performed post hoc

• – A treated relapse rate remained low throughout the study period (all patients: 0.200; switchers: 0.216)

• – Annualized treated relapse rate was higher in patients who had previously received fingolimod or natalizumab compared with platform stable teriflunomide therapies (Table 2)

• – The proportion of patients experiencing a treated relapse was higher in patients who had previously received fingolimod or natalizumab compared with platform stable teriflunomide therapies (Table 2)

• – The proportion of patients experiencing a treated relapse was higher in patients who had previously received fingolimod or natalizumab compared with platform stable teriflunomide therapies (Table 2)