**Teriflunomide in Routine Clinical Practice: Design of the Teri-PRO Study**

**Background**

- Teriflunomide is a once-daily oral immunomodulator approved in the USA, Australia, and Argentina for the treatment of relapsing forms of multiple sclerosis (RMS).
- Teriflunomide selectively and reversibly inhibits dihydro-orotate dehydrogenase, a key mitochondrial enzyme in de novo pyrimidine synthesis required for rapidly dividing lymphocytes.1 2
  - Through this cytostatic effect, teriflunomide limits expansion of stimulated T and B cells thought to be responsible for the damaging inflammatory process associated with RMS.
  - Basic hematopoietic cell functions of resting and slowly dividing cells appear to be preserved, so lymphocytes remain available for ongoing immune surveillance.
- The efficacy and safety of teriflunomide has been investigated in an extensive clinical development program and it has shown efficacy in the two pivotal phase 3 trials, TEMSO (Teriflunomide Multiple Sclerosis Oral: NCT00134563) and TOWER (Teriflunomide Oral in People with Multiple sclerosis: NCT00715811).
- In both studies, teriflunomide 14 mg significantly reduced annualized relapse rate compared with placebo (31.3%, p<0.001 in TEMSO and 36.3%, p<0.001 in TOWER). A significant decrease was also observed with teriflunomide 7 mg in sustained disability progression (confirmed for 12 weeks) compared with placebo (29.8%, p=0.028 in TEMSO and 31.5%, p=0.044 in TOWER). Once-daily treatment with teriflunomide 7 mg also significantly reduced annualized relapse rate in both studies (31.2%, p<0.001 in TEMSO and 22.3%, p<0.002 in TOWER), but did not progress disability.3-6
- Patient-reported outcomes (PROs) provide clinical information to support the evaluation of MS therapies. Patients reported only small changes from baseline in health-related quality of life (HR-QoL) outcomes (EuroQol-5D and Short-Form 36) with no significant differences among the study groups in TEMSO and TOWER.1 7 8
  - In the comparative trial with interferon beta-1a (IFN-1a; TENERE: NCT00883337), patients expressed greater global satisfaction with treatment (related to effectiveness, side-effects, and convenience) in the teriflunomide 7 mg (p=0.030) and 14 mg (p=0.016) groups than in the IFN-1a group, as assessed by the Treatment Satisfaction Questionnaire for Medication (TSQM, secondary outcome).9
- The phase 4 Teri-PRO (Teriflunomide Patient-Reported Outcomes) study will further investigate patient perceptions of teriflunomide on treatment satisfaction, HR-QoL, and effectiveness using PROs, and will provide valuable information on patient adherence and persistence with teriflunomide therapy in real-life settings.

**Primary Objective**

- To describe the efficacy, tolerability, and convenience of teriflunomide treatment through the evaluation of PROs.

**Key Secondary Objectives**

- To describe disease progression using PROs.

**Methods**

**Teri-PRO Study Design**

- Teri-PRO is a prospective, single-arm, multicenter, real-life study to describe the efficacy, tolerability, and convenience of teriflunomide treatment using PROs in patients with RMS who are either naive to disease-modifying treatment (DMT) or switching from another DMT. Teriflunomide will be provided.
- A minimum of 1000 patients across 200 sites will receive teriflunomide once-daily for 48 weeks, with doses given according to local labeling.
- The study design is shown in Figure 1.

**Patient Entry Criteria**

- The key inclusion and exclusion criteria for the Teri-PRO study are shown in Table 1.

**Table 1. Inclusion and Key Exclusion Criteria for the Teri-PRO Study**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>Patients with relapsing forms of MS, considered to have indication for teriflunomide treatment</td>
<td>Under 18 years of age</td>
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<tr>
<td>Signed written informed consent</td>
<td>Current history of treatment with teriflunomide</td>
</tr>
<tr>
<td>History of severe immunodeficiency, bone marrow disease, osteoporosis, or active infections</td>
<td>Previous exposure to teriflunomide within 6 months prior to baseline</td>
</tr>
<tr>
<td>Progressive or relapsing disease with or without active infection</td>
<td>Pre-existing or active liver disease, or those with serum alanine aminotransferase &gt;2 times the upper limit of normal</td>
</tr>
<tr>
<td>Known history of severe immunodeficiency, bone marrow disease, osteoporosis, or active infections</td>
<td>Previous exposure to teriflunomide with severe reaction</td>
</tr>
<tr>
<td>Previous or ongoing treatment with MS therapeutics</td>
<td>Unstable or life-threatening condition</td>
</tr>
<tr>
<td>Use of corticosteroids</td>
<td>Current or history of treatment with teriflunomide</td>
</tr>
<tr>
<td>Use of immunomodulators</td>
<td>Presence of active or severe infection</td>
</tr>
<tr>
<td>Use of corticosteroids with or without immunomodulators</td>
<td></td>
</tr>
</tbody>
</table>

**Primary Endpoint**

- Assessment at 48 weeks (end of treatment [EOT]) of global satisfaction with teriflunomide treatment, measured by score on TSQM, version 1.4 (Table 2 and Table 3).

**Table 2. Patient-Reported Outcome Measures in Teri-PRO**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Description</th>
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<tbody>
<tr>
<td>TSQM</td>
<td>To assess overall level of satisfaction with treatment in terms of its health modification.</td>
</tr>
<tr>
<td>EDSS</td>
<td>To assess disability in patients with MS.</td>
</tr>
<tr>
<td>PDDS</td>
<td>To assess quality of life in patients with MS.</td>
</tr>
<tr>
<td>SF-36</td>
<td>To assess quality of life in patients with different forms of MS.</td>
</tr>
<tr>
<td>TSQM</td>
<td>To assess patient satisfaction with MS treatment.</td>
</tr>
<tr>
<td>SF-36</td>
<td>To assess patient satisfaction with MS treatment.</td>
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</tr>
</tbody>
</table>

**Secondary Endpoint**

- Change in TSQM score from baseline to Week 4 and to EOT in patients switching from another DMT.
- Change in TSQM from Week 4 to Week 48/EOT in treatment-naïve patients.
- Disease progression: change from baseline to Week 24 and Week 48/EOT on the PDDS scale.
- Disease progression: change from baseline to Week 24 and Week 48/EOT on the Multiple Sclerosis Functional Scale.

**Clinical outcomes: treated relapses, time to first treated relapse.**

**Analyses**

- Change in cognition as baseline to Week 48/EOT on the Symbol Digit Modalities Test.
- Occurrence of AEs.
- Adherence (ie, compliance) and persistence (ie, duration of exposure) to teriflunomide treatment over 48 weeks.
- QoL change from baseline to Week 48/EOT measured by Multiple Sclerosis International Quality of Life and Stern Leisure Activity Scale.
- TSQM score at baseline and at Week 48/EOT.
- The timing of efficacy and safety assessments are shown in Table 3.

**Conclusions**

- Teri-PRO will improve clinical knowledge of the benefits of teriflunomide from a patient perspective with regard to efficacy, tolerability, and convenience.
- Teri-PRO will provide valuable information on PROs for MS disability progression, treatment satisfaction, adherence, QoL, and safety in patients with RMS receiving teriflunomide in routine clinical practice.

**references**


**Disclosures**

- The Clinical Research (Bronx, NY), Genzyme, Janssen Research, Teva Neuroscience, Redmond Institute of Health, Oral Pharmacotherapy, Consulting (Bronx, NY), Teva Neuroscience, Accelerated Cure Project, Genzyme, Briston-Moore Squibb, Novartis Pharmaceuticals, Questco, Qality-Action Charitable Trust, Evergreen, Acorda, Sharks Fund, and MS and EI Employees of Genzyme, a Sanofi company.

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