**Teriflunomide Efficacy in Newly Diagnosed Patients With RMS Enrolled in the TEMSO and TOWER Studies: A Post Hoc Analysis**

Jerry S Wolinsky,1 Mark S Freedman,2 Giancarlo Comi,3 Jean-Pierre Bouchard,4 Ludwig Kappos,1 Philippe Truffinet,6 Karthi Nathan Thangavelu,7 Steve Cavalier,8 Paul W O’Connor9

1University of Texas Health Sciences Center at Houston, Houston, TX, USA; 2University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; 3University Vita-Salute San Raffaele, Milan, Italy; 4Laval University, Centre Hospitalier Universitaire de Quebec, Quebec, QC, Canada; 5University Hospital Basel, Basel, Switzerland; 6Genzyme, a Sanofi company, Chilly-Mazarin, France; 7Genzyme, Cambridge, MA, USA; 8St Michael’s Hospital, Toronto, ON, Canada

**INTRODUCTION**

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS.
- In 2 phase 3 studies (TEMSO [NCT00134563]) and TOWER (NCT00751881), teriflunomide demonstrated efficacy on annualized relapse rate (ARR), disability progression,2 and MRI parameters1 in patients with a range of MS disease activity at baseline.
- A previous pooled analysis of TEMSO and TOWER key efficacy outcomes showed that teriflunomide 14 mg reduced ARR by 33.7% (P = 0.0012) and reduced the risk of sustained disability progression (confirmed for 12 weeks) by 30.5% (P = 0.003) compared with placebo.1
- Teriflunomide 7 mg reduced ARR by 27.0% (P < 0.001) and, although not significant, showed a numerical reduction in the risk of disability progression.
- In TEMSO, both doses of teriflunomide improved disease activity (as measured across a range of MRI endpoints), including a significant reduction in the ratio of combined unique active lesions (UALs) (P = 0.001 for both doses)1 (MRI was not performed in TOWER).

**OBJECTIVES**

- To evaluate the efficacy of teriflunomide on ARR and the number of UALs in a subgroup of newly diagnosed patients from the TEMSO and TOWER studies.

**METHODS**

- In this post hoc analysis of the TEMSO and TOWER studies, the effect of teriflunomide 14 mg and 7 mg on ARR and the number of UALs per scan was analyzed in newly diagnosed patients, defined as those diagnosed with relapsing forms of MS (RMS) within 1 year of newly diagnosed patients, defined as those diagnosed with relapsing forms of MS (RMS) within 1 year of enrolment and naïve to disease-modifying therapies.
- ARR was evaluated using data pooled from the TEMSO and TOWER studies.
- Treatment duration for patients in TEMSO was 48 to 152 weeks;2 for patients in TOWER, treatment continued until 48 weeks after the last patient had been randomized and therefore varied between 48 to 152 weeks.1
- UALs per scan were evaluated using data from TEMSO only. MRI scans were obtained at baseline and Weeks 24, 48, 72, and 108.

**RESULTS**

- In the pooled analysis, 587 newly diagnosed patients with RMS received once-daily teriflunomide 14 mg (n = 183), 7 mg (n = 189), or placebo (n = 215).
- Demographic and disease characteristics at baseline were similar in the 3 treatment groups (Table 1).
- A significantly greater proportion of patients were free of UALs in the teriflunomide 14 mg group (73.8%) compared with the placebo group (54.9%, odds ratio 2.31, P = 0.0001).
- In the 7-mg group, 64.0% of patients remained relapse-free (odds ratio 1.46, P = 0.0623 vs placebo).
- UAL (TEMSO Only)
- In TEMSO, 267 newly diagnosed patients with RMS received once-daily teriflunomide (14 mg, n = 80; 7 mg, n = 88) or placebo (n = 99).
- At baseline, the presence of gadolinium-enhancing T1 lesions was similar across the 3 treatment groups, with 36.3%, 34.1%, and 31.3% of patients having ≥1 gadolinium-enhancing T1 lesion in the 14 mg, 7 mg, and placebo groups, respectively.

**CONCLUSIONS**

- Pooled data from TEMSO and TOWER demonstrated significant reductions in ARR in newly diagnosed patients with RMS treated with teriflunomide 14 mg, consistent with results from individual trials.1
- In TEMSO, significant reductions in number of UALs were observed in newly diagnosed patients in both treatment groups, in accordance with the overall study population.
- This post hoc analysis supports a consistent positive effect of teriflunomide on clinical and MRI measures in newly diagnosed patients.

**REFERENCES**


**Disclosures**

CRQ (Cerebrospinal Fluid, Arterial, Venous, Arteriovenous, Brain Health Care) / CRQ: Employees (Beaver HealthCare), contracted research (Bayer HealthCare, Biogen Idec, EMD Serono, Genentech, Genzyme, Novartis, Roche, Sanofi, Teva, Teva Neurosciences, to-BBB, XenoPort); contracted research (Genzyme, Laval University, Centre Hospitalier Universitaire de Quebec, University Hospital Basel, Genzyme, Cambridge, MA, USA; St Michael’s Hospital, Toronto, ON, Canada).

**Acronyms**

- ARR: Annualized relapse rate.
- MS: Multiple sclerosis.
- RMS: Relapsing multiple sclerosis.
- MRI: Magnetic resonance imaging.
- UAL: Unique active lesion.
- TOWER: Treatment of Relapsing Multiple Sclerosis with Teriflunomide (NCT00751881).
- TEMSO: Treatment of Multiple Sclerosis: Oral Teriflunomide (NCT00134563).
- PRMS: Progressive relapsing MS.
- RRMS: Relapsing-remitting MS.
- EDSS: Expanded Disability Status Scale.
- SD: Standard deviation.
- F: Female.
- M: Male.
- ADL: Activities of daily living.
- TOI: Treatment of relapsing multiple sclerosis.
- B: Blood.
- CSF: Cerebrospinal fluid.
- U: Urine.
- PT: Physical therapy.

**TABLE 1. Patient Demographics and Baseline Disease Characteristics: Pooled Data From TEMSO and TOWER**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Teriflunomide 14 mg (n=183)</th>
<th>Teriflunomide 7 mg (n=189)</th>
<th>Placebo (n=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>37.5 (9.9)</td>
<td>37.6 (9.1)</td>
<td>37.2 (9.1)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>126 (68.9)</td>
<td>126 (67.6)</td>
<td>148 (68.8)</td>
</tr>
<tr>
<td>Time since diagnosis, mean (SD), y</td>
<td>0.44 (0.28)</td>
<td>0.46 (0.27)</td>
<td>0.43 (0.25)</td>
</tr>
<tr>
<td>Time since diagnosis, median (min-max), y</td>
<td>0.33 (0.1-0.6)</td>
<td>0.42 (0.3-0.4)</td>
<td>0.42 (0.1-1.1)</td>
</tr>
<tr>
<td>Time since first symptoms of MS, mean (SD), y</td>
<td>4.26 (5.22)</td>
<td>4.17 (4.64)</td>
<td>4.12 (4.73)</td>
</tr>
<tr>
<td>Time since first symptoms of MS, median (min-max), y</td>
<td>2.08 (0.2-2.92)</td>
<td>2.33 (1.2-5.9)</td>
<td>2.08 (0.2-2.41)</td>
</tr>
<tr>
<td>Number of relapses in previous year, mean (SD)</td>
<td>1.5 (0.7)</td>
<td>1.5 (0.6)</td>
<td>1.5 (0.7)</td>
</tr>
<tr>
<td>MS RMS</td>
<td>182 (99.5)</td>
<td>181 (95.8)</td>
<td>208 (96.7)</td>
</tr>
<tr>
<td>PRMS</td>
<td>0</td>
<td>6 (3.2)</td>
<td>5 (2.3)</td>
</tr>
<tr>
<td>EDSS score (SD)</td>
<td>2.23 (1.12)</td>
<td>2.34 (1.29)</td>
<td>2.25 (1.23)</td>
</tr>
</tbody>
</table>

**Figure 1. Adjusted ARR: Pooled Data From TEMSO and TOWER Studies**

**Figure 2. Number of UALs per Scan: Data From the TEMSO Study**

**ARR (TEMSO and TOWER)**

- In newly diagnosed patients, teriflunomide 14 mg was associated with a significant relative reduction in ARR (37.8%, P = 0.0096) compared with placebo (Figure 1).
- Relative reductions in ARR (24.3%, P = 0.0677) were also observed for teriflunomide 7 mg, however, these were not significant.

- Teriflunomide significantly reduced the number of UALs per scan in newly diagnosed patients compared with placebo (Figure 2).
- The relative reduction in number of UALs per scan versus placebo group was 64.6% (P = 0.0012) in the 14-mg group and 47.3% (P = 0.0013) in the 7-mg group.
- A greater proportion of patients were free of UALs in the teriflunomide 14-mg (39.0%, P = 0.0079 vs placebo) and 7-mg (27.1%, not significant vs placebo) groups compared with the placebo group (20.6%).