Consistent Treatment Effect of Teriflunomide in Subgroups Based on Pre-trial Therapy: Pooled Analyses of TEMSO and TOWER

Mark S Freedman, Deborah Du Kovitch, Myram Benamor, Philippe Truffinet, Ludwig Kappos

University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; Sanofi, Bridgewater, NJ, USA; Genzyme, a Sanofi company, Chilly-Mazarin, France; Hospita l Universitaire, Basel, Switzerland

BACKGROUND

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (RMS)
- Teriflunomide has been evaluated in two large phase 3 clinical studies with similar designs and patient populations:
  - TEMSO (TE=Teriflunomide, MS=Multiple Sclerosis) [NCT00145631]
  - TOWER (Teriflunomide Oral in people With relap Sing Multiple Sclerosis) [NCT00751881]

- A previous pooled analysis of TEMSO and TOWER key efficacy outcomes confirmed the consistent and robust effect of teriflunomide 14 mg on annualized relapse rate (ARR) and disability progression seen in the individual studies.
- Teriflunomide 14 mg reduced ARR by 33.7% (P<0.001) and reduced the risk of disability sustained progression (confirmed for 12 weeks) by 30.5% (hazard rate reduction, P=0.033) compared with placebo.

OBJECTIVE

- To assess the consistency of the teriflunomide effect on ARR and disability progression across subgroups based on previous MS therapy in the pooled TEMSO and TOWER database.

METHODS

STUDY DESIGNS

- TEMSO and TOWER were both phase 3, multicenter, multinational, randomized, double-blind, parallel-group, placebo-controlled studies.

- Patients were randomized 1:1:1 to once-daily oral teriflunomide 14 mg or 7 mg, or placebo.

- In TEMSO, treatment was for a fixed duration of 108 weeks.

- In TOWER, individual patients’ treatment duration was based on time of enrollment. The study ended 48 weeks after the last patient was randomized. Mean treatment duration for TOWER was 78 weeks (minimum 48 weeks, maximum 152 weeks).

STUDY POPULATIONS

- TEMSO and TOWER both enrolled patients aged 18-55 years with relapsing forms of MS meeting the McDonald diagnostic criteria (TEMSO, 2001 criteria; TOWER, 2005 criteria) and Expanded Disability Status Scale (EDSS) score ≤5.5.

- Relapse in the 12 months before study entry or ≥2 relapses in the 24 months before study entry was also a requirement.

RESULTS

- Patients were excluded from TEMSO/TOWER if they had received natalizumab, any investigational drug in the last 6 months, interferon beta or glatiramer acetate in the last 4-10 months (TEMSO) or 3-12 months (TOWER), or intravenous immunoglobulins in the last 6 months (TEMSO) or 3 months (TOWER).

- Subgroup analyses are designed to assess homogeneity of treatment effect within each individual subgroup level.

- The key secondary outcome for both studies was sustained disability progression confirmed for 12 weeks.

- The treatment effect of teriflunomide 14 mg on reducing the risk of disability progression was numerically greater in patients with one or more prior DMT compared with treatment-naïve patients in TEMSO (78.6%) and TOWER (82.8%).

- Patients with prior DMT use had longer times since first MS symptoms (>1 Prior DMT) and, although not significant, showed a reduction in disability progression (15.3%, P=0.13).

- Teriflunomide 14 mg and 7 mg had similar safety and tolerability profiles across studies and in pooled analyses.

- Where studies of comparable size have similar enrollment criteria, interventions, and endpoints, pooled data analyses can provide additional valuable insight into treatment outcomes.

- Both TEMSO and TOWER included some patients who had received, and then discontinued treatment with, other disease-modifying therapies (DMTs) in the 2 years before study entry. These patients may be considered sub-optimal responders to their prior treatments and could be at higher risk of relapse or disease progression.

- This poster presents pooled subgroup analyses from TEMSO and TOWER by pre-trial DMT use.

CONCLUSIONS

- The placebo arms of the individual and pooled data sets show a higher ARR and risk of disability progression in patients experiencing one or more DMT prior to entering this study, confirming the suspicion that these patients are indeed at higher risk of disease activity.

- Teriflunomide 14 mg showed a consistent treatment effect on relapse rate and disability progression across subgroups defined by pre-trial DMT use in analyses of pooled TEMSO and TOWER clinical trial data.

- Teriflunomide 7 mg showed a similar consistent effect on relapse rate.

- The treatment effect of teriflunomide 14 mg appeared to be greatest in patients with experience of more than one prior DMT.

- These findings support the beneficial effects of teriflunomide across a broad range of patients with RMS, including robust activity in those patients who have previously used and discontinued other DMT.

REFERENCES

- Rubatto, Novartis, and Roche Research Foundations.

Acknowledgments

This paper was commissioned by Thierry Rapin, PhD, of Sanofi, a French company. Editorial support for this manuscript was provided by Sheila Mathre of MedCom Agency, and was funded by Sanofi.

Disclosures

MIP has received research and educational grant support: Roche Healthcare, Genzyme, a Sanofi company, Teva Canada; and consulting fees: Genzyme, a Sanofi company, Teva Canada, Novartis; Research grants: Roche Healthcare, Genzyme, a Sanofi company, Teva Canada.

Sanofi, Bridgewater, NJ, USA; Genzyme, a Sanofi company, Chilly-Mazarin, France; Hospital Universitaire, Basel, Switzerland.

Presented at the 2014 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) and the Sixth Cooperative Meeting with American Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS). May 28, 2014-31, Dallas, TX, USA.

Funding provided by Genzyme, a Sanofi company.