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

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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,[1,2] and MRI parameters[1] 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<0.001) and reduced the risk of sustained disability progression (confirmed for 12 weeks) by 30.5% (P=0.003) compared with placebo[3]
  - 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 number 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 enrollment 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 108 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
- A Poisson model, with treatment, baseline Expanded Disability Status Scale strata, region, and baseline value (analysis of UALs only) as covariates and study as an additional covariate in the pooled analysis, was used for assessment of outcomes
- A logistic regression model was used to make treatment group comparisons vs placebo for patients free of relapse and patients free of UALs (TEMSO only)

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**)

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

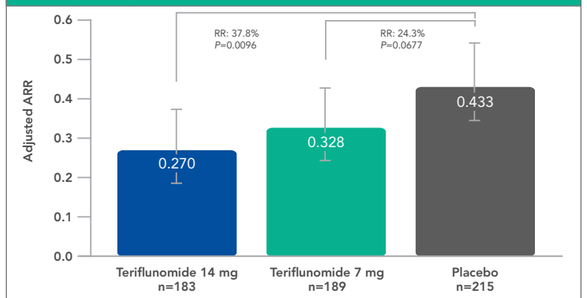
	Teri 14 mg (n=183)	Teri 7 mg (n=189)	Placebo (n=215)
Age, mean (SD), y	36.7 (9.9)	35.1 (9.6)	37.2 (9.1)
Female, n (%)	126 (68.9)	126 (66.7)	148 (68.8)
Time since diagnosis, mean (SD), y	0.44 (0.28)	0.46 (0.27)	0.43 (0.25)
Time since diagnosis, median (min:max), y	0.33 (0.0:1.0)	0.42 (0.0:1.0)	0.42 (0.1:1.0)
Time since first symptoms of MS, mean (SD), y	4.26 (5.22)	4.17 (4.84)	4.12 (4.73)
Time since first symptoms of MS, median (min:max), y	2.08 (0.2:29.2)	2.33 (0.1:29.5)	2.08 (0.2:24.1)
Number of relapses in previous year, mean (SD)	1.5 (0.7)	1.5 (0.6)	1.5 (0.7)
MS subtype, n (%) RRMS SPMS PRMS	 182 (99.5) 1 (0.5) 0	 181 (95.8) 2 (1.1) 6 (3.2)	 208 (96.7) 2 (0.9) 5 (2.3)
EDSS score mean (SD)	2.23 (1.22)	2.34 (1.29)	2.25 (1.23)

EDSS, Expanded Disability Status Scale; PRMS, progressive relapsing MS; RRMS, relapsing-remitting MS; SD, standard deviation; SPMS, secondary progressive MS.

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

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



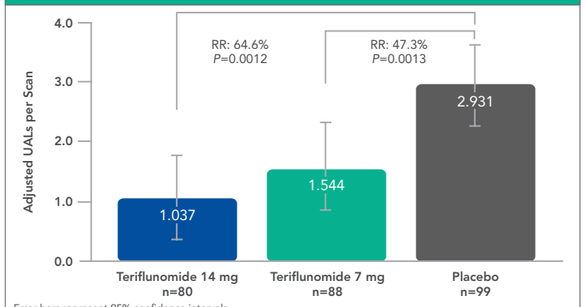
Error bars represent 95% confidence intervals.
Poisson model, with total number of confirmed relapses between randomization and last dose as response variable; treatment, baseline Expanded Disability Status Scale strata, region, and study as covariates; and log-transformed treatment duration as an offset variable.
ARR, annualized relapse rate; RR, relative reduction.

- A significantly greater proportion of patients were relapse-free 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

Figure 2. Number of UALs[a] per Scan: Data From the TEMSO Study



Error bars represent 95% confidence intervals.
[a]Total number of combined UALs that occurred during the study divided by the total number of scans during the study. Poisson model, with total number of combined UALs as response variable; treatment, baseline Expanded Disability Status Scale strata, region, and baseline number of combined UALs as covariates; and log-transformed number of scans as an offset variable.
RR, relative reduction; UAL, unique active lesion.

- 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%)

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[1,2]
- 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[1]
- This post hoc analysis supports a consistent positive effect of teriflunomide on clinical and MRI measures in newly diagnosed patients

REFERENCES

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Disclaimer

Teriflunomide is approved in many countries, including the US and the European Union, for the treatment of relapsing multiple sclerosis or relapsing-remitting multiple sclerosis.
This material may contain information that is outside of the approved labeling in some countries.

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