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Improvements in Patient-Reported Outcomes (PROs) With Teriflunomide: Results From the US Cohort of the Teri-PRO Phase 4 Study

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OBJECTIVE

- **To report treatment satisfaction and safety outcomes up to Week 48 for US patients enrolled in the global Teri-PRO (Teriflunomide Patient-Reported Outcomes) study, based on an interim data cut**

INTRODUCTION

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS
  - Teriflunomide was approved by the US Food and Drug Administration in September 2012[1]
- The consistent efficacy of teriflunomide on both clinical measures (relapse and disability) and magnetic resonance imaging parameters has been demonstrated in placebo-controlled studies of patients with relapsing forms of MS,[2–4] and in those who experienced a first clinical episode suggestive of MS.[5] Teriflunomide also has a manageable and well-characterized safety and tolerability profile[2–6]
- The use of patient-reported outcomes complements clinical assessment and provides clinicians with additional understanding of the effects of treatment on patients' daily lives and their satisfaction with therapy. Consequently, such tools can be useful when discussing treatment options with patients
- The phase 4 Teri-PRO study (NCT01895335) evaluated efficacy, tolerability, and patient treatment satisfaction with teriflunomide in routine clinical practice

METHODS

Study Design and Patients

- Teri-PRO is a prospective, global, multicenter, single-arm, open-label study
- The study design and full eligibility criteria have been presented previously.[7] In brief:
  - Patients ≥18 years of age with relapsing forms of MS were recruited from sites in the US, Canada, Europe, and Latin America
  - No disease activity eligibility criteria were used, in line with the clinical practice setting
  - Patients were prescribed teriflunomide 7 mg or 14 mg once daily for 48 weeks in accordance with local labeling; in the US, where the 7-mg dose is available, choice of dose was determined by the treating neurologist
- Patients could enter the study irrespective of previous disease-modifying therapy (DMT) use and were classified into the following groups:
  - Patients with no DMT intake in the prior 2 years
  - Patients with last DMT intake within 2 years of study entry:
    - Patients with last DMT intake 6–24 months prior to study entry
    - Patients with last DMT intake within 6 months of study entry

Study Outcomes

- The primary endpoint was global satisfaction with teriflunomide treatment, as measured by the Treatment Satisfaction Questionnaire for Medication (TSQM; version 1.4), at Week 48
  - The TSQM consists of 14 questions assessing the effectiveness, side effects, convenience, and global satisfaction of medication over the previous 2–3 weeks or since last use of medication
  - A higher TSQM score indicates greater treatment satisfaction
- Secondary endpoints included:
  - Change in TSQM score from baseline to Week 4 and Week 48 in patients switching from another DMT
  - Occurrence of treatment-emergent adverse events (AEs)

TSQM Assessments

- TSQM score was assessed at:
  - Week 4 and Week 48 (or end of treatment; EOT) in all patients
  - Baseline, Week 4, and Week 48 (or EOT) in patients switching from another DMT
- Results presented here are based on an interim analysis with a cutoff date of September 14, 2015

CONCLUSIONS

- **High levels of patient treatment satisfaction with teriflunomide were seen across all TSQM domains in these interim results from the US cohort in the real-world Teri-PRO study, supporting its use as a first-line treatment in relapsing-remitting MS**
- **In patients switching from other DMTs, clinically significant improvements in patient treatment satisfaction with teriflunomide were reported early in treatment across all 4 domains of the TSQM, and sustained over the course of the study**
- **The safety and tolerability profile of teriflunomide in the Teri-PRO study was consistent with that seen in phase 2 and 3 studies**
  - **The low rate of treatment discontinuation due to AEs reflects routine clinical practice**

Effect Size

- Effect size (ES), potentially useful in evaluating whether statistically significant differences in groups over time are clinically meaningful and relevant to patients,[8] was defined as the change from baseline divided by the standard deviation (SD) of the change
- Clinical significance was defined as per the ES limits set out by Cohen[8]: <0.2, negligible; ≥0.2 to <0.5, small; ≥0.5 to ≤0.8, moderate; and >0.8, high

Analysis Population

- All patients who received ≥1 dose of teriflunomide were included in the efficacy and safety analyses

RESULTS

- A total of 545 US patients were included in the Teri-PRO study; the majority received teriflunomide 14 mg (n=473, 86.8%) and the remainder received teriflunomide 7 mg (n=72, 13.2%)
- Demographics and baseline disease characteristics are summarized in **Table 1**

Table 1. Demographics and Baseline Disease Characteristics of US Patients

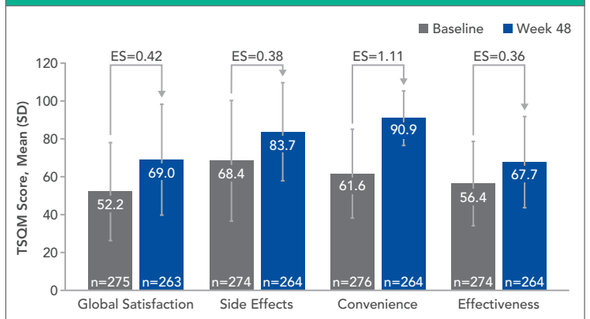
	Patients (N=545)
Age, mean (SD), y	50.6 (10.5)
Female, n (%)	414 (76.0)
Race, n (%)	
Black	49 (9.0)
Caucasian/White	489 (89.7)
Other	7 (1.3)
Time since first symptom of MS, mean (SD), y	14.7 (9.8)
Number of relapses within past 2 years, mean (SD)[a]	1.3 (1.7)
Baseline EDSS score, mean (SD)[b]	3.7 (1.9)
Previous DMT within past 2 years, n (%)	
No	160 (29.4)
Yes	385 (70.6)
Not within past 6 months	69 (12.7)
Within past 6 months	316 (58.0)

[a]n=544; [b]n=543.
DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Treatment Satisfaction

- Among the group of patients that switched from another DMT within the past 6 months, improvements from baseline to Week 48 in TSQM scores were seen across all TSQM domains (**Figure 1**). These improvements were already seen at Week 4
  - Mean (SD) change: Global Satisfaction, 16.3 (38.8); Side Effects, 14.8 (39.1); Convenience, 29.2 (26.4); Effectiveness, 11.1 (31.1)
  - A high ES was observed in the Convenience domain (1.11) while smaller ESs were seen for the Global Satisfaction (0.42), Side Effects (0.38), and Effectiveness (0.36) domains
- At Week 4 and Week 48, high mean treatment satisfaction scores were observed with teriflunomide for all US patients (**Figure 2**)

Figure 1. Improvement in Treatment Satisfaction by TSQM Domain at Baseline and Week 48 in US Patients Switching From Another DMT Within Past 6 Months

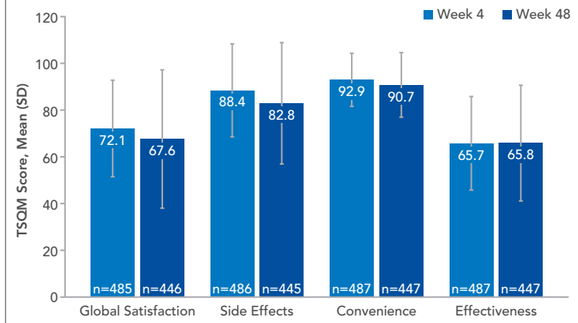


Patient numbers used for the calculation of ES were as follows: Global Satisfaction and Side Effects, n=230; Convenience, n=231; Effectiveness, n=229.
DMT, disease-modifying therapy; ES, effect size; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication (version 1.4).

Safety

- A total of 433 patients (79.4%) reported at least 1 treatment-emergent AE. A summary of treatment-emergent AEs, including those reported in ≥5% of patients, is shown in **Table 2**
- A total of 66 patients (12.1%) experienced a serious treatment-emergent AE (**Table 2**)
  - The most common serious AEs were MS relapse, reported in 6 patients (1.1%), and pneumonia, urinary tract infections, hypertension, non-cardiac chest pain, and alanine aminotransferase (ALT) increase, each reported in 3 patients (0.6%)
- As a result of an AE, 61 patients (11.2%) permanently discontinued treatment (**Table 2**)
  - AEs leading to treatment discontinuation in ≥2 patients were: diarrhea (n=11), hair thinning (n=5), ALT increase (n=3), fatigue (n=3), influenza-like illness (n=3), *Clostridium* test positive (n=2), headache (n=2), MS relapse (n=2), nausea (n=2), urticaria (n=2), and vomiting (n=2)
- Four AEs leading to death were reported (MS relapse, pneumonia, arrhythmia, and non-small cell lung cancer Stage IV); none of these were considered treatment-related

Figure 2. Treatment Satisfaction by TSQM Domain at Week 4 and Week 48 in All US Patients



SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication (version 1.4).

Table 2. Summary of Adverse Events

AE	Patients, n (%) (N=545)
All AEs	433 (79.4)
AEs reported in ≥5% of patients	
Hair thinning[a]	89 (16.3)
Diarrhea	83 (15.2)
Nausea	49 (9.0)
Urinary tract infection	44 (8.1)
Headache	36 (6.6)
Fatigue	28 (5.1)
Paresthesia	28 (5.1)
Serious AEs	66 (12.1)
AEs leading to treatment discontinuation	61 (11.2)
Deaths	4 (0.7)

[a]Medical Dictionary for Regulatory Activities (version 18.0)[9] preferred term is alopecia.
AE, adverse event.

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