Improvements in Patient-Reported Treatment Satisfaction With Teriflunomide: Results From the Phase 4 Teri-PRO Study

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OBJECTIVE

- **To report treatment satisfaction for patients enrolled in the 48-week phase 4 Teri-PRO (Teriflunomide Patient-Reported Outcomes) study**

INTRODUCTION

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS in 69 countries. Approximately 55,000 patients have been treated with teriflunomide as of April 2016, with total exposure to the 14-mg dose approaching 70,000 patient-years
- The consistent efficacy of teriflunomide has been demonstrated in placebo-controlled studies of patients with relapsing forms of MS (RMS),[1–3] and in those who experienced a first clinical episode suggestive of MS[4]
- Teriflunomide also has a well-characterized tolerability and safety profile, as demonstrated across phase 2 and 3 clinical studies,[1–5] and their extensions[6–9]
- The global phase 4 Teri-PRO study (NCT01895335) evaluated patient-reported treatment satisfaction and the efficacy, safety, and tolerability of teriflunomide in routine clinical practice
  - 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
- Here, we report the patient treatment satisfaction outcomes of the Teri-PRO study, as measured using the Treatment Satisfaction Questionnaire for Medication (TSQM; Version 1.4)
  - The TSQM was shown to have good measurement properties in an analysis using traditional psychometric methodology applied to data from the TENERE phase 3 clinical trial of patients with RMS receiving either teriflunomide or subcutaneous interferon B-1a (NCT00883337)[10]; a similar assessment has also been conducted using data from the Teri-PRO study[11]

METHODS

Study Design and Patients

- Teri-PRO was a prospective, global, multicenter, single-arm, open-label study
- The study design and full eligibility criteria have been presented previously.[12] In brief:
  - Patients ≥18 years of age with RMS were recruited from sites in the US, Canada, Europe, and Latin America
  - In line with the clinical practice setting, there were no disease activity eligibility criteria for patient recruitment into the study
  - 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, subdivided into:
    - Patients with last DMT intake 6–24 months prior to study entry
    - Patients with last DMT intake within 6 months of study entry ("switchers")

Study Outcomes

- The primary endpoint was global satisfaction with teriflunomide treatment, as measured by the TSQM, Version 1.4, at Week 48
  - The TSQM consists of 14 questions across 4 domains 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 patient-reported treatment satisfaction in that domain
- Secondary endpoints included change in TSQM score from baseline to Week 4 and Week 48 in patients switching from another DMT

TSQM Assessments

- TSQM score was assessed at:
  - Week 4 and Week 48 (or end of treatment) in all patients
  - Baseline, Week 4, and Week 48 (or end of treatment) in patients switching from another DMT
- Effect size (ES), potentially useful in evaluating whether differences in groups over time are clinically meaningful and relevant to patients, was defined as the mean change from baseline divided by the standard deviation of the change
- Clinical significance was defined as per the ES limits set out by Cohen[13]: <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 TSQM analysis

Statistical Analysis

- In a post hoc analysis, *P* values were derived from an ANCOVA model of change from baseline adjusted for baseline score and baseline Expanded Disability Status Scale score categorized as ≤3.5 or >3.5
- Analyses based on reason for treatment with teriflunomide and on prior DMT in switcher patients were also performed post hoc; ES value calculations were not performed for these analyses

RESULTS

Baseline Characteristics

- A total of 1001 patients were included in the Teri-PRO study, and 1000 received teriflunomide; most received teriflunomide 14 mg (n=928, 92.8%), with only a small number receiving teriflunomide 7 mg (n=72, 7.2%)
- Demographics and baseline disease characteristics are summarized in **Table 1**

Prior Treatments and Reasons for Treating With Teriflunomide

- The most frequent reason given by physicians for choosing treatment with teriflunomide was the convenience associated with an oral therapy; this was followed by side effects/risk of side effects with previous DMT and intolerance to administration mode of previous DMT (**Figure 1**)
- For patients who switched to teriflunomide within 6 months of discontinuing another DMT (switchers), the most common prior therapies before study entry included interferon B, glatiramer acetate, and dimethyl fumarate (**Figure 2**)

CONCLUSIONS

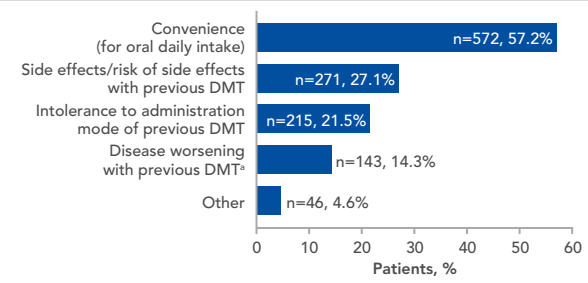
- **At Weeks 4 and 48, high levels of patient treatment satisfaction with teriflunomide were seen across all TSQM domains in the real-world Teri-PRO study**
- **In patients switching from other DMTs, statistically significant improvements in patient treatment satisfaction with teriflunomide were reported early at Week 4 and sustained over the course of the study across all 4 domains of the TSQM**
  - **These statistically significant improvements were seen regardless of the reason for choosing teriflunomide, and for patients switching from both platform injectable therapies and dimethyl fumarate**
  - **In combination with other Teri-PRO outcomes, these treatment satisfaction results are in accordance with results from the teriflunomide clinical trial program, and support the use of teriflunomide for relapsing-remitting MS**

Table 1. Demographics and Baseline Disease Characteristics[14]

Characteristic	N=1000
Age, mean (SD), y	47.1 (11.0)
Female, n (%)	756 (75.6)
Race, n (%) Asian/Oriental Black Caucasian/White Other	 3 (0.3) 50 (5.0) 938 (93.8) 9 (0.9)
Time since first symptoms of MS, mean (SD), y	13.2 (9.5)
Time since most recent relapse onset, mean (SD), mo[a]	31.2 (46.5)
Number of relapses within past 2 years, mean (SD)[b]	1.2 (1.5)
Baseline EDSS score, mean (SD)[c]	3.1 (2.0)
Previous DMT within past 2 years, n (%) No Yes	 285 (28.5) 715 (71.5)
Previous DMT within past 6 months (switchers), n (%)	594 (59.4)

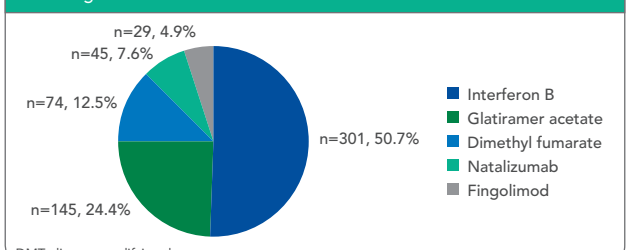
[a]n=971; [b]n=999; [c]n=996.
DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Figure 1. Reasons for Treating Patients With Teriflunomide According to Physicians[14]



[a]Worsening as defined by investigator. More than 1 reason per patient for treating could be documented. DMT, disease-modifying therapy.

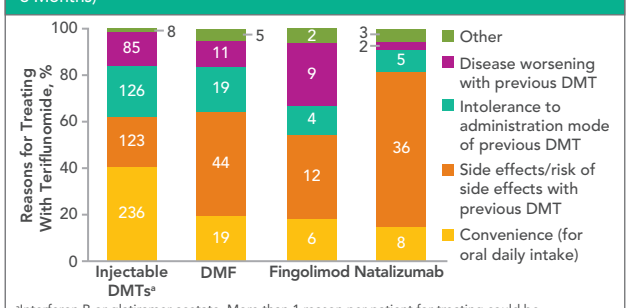
Figure 2. Last DMT Taken Before First Teriflunomide Intake by Patients Switching to Teriflunomide[14]



DMT, disease-modifying therapy.

- For patients switching from injectable therapies, the most common reason for physician choice of teriflunomide was the convenience of an oral therapy. For those switching from other oral therapies or natalizumab, the most frequently cited reason for choosing teriflunomide was the side effects/risk of side effects associated with the previous DMT (**Figure 3**)

Figure 3. Physician-Reported Reasons for Treating With Teriflunomide Based on Last DMT Taken (Patients Switching From Another DMT Within Past 6 Months)[14]

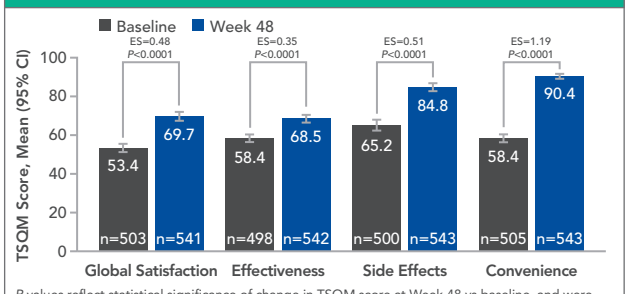


[a]Interferon B or glatiramer acetate. More than 1 reason per patient for treating could be documented. Percentages were calculated by using the sum of the number of patient responses as the denominator. DMF, dimethyl fumarate; DMT, disease-modifying therapy.

Treatment Satisfaction – Patients Switching From Another DMT

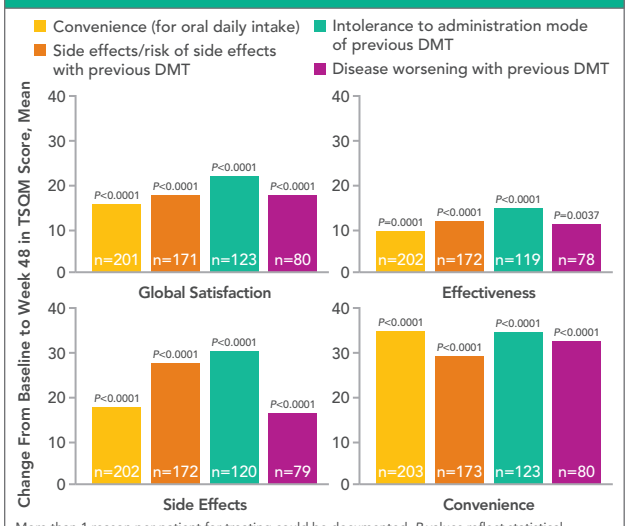
- In patients switching to teriflunomide from another DMT within the preceding 6 months, statistically significant improvements from baseline to Week 48 in TSQM scores were seen across all domains (**Figure 4**)
  - These improvements were already significant at Week 4: moderate or high ES values were seen for Global Satisfaction (0.78), Side Effects (0.69), and Convenience (1.31), and a small ES was seen for effectiveness (0.47); *P*<0.0001 vs baseline for all domains
- Increases in satisfaction on the Convenience domain were similar regardless of the reason for treatment with teriflunomide. Increases in treatment satisfaction in the Side Effects domain were greater in patients for whom intolerance to administration mode of previous DMT or side effects (or risk of side effects) with previous DMT were given as reasons for treating with teriflunomide, vs those citing other reasons (**Figure 5**)

Figure 4. Treatment Satisfaction by TSQM Domain at Baseline and Week 48 in Patients Switching From Another DMT Within Prior 6 Months[14]



P values reflect statistical significance of change in TSQM score at Week 48 vs baseline, and were derived from an ANCOVA model of change from baseline adjusted for baseline score and baseline Expanded Disability Status Scale score categorized as ≤3.5 or >3.5. CI, confidence interval; DMT, disease-modifying therapy; ES, effect size; TSQM, Treatment Satisfaction Questionnaire for Medication, Version 1.4.

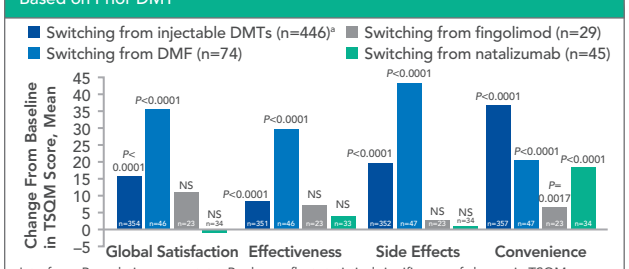
Figure 5. Change From Baseline to Week 48 in Treatment Satisfaction in Patients Switching From Another DMT Based on Reason for Treating With Teriflunomide[14]



More than 1 reason per patient for treating could be documented. *P* values reflect statistical significance of change in TSQM score at Week 48 vs baseline, and were derived from an ANCOVA model of change from baseline adjusted for baseline score and baseline Expanded Disability Status Scale score categorized as ≤3.5 or >3.5. DMT, disease-modifying therapy; TSQM, Treatment Satisfaction Questionnaire for Medication, Version 1.4.

- At Week 48, statistically significant increases in treatment satisfaction across all TSQM domains were seen in patients switching from injectable DMTs or dimethyl fumarate. In patients switching from natalizumab or fingolimod, statistically significant improvements were seen in the Convenience domain (**Figure 6**)

Figure 6. Improvement in Treatment Satisfaction by TSQM Domain at Week 48 in Patients Switching From Another DMT Within Past 6 Months, Based on Prior DMT[14]

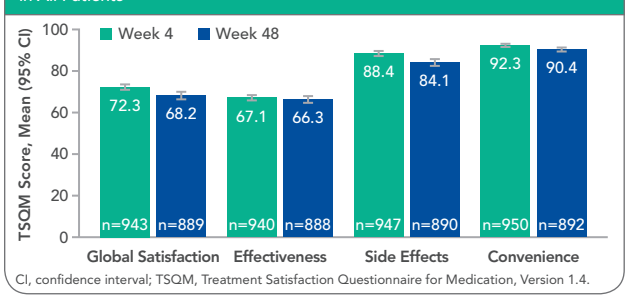


[a]Interferon B or glatiramer acetate. *P* values reflect statistical significance of change in TSQM score at Week 48 vs baseline, and were derived from an ANCOVA model of change from baseline adjusted for baseline score and baseline Expanded Disability Status Scale score categorized as ≤3.5 or >3.5. DMF, dimethyl fumarate; DMT, disease-modifying therapy; NS, nonsignficant; TSQM, Treatment Satisfaction Questionnaire for Medication, Version 1.4.

Treatment Satisfaction – All Patients

- At Week 4 and Week 48, high mean treatment satisfaction scores were observed with teriflunomide for all patients (**Figure 7**)

Figure 7. Treatment Satisfaction by TSQM Domain at Week 4 and Week 48 in All Patients[14]



CI, confidence interval; TSQM, Treatment Satisfaction Questionnaire for Medication, Version 1.4.

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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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