P3-363

Patient-Reported Outcomes (PROs) in Patients Switching to Teriflunomide From a Prior Disease-Modifying Therapy (DMT): Results From the Phase 4 Teri-PRO Study

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OBJECTIVE

- **To evaluate patient-reported treatment satisfaction, disability, and quality of life (QoL) during the Teri-PRO (Teriflunomide Patient-Reported Outcomes) study in patients who had received a disease-modifying therapy (DMT) other than teriflunomide within 6 months or 6–24 months prior to study entry**

INTRODUCTION

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS in 70 countries, and approximately 71,000 patients are currently being treated with teriflunomide worldwide
- The phase 4 Teri-PRO study (NCT01895335) evaluated treatment satisfaction, disability, and QoL with teriflunomide using patient-reported outcomes (PROs). The effectiveness, safety, and tolerability of teriflunomide when used in routine clinical practice were also assessed
  - High levels of treatment satisfaction with teriflunomide were reported over the course of the 48-week study[1]
- PROs are important in understanding the impact of treatment from a patient's perspective
  - Owing to the large number of DMTs currently available, patients often switch between different agents for many reasons. Understanding the reasons for choosing a particular DMT, and evaluating treatment outcomes from the patient's perspective using PROs, enhances understanding of treatment benefits
- Complementary data from the Teri-PRO study, describing clinical and safety outcomes as well as PROs in treatment-naïve patients are presented at this congress in posters P5-384 (Gold et al)[2] and P3-348 (Gold et al),[3] respectively

METHODS

Study Design and Patients

- Teri-PRO was a prospective, global, multicenter, single-arm, open-label study
  - Patients were treated with teriflunomide 14 mg or 7 mg (US only) according to local labeling
  - The full study design and eligibility criteria have been presented previously[4]
- Patients with last DMT intake (other than teriflunomide) within 2 years of study entry were divided into 2 groups:
  - Patients who received another DMT within the 6 months prior to study start ("switchers")
  - Patients who received another DMT 6–24 months prior to study start ("DMT experienced")

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
- Secondary endpoints included:
  - Change in TSQM scores from baseline to Week 4 and Week 48, or end of treatment (EoT), in patients receiving another DMT in the previous 6 months
  - Change in patient-reported disability (as measured by the Multiple Sclerosis Performance Scale [MSPS] score[5,6]) and QoL (as measured by the Multiple Sclerosis International Quality of Life [MusiQoL] score[7]) from baseline to Week 48 or EoT
- 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[8]: <0.2, negligible; ≥0.2 to <0.5, small; ≥0.5 to ≤0.8, moderate; and >0.8, high

Treatment Satisfaction

- The TSQM consists of 14 questions across 4 domains assessing Global Satisfaction, Effectiveness, Side Effects, and Convenience of medication over the previous 2–3 weeks or since last use of medication[9]
- The TSQM has shown good measurement properties using traditional psychometric methods applied to data from both this study[10] and the TENERE (NCT00883337) phase 3 trial[11]
- A higher TSQM score indicates greater treatment satisfaction in that domain
- TSQM scores were assessed at Week 4 and Week 48 (or EoT) in all patients (including DMT-experienced patients)
  - Baseline TSQM scores were not collected for DMT-experienced patients, as they were not receiving a DMT directly before study start

Patient-Reported Disability

- The MSPS questionnaire requires patients to indicate their level of disability experience during the past month
- A total MSPS score (ranging from 0 to 41) is calculated as the sum of the scores on 8 individual subscales, with a higher score reflecting greater disability
  - Subscales are: Mobility, Hand Function, Vision, Fatigue, Cognitive Symptoms, Bladder/Bowel, Sensory Symptoms, and Spasticity Symptoms
- MSPS scores were assessed at baseline, Week 24, and Week 48 (or EoT) in all patients (including switchers and DMT-experienced patients)

Quality of Life

- MusiQoL consists of 31 questions, divided into 9 dimensions: Activities of Daily Living, Psychological Well-being, Symptoms, Relationships With Friends, Relationships With Family, Sentimental and Sexual Life, Coping, Rejection, and Relationship With Healthcare System
- A total MusiQoL score is calculated as the mean of the dimension scores,[12] with higher scores reflecting higher QoL
- MusiQoL scores were assessed at baseline and Week 48 (or EoT) in all patients (including switchers and DMT-experienced patients)

Statistical Analysis

- All patients who received ≥1 dose of teriflunomide were included in the analysis
- In a post hoc analysis, *P* values for change vs baseline were derived for TSQM, MSPS, and MusiQoL scores from an analysis of covariance model adjusted for baseline score and baseline Expanded Disability Status Scale score (≤3.5 or >3.5). In patients switching to teriflunomide from another DMT, analyses for TSQM based on prior DMT and reasons for treating with teriflunomide were also performed post hoc

RESULTS

- Of the total Teri-PRO cohort (N=1000), 594 (59.4%) patients had received another DMT within 6 months prior to study entry (switchers), and 121 (12.1%) had received another DMT 6–24 months prior to study entry (DMT experienced)
  - In both switcher and DMT-experienced cohorts, the majority of patients received teriflunomide 14 mg (switchers: n=556, 93.6%; DMT experienced: n=108, 89.3%)
- Demographics and baseline disease characteristics are shown in **Table 1**

Table 1. Baseline demographics and disease characteristics

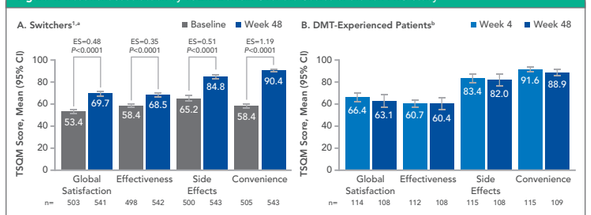
Characteristic	All Patients[a] (N=1000)	Switchers[b] (n=594)	DMT-Experienced Patients[c] (n=121)
Age, mean (SD), y	47.1 (11.0)	47.5 (11.0)	44.9 (11.1)
Female, n (%)	756 (75.6)	454 (76.4)	95 (78.5)
Race, n (%)			
Asian/oriental	3 (0.3)	2 (0.3)	1 (0.8)
Black	50 (5.0)	27 (4.5)	8 (6.6)
Caucasian/white	938 (93.8)	560 (94.3)	110 (90.9)
Other	9 (0.9)	5 (0.8)	2 (1.7)
Time since first symptoms of MS, mean (SD), y	13.2 (9.5)	13.8 (9.3)	12.4 (7.7)
No. of relapses in past 2 years, mean (SD)	1.2 (1.5)[d]	1.2 (1.5)	1.4 (1.3)
Time since most recent relapse onset, mean (SD), mo	31.2 (46.5)[e]	37.8 (51.5)[f]	25.2 (35.5)[g]
Baseline EDSS score, mean (SD)	3.1 (2.0)[h]	3.1 (2.0)[i]	3.1 (1.9)[j]

[a]Includes patients who have not previously received a DMT; [b]switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [c]DMT-experienced patients are defined as those who received a DMT other than teriflunomide in the 6–24 months prior to study start; [d]n=999; [e]n=971; [f]n=578; [g]n=120; [h]n=996; [i]n=592; [j]n=119. DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Treatment Satisfaction

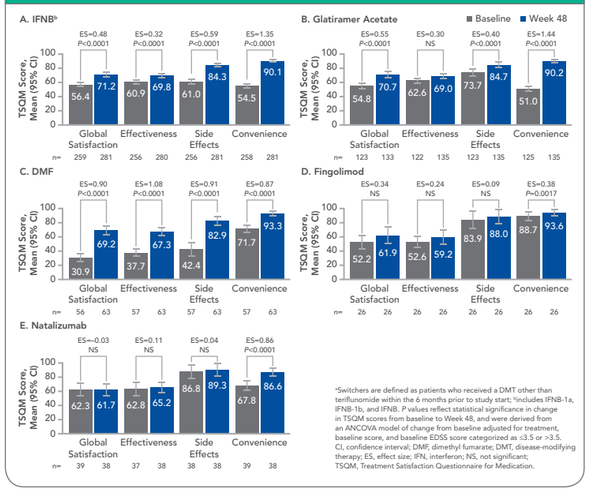
- In switchers, treatment satisfaction was significantly improved at Week 48 compared with baseline across all TSQM domains (**Figure 1A**). These improvements were observed as early as Week 4 (*P*<0.0001 for all domains)
  - At Week 48, moderate or high ES values were seen for Side Effects (0.51) and Convenience (1.19), and small ES values seen for Global Satisfaction (0.48) and Effectiveness (0.35)
- In DMT-experienced patients, high levels of treatment satisfaction were reported at Week 4 and were maintained to Week 48 (**Figure 1B**)
- In patients who had received interferon (IFN) B or dimethyl fumarate (DMF) in the previous 6 months, treatment satisfaction was significantly improved at Week 48 vs baseline across all TSQM domains (**Figure 2A** and **2C**). Improvements were seen as early as Week 4 (*P*<0.0001 for all domains)
  - At Week 48, high ES values vs baseline were seen in the Convenience domain for IFNB (1.35) and across all TSQM domains in patients who had received DMF (Global Satisfaction, 0.90; Effectiveness, 1.08; Side Effects, 0.91; Convenience, 0.87)
- Significant improvements were observed at Week 48 vs baseline in the domains of Global Satisfaction, Side Effects, and Convenience in patients who had previously received glatiramer acetate (GA) (**Figure 2B**). Improvements were seen as early as Week 4 (*P*<0.0001 for all domains)
  - At Week 48, high ES values were seen in the Convenience domain (1.44)
- Statistically significant improvements were seen in the Convenience domain at Week 48 in patients who had received fingolimod or natalizumab in the previous 6 months (**Figure 2D** and **2E**). Improvements in TSQM scores were seen as early as Week 4 and were statistically significant in some, but not all, TSQM domains (fingolimod: Global Satisfaction *P*=0.0004, Effectiveness *P*=0.0013, Side Effects not significant [NS], Convenience NS; natalizumab: Global Satisfaction *P*=0.0468, Effectiveness NS, Side Effects NS, Convenience *P*<0.0001)
  - At Week 48, high ES values were seen in the Convenience domain (0.86) for patients previously receiving natalizumab

Figure 1. Treatment Satisfaction by TSQM Domain Over the Course of the Teri-PRO Study



[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [b]DMT-experienced patients are defined as those who received a DMT other than teriflunomide in the 6–24 months prior to study start. *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 EDSS score categorized as ≤3.5 or >3.5. *P* values and ES calculations were not performed for the DMT-experienced cohort, Week 4 vs Week 48. ANCOVA, analysis of covariance; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; ES, effect size; TSQM, Treatment Satisfaction Questionnaire for Medication.

Figure 2. Treatment Satisfaction at Baseline and Week 48 in Switchers[a] According to Previous DMT



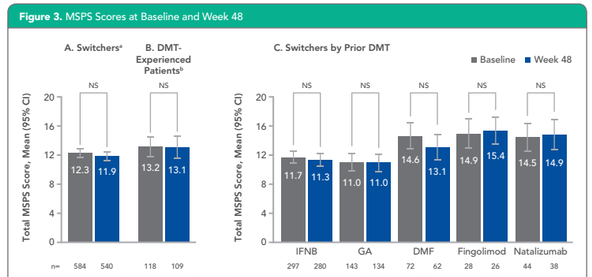
[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [b]includes IFNB-1a, IFNB-1b, and IFNB. *P* values reflect statistical significance in change in TSQM scores from baseline to Week 48, and were derived from an ANCOVA model of change from baseline adjusted for treatment, baseline score, and baseline EDSS score categorized as ≤3.5 or >3.5. CI, confidence interval; DMF, dimethyl fumarate; DMT, disease-modifying therapy; ES, effect size; IFN, interferon; NS, not significant; TSQM, Treatment Satisfaction Questionnaire for Medication.

- Treatment satisfaction was significantly improved at Week 48 across all TSQM domains in switchers regardless of reason for treating with teriflunomide (reasons were disease worsening with previous DMT, convenience for oral daily intake, intolerance to administration mode of previous DMT, side effects/risk of side effects with previous DMT, or other)

Patient-Reported Disability

- Total MSPS scores remained low and stable over the course of the study in both switcher and DMT-experienced cohorts (**Figure 3A** and **3B**)
- Scores remained low and stable in switchers regardless of prior DMT received (**Figure 3C**)

Figure 3. MSPS Scores at Baseline and Week 48

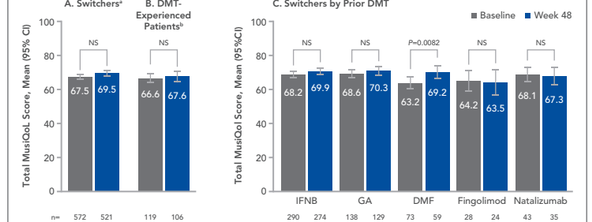


[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [b]DMT-experienced patients are defined as those who received a DMT other than teriflunomide in the 6–24 months prior to study start. No significant differences were observed over the course of the study. Statistical significance in MSPS scores from baseline to Week 48 was assessed using an ANCOVA model of change from baseline adjusted for treatment, baseline score, and baseline EDSS score categorized as ≤3.5 or >3.5. ANCOVA, analysis of covariance; CI, confidence interval; DMF, dimethyl fumarate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; GA, glatiramer acetate; IFN, interferon; MSPS, Multiple Sclerosis Performance Scale; NS, not significant.

Quality of Life

- Total scores on the MusiQoL scale remained high and stable over the course of the study in both switcher and DMT-experienced cohorts (**Figure 4A** and **4B**)
- Scores remained high in switchers regardless of prior DMT received (**Figure 4C**)
  - Statistically significant improvements were observed in total MusiQoL scores at Week 48 compared with baseline in patients who had previously received DMF prior to study entry

Figure 4. Total MusiQoL Scores at Baseline and Week 48



[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [b]DMT-experienced patients are defined as those who received a DMT other than teriflunomide in the 6–24 months prior to study start. Statistical significance in change in MSPS scores from baseline to Week 48 was assessed using an ANCOVA model of change from baseline adjusted for treatment, baseline score, and baseline EDSS score categorized as ≤3.5 or >3.5. ANCOVA, analysis of covariance; CI, confidence interval; DMF, dimethyl fumarate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; GA, glatiramer acetate; IFN, interferon; MusiQoL, Multiple Sclerosis International Quality of Life; NS, not significant.

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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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