QL04

Outcomes in the African American Subpopulation From the Phase 4 Teri-PRO Study of Teriflunomide

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OBJECTIVE

- **To report patient-reported outcomes (PROs), effectiveness, safety, and tolerability of teriflunomide for African American (AA) patients enrolled in the phase 4 Teri-PRO study**

INTRODUCTION

- Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting MS in 70 countries, with more than 71,000 patients currently being treated with teriflunomide worldwide
- Teriflunomide has established efficacy on clinical outcomes, and a manageable safety and tolerability profile in patients with RMS (phase 3 studies TEMSO [NCT00134563][1] and TOWER [NCT00751881][2]), and with a first episode suggestive of MS (TOPIC [NCT00622700])[3]
- The global Teri-PRO study (NCT01895335) evaluated treatment satisfaction, disability, and quality of life (QoL) associated with teriflunomide treatment using PROs, as well as the effectiveness, safety, and tolerability of teriflunomide in routine clinical practice
  - High levels of treatment satisfaction were reported over 48 weeks in the total study population[4]
- Approximately 10% of patients enrolled in Teri-PRO in the US were of AA origin, which is a population that tends to show a poorer prognosis than Caucasian patients[5–7]
  - AA patients show a more aggressive disease course[5] and a higher incidence of cerebellar dysfunction[6]
  - This population has also been shown to have a higher risk of disability[5–7]

METHODS

Study Design

- Teri-PRO was a prospective, global, multicenter, single-arm, open-label study; the study design and inclusion criteria have been presented previously[8]
- Patients received once-daily teriflunomide 14 mg or 7 mg, per local labeling
- Teri-PRO patients enrolled in the US were included in this analysis and divided into 2 cohorts: AA patients and non-AA patients
- "Switchers" are defined as patients who received a disease-modifying therapy (DMT) other than teriflunomide within the 6 months prior to study start

Study Outcomes

- The primary outcome was global treatment satisfaction at Week 48, measured using the Treatment Satisfaction Questionnaire for Medication (TSQM, Version 1.4)[9]
- Secondary outcomes included change from baseline to Week 48, or end of treatment (EoT), in:
  - TSQM scores in patients receiving a prior DMT in the previous 6 months (switchers)
  - Patient-reported QoL (measured by Multiple Sclerosis International Quality of Life [MusiQoL] score[10,11]) and disability (measured by Multiple Sclerosis Performance Scale [MSPS] score[12,13] and Patient-Determined Disease Steps [PDDS] score[14])
  - Expanded Disability Status Scale (EDSS) score
- Annualized treated relapse rate was also a secondary outcome in this study
- 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[15]: <0.2, negligible; ≥0.2 to <0.5, small; ≥0.5 to ≤0.8, moderate; and >0.8, high
- Adverse events (AEs) were reported at each study visit (baseline, Week 4, Week 24, and Week 48)

Treatment Satisfaction

- The TSQM measures patient-reported satisfaction with treatment and consists of 4 domains: Effectiveness, Side Effects, Convenience, and Global Satisfaction
  - A higher TSQM score indicates greater treatment satisfaction in that domain
- The TSQM has shown good measurement properties using traditional psychometric methods applied to data from both this study[16] and the TENERE (NCT00883337) phase 3 trial[17]
- Treatment satisfaction was measured according to prior treatment experience:
  - At Week 4 and Week 48/EoT for all patients
  - At baseline, Week 4, and Week 48/EoT for switchers

Disability

- Physician-reported disability was measured using the EDSS
- Patient-reported disability was measured using the PDDS scale and the MSPS questionnaire, where higher scores reflect greater disability
  - The PDDS scale focuses mainly on ambulatory function, and is scored from 0 (normal) to 8 (bedridden)
  - The MSPS questionnaire measures the level of disability (ranging from 0 to 41) experienced by the patient during the past month; total MSPS score is calculated as the sum of the scores on 8 individual subscales: Mobility, Hand Function, Vision, Fatigue, Cognitive Symptoms, Bladder/Bowel, Sensory Symptoms, and Spasticity Symptoms

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, with higher scores reflecting higher QoL

Statistical Analysis

- *P* values for change vs baseline in the AA and non-AA cohorts were derived post hoc for TSQM, MSPS, PDDS, and MusiQoL scores, from an analysis of covariance model adjusted for baseline score and baseline EDSS score (categorized as ≤3.5 or >3.5)

RESULTS

- Of the 545 patients enrolled in the Teri-PRO study in the US, 49 (8.9%) were AA
- Baseline demographics and disease characteristics were comparable between AA and non-AA cohorts, with the exception that AA patients were younger and had a shorter time since symptom onset (**Table 1**)
- Similar proportions of patients in both the AA cohort (55.1%) and the non-AA cohort (58.3%) switched from a prior DMT to teriflunomide within the 6 months prior to study entry (switchers)

Table 1. Baseline Demographics and Disease Characteristics

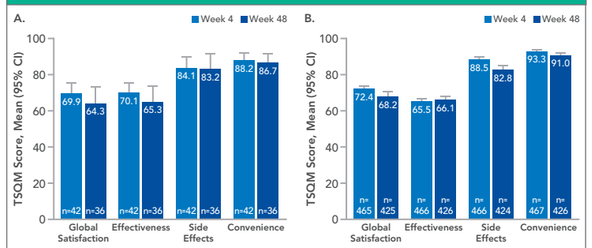
	AA Patients (n=49)	Non-AA Patients (n=496)	AA Switchers[a] (n=27)	Non-AA Switchers[a] (n=289)
Age, mean (SD), y	45.0 (10.9)	51.2 (10.2)	48.0 (10.7)	51.4 (10.2)
Female, n (%)	40 (81.6)	373 (75.2)	23 (85.2)	222 (76.8)
Time since first MS symptoms, mean (SD), y	11.2 (8.2)	15.1 (9.8)	13.2 (9.5)	15.4 (9.7)
Time since most recent relapse onset, mean (SD), mo	31.4 (52.8)[b]	32.3 (51.6)[c]	42.4 (66.7)[d]	37.3 (57.6)[e]
Number of relapses in past 2 years, mean (SD)	1.3 (1.7)	1.3 (1.7)[f]	1.3 (1.8)	1.3 (1.8)
Baseline EDSS score, mean (95% CI)	3.6 (3.0, 4.2)	3.7 (3.6, 3.9)[g]	4.3 (3.4, 5.1)	3.7 (3.5, 4.0)[h]

[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start; [b]n=48; [c]n=471; [d]n=26; [e]n=276; [f]n=495; [g]n=494; [h]n=288. AA, African American; CI, confidence interval; EDSS, Expanded Disability Status Scale; SD, standard deviation.

Treatment Satisfaction

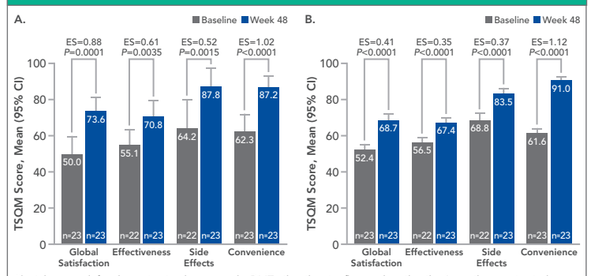
- TSQM scores were comparable between the AA and non-AA cohorts, with treatment satisfaction remaining high over the study period in all domains (**Figure 1**)
- In AA switchers, statistically significant increases in scores across all TSQM domains were observed from baseline to Week 48 (**Figure 2**)
  - A statistically significant increase was also seen in all domains for the non-AA switcher cohort (**Figure 2**)
  - Improvements in TSQM scores were already observed by Week 4 across all domains in both cohorts of switchers (data not shown)

Figure 1. Treatment Satisfaction in (A) African American and (B) Non-African American Patients



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

Figure 2. Treatment Satisfaction in (A) African American Switchers and (B) Non-African American Switchers



[a]Switchers are defined as patients who received a DMT other than teriflunomide within the 6 months prior to study start. CI, confidence interval; ES, effect size; TSQM, Treatment Satisfaction Questionnaire for Medication.

Disability

- There was little variation in disability outcomes reported for AA and non-AA patients
  - Baseline MSPS, PDDS, and EDSS scores were similar for the AA and non-AA cohorts, and remained stable over the treatment period (**Table 2**)

Table 2. Evolution of MSPS, PDDS, and EDSS Scores in African American and Non-African American Patients

	AA Patients (n=49)		Non-AA Patients (n=496)	
	Baseline	Week 48	Baseline	Week 48
MSPS overall score, mean (95% CI)	13.1 (11.2, 15.0)[a]	14.0 (11.5, 16.4)[b]	15.3 (14.6, 15.9)[c]	14.7 (14.0, 15.4)[d]
PDDS score, mean (95% CI)	2.5 (1.9, 3.1)[e]	2.7 (2.0, 3.5)[f]	2.9 (2.7, 3.0)[g]	2.8 (2.6, 3.0)[h]
EDSS score, mean (95% CI)	3.6 (3.0, 4.2)[i]	3.7 (3.0, 4.5)[j]	3.7 (3.6, 3.9)[k]	3.7 (3.5, 3.9)[l]

[a]n=48; [b]n=35; [c]n=488; [d]n=426; [e]n=47; [f]n=35; [g]n=486; [h]n=424; [i]n= 48; [j]n=36; [k]n=488; [l]n=417.
AA, African American; CI, confidence interval; EDSS, Expanded Disability Status Scale; MSPS, Multiple Sclerosis Performance Scale; PDDS, Patient-Determined Disease Steps.

Relapses Requiring Treatment

- Annualized treated relapse rate during the study was higher for AA patients (0.35) compared with non-AA patients (0.16) (**Table 3**)
  - This difference was more pronounced in switchers, with a relapse rate of 0.50 for AA switchers vs 0.18 for non-AA switchers

Table 3. Treated Relapses During the Teri-PRO Study in African American and Non-African American Patients

	AA Patients (n=49)	Non-AA Patients (n=496)	AA Switchers (n=27)	Non-AA Switchers (n=289)
Annualized treated relapse rate (95% CI)[a]	0.35 (0.16, 0.54)	0.16 (0.12, 0.20)	0.50 (0.21, 0.80)	0.18 (0.13, 0.24)
Number of patients free from relapse, n (%)	40 (81.6)	440 (88.7)	20 (74.1)	249 (86.2)

[a]Annualized treated relapse rate presented for the study duration. AA, African American; CI, confidence interval.

- In the 2 years prior to initiating treatment with teriflunomide, the percentage of patients across all 4 subgroups that was free from relapse was lower (≤52%) than during Teri-PRO (≥74%)

Quality of Life

- Total mean (95% CI) MusiQoL scores at baseline and Week 48 for AA patients were 65.50 (60.77, 70.24) and 63.36 (57.57, 69.14), respectively
  - All subdomain scores in MusiQoL remained stable over the course of the study

Safety

- AEs were reported in similar proportions of patients in the AA and non-AA cohorts, and were mostly of mild to moderate intensity
- The numbers of serious AEs and AEs leading to permanent discontinuation were also comparable between AA and non-AA patients, with no serious AE of any type seen in more than 1 AA patient
- There were 4 deaths reported in Teri-PRO, none of which was considered related to teriflunomide treatment; there were no deaths in AA patients within Teri-PRO

CONCLUSIONS

- **African American patients with MS are known to have a more aggressive disease course with poorer long-term prognosis, which is consistent with the higher relapse rate observed in the African American cohort of Teri-PRO**
- **Despite this, in the small sample of African American patients in Teri-PRO, high levels of treatment satisfaction were reported, with significant increases seen in those switching from other DMTs, consistent with the overall Teri-PRO study cohort**

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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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