Effectiveness of Relapsing Multiple Sclerosis Patients Switching to Teriflunomide Following Disease Progression in a Real-World Setting

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OBJECTIVE

- **To describe patient demographics and examine the effectiveness of teriflunomide in patients with relapsing multiple sclerosis (RMS) who switched from other disease-modifying treatments (DMTs) following disease progression, in a real-world setting.**

BACKGROUND

- MS is a progressive demyelinating and neurodegenerative disease, with an unpredictable disease course, and broad clinical spectrum.[4-6]
  - Relapsing or progressive MS may be characterized by severity of signs and symptoms, frequency of relapses, rate of worsening, residual disability, and impairment.[4]
  - Patients with RMS commonly initiate DMTs to decrease relapse and slow disease progression.[7]
- Several DMTs are currently available to treat MS, such as teriflunomide, a once-daily, oral immunomodulatory therapy with demonstrated efficacy in phase 2 and phase 3 trials in patients with RMS.[8]
  - Teriflunomide is approved in >80 countries for treating RMS, including clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), active secondary progressive MS (aSPMS), and pediatric MS patients aged ≥10 years, depending on the local label.
- Real-world studies of teriflunomide have shown stability in EDSS scores and MRI lesion analyses for, in some cases, up to 4 years of follow-up.[1-3]
  - Post-hoc analyses of phase 3 data also support the efficacy of teriflunomide across a broad range of patients with RRMS, including those who have discontinued previous DMTs.[9]
  - Patients also report high treatment satisfaction with teriflunomide, with patients who switched to teriflunomide from other DMTs ("switchers") reporting improved satisfaction.[10]
  - However, the effectiveness of teriflunomide has not been studied in an exclusively disease-progressing RMS population.
- By analyzing RMS patients who switch to teriflunomide following disease progression, in a real-world setting, we can better understand the patient characteristics and effectiveness outcomes measures pre- and post-switch (relapses, disability, and MRI).

METHODS

- A retrospective, observational, cohort study was conducted by extracting medical chart data from a single US neurology center for 115 adult patients with RMS and disease progression who switched to teriflunomide from a prior DMT.
- Disease progression was defined as a ≥1-point increase in EDSS score sustained over 6 months in the absence of new clinical relapse and/or new MRI activity.
- Data were collected 1 year pre-index, at index, and for 1-year post-index.
- Descriptive statistics were conducted for all outcome measures (relapses, disability, MRI).
- All patients aged >18 years who had been diagnosed with MS and switched to, and received, teriflunomide at the neurology center between September 2012 and February 2019 were screened.
  - MS patients who were pregnant or wished to become pregnant were excluded.

RESULTS

Study cohort

- Patients were mainly female (85.2%) and White (98.3%). While the majority of patients had never smoked, 38.6% of patients had a past history of smoking and 8.8% were current smokers. (**Table 1**).
- At index, the mean age was 55.1 ± 10.1 years (range: 24.0–75.0 years), and disease duration was 19.0 ± 10.7 years (range: 2.0–53.0 years).
- Patients often had comorbid depression, spasticity, anxiety, and neurogenic bladder (**Table 1**).

Switching to teriflunomide from prior DMTs

- The most common prior DMTs used during the pre-index period (prior to switching) were:
  - Interferon beta-1a → 33.9%
  - Glatiramer acetate → 27.0%
  - Dimethyl fumarate → 18.3%.
- Patients switched to teriflunomide for reasons of tolerability, safety, or efficacy; however, over half of patients switched for "Other" reasons (**Table 2**).

Change in EDSS score following switching to teriflunomide from other DMTs

- Mean EDSS score reduced from 2.71 ± 2.31 (1 year pre-index) to 2.60 ± 2.15 (1 year post-index); mean change −0.05; *P*=0.325 (**Figure 1**).

Use of ambulatory aids following switching to teriflunomide from other DMTs

- Of the 48 patients with RMS who had data on ambulatory aid use in the pre- and post-index periods, 40 (83.3%) did not require an ambulatory aid 1 year after switching to teriflunomide, vs 79.2% (n=38/48) at 1 year pre-index (**Figure 2**).
  - A small proportional increase in wheelchair use was seen after switching (+2.0%), but this translated to 1 additional patient using a wheelchair in the post-index (n=4) vs pre-index period (n=3), in patients with available data.

CONCLUSIONS

- **Patients with RMS who had disease progression and who switched to teriflunomide treatment demonstrated numerical reductions in Expanded Disability Status Scale (EDSS) scores, and most patients showed an improvement or remained stable in annualized relapse rate (ARR) and/or evidence of MRI lesions.**
  - **These observations are in line with previous real-world observational studies of MS patients on teriflunomide who demonstrated stability in EDSS scores and in MRI lesion analyses.[1-3]**
  - **However, the small sample size needs to be considered when interpreting our observations.**
- **Longer-term assessment of this cohort may aid further understanding of the impact of teriflunomide use on clinical outcomes specifically in patients with disease-progressing RMS.**

Annualized relapse rate

- ARR was stable for almost two-thirds (n=75) of patients; 16 patients showed possible improvement with fewer relapses (**Table 3**).
- At 1 year post-index, ARR remained stable in 65.3% of patients (**Table 3**, green text); 13.9% of patients showed improvement (**Table 3**, blue text), with fewer relapses vs 1 year pre-index.

MRI observations

- MRI lesions remained stable in most patients (75%) during the 1-year post-index period after switching to teriflunomide, and improved in 3 patients (**Table 4**).

Table 1. Baseline Characteristics and Demographics of Study Cohort with RMS and Disease Progression

Demographics	RMS patients who started teriflunomide (N=115)[a]
Age, mean ± SD [median], y	55.1 ± 10.1 [57.0]
Age group, n (%), y	
<30	2 (1.7)
30–39	9 (7.8)
40–49	16 (13.9)
50–59	44 (38.3)
60–69	41 (35.7)
≥70	3 (2.6)
Female, n (%)	98 (85.2)
Race, n (%)	
White	113 (98.3)
Black or Multiracial	2 (1.8)
Not Hispanic or Latino	115 (100.0)
Smoking status, n (%)[b]	
Current smoker	10 (8.8)
Never smoked	60 (52.6)
Past smoker	44 (38.6)
Insurance type, n (%)[b]	
Medicaid insurance	4 (3.5)
Medicare insurance	27 (23.7)
Private insurance	83 (72.8)
MS disease duration, mean ± SD [median], y	19.0 ± 10.7 [18.0]
Comorbid conditions, n (%)	
Depression	63 (54.8)
Spasticity	51 (44.3)
Anxiety	49 (42.6)
Neurogenic bladder	49 (42.6)
Hypertension	47 (40.9)
Thyroid disorder	42 (36.5)
Migraine	33 (28.7)
Peripheral neuropathy	22 (19.1)
Rheumatoid arthritis	16 (13.9)
Diabetes	13 (11.3)
Irritable bowel syndrome	4 (3.5)
Pseudobulbar affect	1 (0.9)

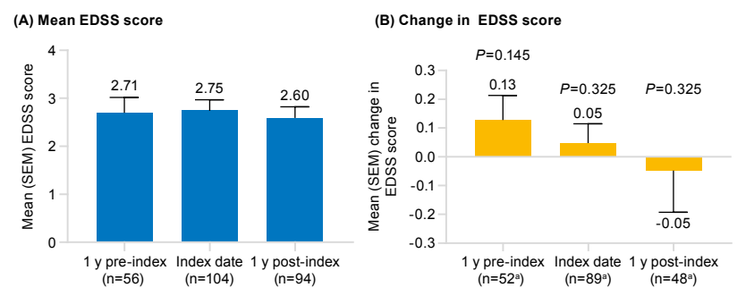
MS=multiple sclerosis; RMS=relapsing multiple sclerosis; SD=standard deviation.
[a]115 patients, unless otherwise noted.
[b]114 patients; 1 patient with missing data.

Table 2. Reasons for Switching to Teriflunomide From Existing DMTs

Reason given, n (%)	RMS patients who started teriflunomide (N=115)
Efficacy – new MRI lesions[a]	12 (10.4)
Efficacy – relapse	2 (1.7)
Needle fatigue	7 (6.1)
Safety	13 (11.3)
Tolerability	19 (16.5)
Other	62 (53.9)

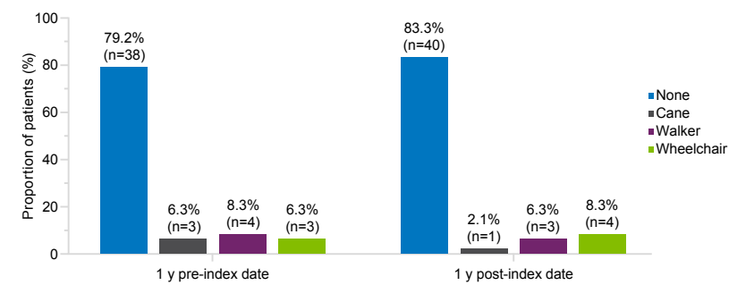
DMTs=disease-modifying treatments; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis.
[a]Combined unique lesions (new gadolinium [Gd]-enhancing lesions and/or new or enlarging T2 lesions).

Figure 1. Change in EDSS Score Following Switching to Teriflunomide From Other DMTs



DMTs=disease-modifying treatments; EDSS=Expanded Disability Status Scale; SEM, standard error of the mean.
[a]Sample sizes for pre- and post-index comparisons differed from those for measurements at single time points.

Figure 2. Use of Ambulatory Aid Following Switching to Teriflunomide From Other DMTs[a]



DMTs=disease-modifying treatments.
[a]Patients with missing data were excluded.

Table 3. Annualized Relapse Rate in the 1-Year Post-Index Period for Patients Who Switched to Teriflunomide From Other DMTs

		Relapses in 1-year post-index period			RMS patients who started teriflunomide (N=115)
		0	1	2	
Patients, n (%)		81 (70.4)	29 (25.2)	5 (4.3)	115
Relapses in 1-year pre-index period					
0	n (%)	**67 (58.3)**	20 (17.4)	1 (0.9)	88 (76.5)
	(% of column)	67/81 (82.7)	20/29 (69.0)	1/5 (20.0)	
	[% of row]	67/88 [76.1]	20/88 [22.7]	1/88 [1.1]	
1	n (%)	**13 (11.3)**	**7 (6.1)**	3 (2.6)	23 (20.0)
	(% of column)	13/81 (16.0)	7/29 (24.1)	3/5 (60.0)	
	[% of row]	13/23 [56.5]	7/23 [30.4]	3/23 [13.0]	
2	n (%)	**1 (0.9)**	**2 (1.7)**	**1 (0.9)**	4 (3.5)
	(% of column)	1/81 (1.2)	2/29 (6.9)	1/5 (20.0)	
	[% of row]	1/4 [25.0]	2/4 [50.0]	1/4 [25.0]	

DMTs, disease-modifying therapies; RMS=relapsing multiple sclerosis.
Green text=patients with stable relapse rate; Blue text=patients with fewer relapses in post-index period.
Bowker's exact symmetric test, *P*=0.780.
n/N given for calculations by column (as a proportion of those with 0, 1, 2 relapses in the post-index period) or by row (as a proportion of those with 0, 1, 2 relapses in the pre-index period).

Table 4. MRI Observations in the 1-Year Post-Index Period for Patients Who Switched to Teriflunomide From Other DMTs

	RMS patients who started teriflunomide (with complete MRI data) (n=68[a])
MRI lesions[b] 1 year post-index, n (%)	
Improved	3 (4.4)
Stable	51 (75.0)
Worsened	14 (20.6)

DMTs, disease-modifying therapies; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis.
[a]Patients with missing data were excluded (n=47).
[b]Combined unique lesions (new gadolinium [Gd]-enhancing lesions and/or new or enlarging T2 lesions) with status compared to prior scan (worsened, stable, improved).

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