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ORIGINAL RESEARCH

Effectiveness and Safety of Teriflunomide in Relapsing–Remitting Multiple Sclerosis and Improvements in Quality of Life: Results from the Real-World TERICARE Study

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ABSTRACT

Introduction: Teriflunomide is a once-daily oral immunomodulator approved for relapsing forms of multiple sclerosis (MS) or relapsing–remitting multiple sclerosis (RRMS; depending on the local label), based on extensive evidence from clinical trials and a real-world setting on efficacy, tolerability and

patient-reported benefits. The TERICARE study assessed the impact of teriflunomide treatment over 2 years on health-related quality of life (HRQoL) and some of the most common and disabling symptoms of MS, such as fatigue and depression.

Methods: This prospective observational study in Spain included RRMS patients treated with teriflunomide for ≤ 4 weeks. The following patient-reported outcomes (PROs) were collected at baseline and every 6 months for 2 years: the 29-item Multiple Sclerosis Impact Scale version 2 (MSIS-29), the 21-item Modified Fatigue Impact Scale (MFIS-21), the Beck Depression Inventory (BDI-II), the Short Form (SF)-Qualiveen and the Treatment Satisfaction Questionnaire for Medication v1.4 (TSQM). Annualised relapse rate (ARR), disability progression according to the Expanded Disability Status Scale (EDSS), and no evidence of disease activity (NEDA-3) were also assessed.

Results: A total of 325 patients were analysed. Patients had a mean (SD) age of 43.2 years (10.4), a mean baseline EDSS score of 1.75 (1.5), a mean number of relapses in the past 2 years of 1.5 (0.7), and 64% had received prior disease-modifying therapy (DMT). Patients showed significant improvements in the psychological domain of MSIS-29 from 35.9 (26.6) at baseline to 29.4 (25.5) at 18 months ($p = 0.004$) and 29.0 (24.6) at 24 months ($p = 0.002$). Levels of fatigue and depression were also reduced. After 2 years of treatment with teriflunomide, ARR was reduced to 0.17 (95% CI 0.14–0.21) from the baseline of 0.42 (95% CI 0.38–0.48), representing a 60.1% reduction. Mean EDSS scores remained stable during the study, and 79.9% of patients showed no disability progression. 54.7% of patients achieved NEDA-3 in the first 12 months, which increased to 61.4% during months 12–24. Patients reported increased satisfaction with treatment over the course of the study, regardless of whether they were DMT naive or not.

Conclusion: Teriflunomide improves psychological aspects of HRQoL and maintains low levels of fatigue and depression. Treatment with teriflunomide over 2 years is effective in reducing ARR and disability progression.

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Keywords: Annualised relapse rate; Clinical practice; Disability; Health-related quality of life; Multiple sclerosis; Teriflunomide

Key Summary Points

The heterogeneity of multiple sclerosis (MS) and the current therapeutic landscape require an integrated assessment that includes individual needs to optimise treatment benefits. Having data on patients' symptoms, overall health and satisfaction with treatment—which are often undetected by clinicians—is a good start with regard to offering better patient-centred care.

The objective of this study was to assess the effect of teriflunomide on health-related quality of life (HRQoL) and symptoms such as fatigue and depression, which complement effectiveness and safety outcomes for determining whether the clinical benefits of teriflunomide are reflected in patient's lives.

The improvements observed in the psychological domain of HRQoL and the lack of worsening of fatigue and depression over 2 years on teriflunomide reflect how MS patients perceived the clinical benefits of the treatment and how it may contribute to their general well-being.

Moreover, the effectiveness at reducing the annualized relapse rate (ARR) and disability worsening in mildly affected patients with relapsing–remitting MS reinforces the importance of appropriate patient selection in achieving better outcomes.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) that usually debuts in young adults with a typical initial clinical course of relapses and remissions of neurological symptoms, leading to significant impairment in different aspects of patients' lives.

Although MS remains incurable, the increasing number of available disease-modifying therapies (DMTs) with proven long-term benefits and a manageable safety profile provide patients and neurologists with a better chance of an individualised approach based on the patient's perspective, ensuring the right drug is used by the right patient.

Teriflunomide is indicated as a once-daily oral immunomodulator for the treatment of relapsing forms of MS or relapsing–remitting multiple sclerosis (RRMS; depending on the local label). In the phase 3 clinical trials TEMSO [1], TOWER [2] and TENERE [3], teriflunomide was demonstrated to significantly reduce disease activity and risk of relapse and to delay disease progression, with these benefits being maintained for the long term in the respective extension studies [4–8]. These findings have also been replicated in large phase 4 [9–11] and other real-world [12] studies. In addition to clinical outcome measures, teriflunomide has

been demonstrated to improve health-related quality of life (HRQoL) [9–11, 13, 14], increase the satisfaction of patients with the effectiveness, side-effect profile and convenience of treatment [3, 9–12, 14], and improve or stabilise cognitive functioning [10, 15].

Obtaining data on patient symptoms, overall health, disability and treatment satisfaction, which are often undetected by routine clinical examination, represents a good start in the move towards patient-centred management, as they help to determine the relative effectiveness of a drug and thus its effects on patient status [16]. The complexity of MS and the current therapeutic landscape require an integrated assessment that includes patients' needs in order to optimise patient benefits.

This study aimed to assess the impact of teriflunomide treatment over 2 years on HRQoL and some of the most common and disabling symptoms of MS. Moreover, we investigated the effectiveness and safety of this treatment to better understand whether the clinical benefits of teriflunomide are reflected in the patient's perception of their disease.

METHODS

Study Design and Patients

TERICARE was a 2-year observational prospective study in patients diagnosed with RRMS from 48 centres in Spain. Patients were included in this study if they were receiving teriflunomide for no more than 4 weeks and they had no relapses within the last 30 days prior to inclusion. Both DMT-naive patients and DMT-experienced patients could enter the study.

The Ethics Committee "Corporació Sanitària Parc Taulí of Sabadell (Barcelona, Spain; reference number 2015619) approved the protocol. The study was conducted in accordance with the Declaration of Helsinki and local regulations, and all patients provided written informed consent.

Assessments

The observation period was 2 years after patient enrolment. Data collection and patient observations occurred at baseline and 6, 12, 18, and 24 months within the normal course of clinical care. Any treatment decision during the study was made at the physician's discretion.

The primary endpoint of this study was HRQoL as measured by the 29-item Multiple Sclerosis Impact Scale version 2 (MSIS-29) [17]. Secondary assessments included changes from baseline in fatigue status measured by the Modified Fatigue Impact Scale (MFIS-21) [18], emotional functioning using the Beck Depression Inventory-II (BDI-II) [19] and urinary function as measured by the Short Form (SF)-Qualiveen [20].

Data collection also included demographics, medical history of MS, clinical relapses (the appearance of a new clinical sign/symptom or clinical worsening of a previous sign/symptom that persisted for ≥ 24 h in the absence of fever), disability progression according to EDSS scores (increase of ≥ 1 point in patients with baseline scores < 5.5, or of ≥ 0.5 points in those with baseline scores ≥ 5.5), and magnetic resonance imaging (MRI) activity at months 12 and 24 (gadolinium-enhancing T1-weighted hyperintense lesions and new or enlarging T2-weighted lesions). Patients had to rate their satisfaction with teriflunomide using the Treatment Satisfaction Questionnaire for Medication (TSQM v1.4) [21]. Adverse events (AEs) and AEs of special interest (AESIs; serious or non-serious) were collected throughout the study. An AESI is a medical concern that requires close monitoring of the patient. Predefined AESIs were an overdose, ALT levels > 3 times the upper limit of the normal range, leukocyte count < 1000 cells/μl, increased blood pressure (SBP ≥ 160 mmHg, DBP > 100 mmHg), respiratory symptoms compatible with diffuse interstitial lung disease, peripheral neuropathy, acute renal failure, hyperkalaemia, and severe skin/allergic reactions. Liver function was regularly monitored according to the summary of product characteristics (SmPC).

Statistical Analysis

Descriptive analysis included the mean, standard deviation, median, and range for continuous variables and the frequency distribution of patients for categorical variables. Patients who stopped teriflunomide were analysed until the last visit they made.

ANOVA of the change from baseline at 6, 12, 18, and 24 months in MSIS-29, MFIS-21, BDI-II, SF-Qualiveen, and EDSS scores was performed. Paired *t*-tests were performed to compare MSIS-29, MFIS-21, BDI-II, SF-Qualiveen, and EDSS scores between baseline and each time point after baseline.

MSIS-29 scores of 0–19 categorise as 'no problems', 20–39 as 'few problems', 40–59 as 'moderate problems', 60–79 as 'quite a few problems', and 80–100 as 'extreme problems' [17]. The total MFIS-21 score ranges from 0 to 84 and uses a cutoff of 38 to discriminate between fatigued and non-fatigued patients [18]. BDI-II scores for depression are classified as minimal (0–13), mild (14–19), moderate (20–28), and severe (29–63) [19]. The SF-Qualiveen scale ranges from 0 (no impact of urinary problems on QoL) to 4 (a highly adverse impact of urinary difficulty) [20].

Correlations between MFIS-21, BDI-II and SF-Qualiveen and the MSIS-29 physical and psychological components were examined by the Spearman rank correlation coefficient (*r*). A post-hoc analysis was performed to compare the differences in HRQoL between patients suffering relapses (as defined in the protocol) during the study and those who did not. The absolute and percent differences in MSIS-29 physical and psychological scores at month 24 between these two independent groups were analysed using the Mann–Whitney test. The annualised relapse rate (ARR) was calculated as the total number of relapses divided by the total patient time at risk of relapse (time in follow-up). Annual NEDA-3 [no evidence of disease activity, defined as no protocol-defined relapses, no Gd-enhancing lesions or new/enlarging T2 lesions, and no 6-month confirmed disability progression (as protocol defined)] was also analysed post hoc. Patients who progressed in the last 6 months of the planned 24 months of follow-up were excluded from the analysis of the period from month 12 to month 24 because they did not have an additional follow-up assessment to confirm progression.

A statistical analysis plan was generated prior to database locking. Missing data were not considered in the analysis and a significance level of 0.05 was used for statistical testing. The Statistical Package for the Social Sciences version 22.0 was used for all analyses (SPSS Inc, Chicago, IL, USA).

RESULTS

Patient Characteristics

Of the 336 patients who were enrolled, 325 were analysed and 11 were excluded as screening failures. Demographics and clinical characteristics are summarised in Table 1. The mean (SD) age was 43.2 years (10.4), with a range from 36.4 to 50.5 years. Seventy-one percent were female, and the mean time since diagnosis was 7.2 years (7.3), with a range from 0.5 to 12 years. The median EDSS score was 1.5 (1–2.5), and 190 (58.5%) patients had experienced at least a relapse in the past 2 years. Sixty-four percent of patients were switched to teriflunomide from other DMTs. During the 2-year follow-up, 88 (27%) patients discontinued the study. The reasons were treatment discontinuation because of a lack of effectiveness (n = 37, 11.4%) and AE occurrence (n = 31, 9.5%), loss to follow-up (n = 6, 1.8%), investigator's decision (n = 3, 0.9%) and patient's willingness (n = 11, 3.4%). Patients discontinuing teriflunomide due to a lack of effectiveness were numerically younger, less likely to be relapse free and more frequently DMT-naive at baseline than patients who discontinued for safety reasons (see Table S1 in the electronic supplementary material for details).

Health-Related Quality of Life

MSIS-29 scores showed a significant reduction in the psychological impact of MS from baseline to month 18 (35.9 (26.6) vs 29.4 (25.5); p = 0.004) and month 24 (35.9 (26.6) vs 29.0

(24.6); $p = 0.002$). No change in physical impact was observed (Fig. 1a).

The analysis of HRQoL comparing relapsing and relapse-free patients did not show significant differences in the absolute and relative changes in MSIS-29 physical and psychological scores at month 24 (see Table S2 in the electronic supplementary material for details).

Fatigue, Depression and Urinary Function

At baseline, the patients exhibited a mean MFIS-21 score of 27.4 (21.2), which was significantly reduced at month 24 to 23.2 (20.5); $p = 0.027$ (Fig. 1b). The mean baseline BDI-II score of 12.9 (10.8) was significantly reduced at month 24 to 10.9 (11.2); $p = 0.041$ (Fig. 1c). The mean SF-Qualiveen score was 0.95 (0.8) at baseline, suggestive of no impact of urinary problems on QoL, and did not change significantly over time (Fig. 1d).

Correlation Analysis Between Fatigue, Depression, Urinary Dysfunction and HRQoL

We found a strong correlation between MFIS-21 and the MSIS-29 physical ($r = 0.88$; $p < 0.001$) and psychological ($r = 0.87$; $p < 0.001$) components over 1 year of treatment with teriflunomide (See Fig. S1 in the electronic supplementary material for details). The correlation between BDI-II and the physical domain of MSIS-29 was moderate ($r = 0.71$; $p < 0.001$), while that with the psychological MSIS-29 component was strong ($r = 0.87$; $p < 0.001$). The correlation between SF-Qualiveen and both components of MSIS-29 was moderate. The changes in the MFIS-21, BDI-II and MSIS-29 scores at month 24 were also found to be significantly correlated (see Fig. S2 in the electronic supplementary material for details).

Disease Activity

The mean number of relapses in the past 2 years was 1.5 (0.7). In the first 12 and 24 months of treatment, the mean number of relapses was 1.2 (0.5) and 1.1 (0.2), respectively. Converted to an ARR, the overall relapse rate per year was 0.43 (95% CI 0.38–0.48) at baseline, 0.22 (95% CI 0.17–0.28) at 12 months and 0.17 (95% CI 0.14–0.21) at 24 months. This represents a 60.1% reduction in the ARR after 2 years of treatment with teriflunomide (Fig. 2). Seventy-five patients (24.4%) had relapses during the study, and 232 (75.6%) were in relapse remission.

Mean EDSS scores remained stable during the study (Fig. 3a), with 75% of patients having EDSS < 2.5. At 2 years, 79.9% (191/240) of the patients did not show disability progression according to EDSS (Fig. 3b). Baseline characteristics of the patients by progression status based on EDSS after 2 years of teriflunomide use are shown in Supplementary Table S3. Except for a numerically higher proportion of DMT-naive patients among those who progressed (45.8%) compared to patients with stable EDSS (36.1%), the remaining baseline characteristics were found to be similar.

Overall, the presence of gadolinium-enhanced lesions was reported in 10.2% of patients (28/195) at month 12 and 9.2% (14/152) at month 24. The percentage of patients with new or enlarging T2-weighted lesions was 30% (62/207) at month 12 and 25.6% (41/160) at month 24.

In the first 12 months on teriflunomide, 54.7% (150/274) of patients achieved annual NEDA-3, which increased to 61.4% (140/228) during months 12–24.

Treatment Satisfaction

In patients switching to teriflunomide from other DMTs, statistically significant increases were observed in mean effectiveness, convenience, side effects, and global satisfaction score from baseline to months 18 and 24 (Fig. 4a). The increase in mean convenience was observed as early as month 6.

In DMT-naive patients, increases in mean convenience, side effects, and global satisfaction scores were observed from baseline to month 18. Increases in mean side effects remained at month 24 (Fig. 4b).

Table 1 Demographic and clinical characteristics at baseline

Characteristic	Value
Age, years	43.2 (10.4)
Female	229 (71%)
Years since diagnosis of MS	7.2 (7.3)
Median (range)	5 (0.5–12)
Frequency of relapses in past 2 years	
0	135 (41.5%)
1	119 (36.6%)
≥ 2	72 (21.8%)
Mean number of relapses (excluding zero)	1.5 (0.7)
Median (range), excluding zero	1 (1–2)
Baseline ARR (95%CI)	0.42 (0.38–0.48)
EDSS	
Mean (SD)	1.75 (1.5)
Median (range)	1.5 (1–2.5)
Patients with gadolinium-enhancing lesions*	94 (30.1%)
Mean number of gadolinium-enhancing lesions	2.1 (1.8)
Patients who switched DMT	208 (64%)
Mean number of previous DMTs	1.5 (0.9)
Last DMT before teriflunomide administration	
Interferons	106 (51%)
Glatiramer acetate	51 (24.5%)
Dimethyl fumarate	27 (13%)
Immunosuppressants†	8 (5.3%)

Data are shown as mean (SD) or number (%) unless otherwise stated. *MRI was available in 312 patients. †Fingolimod (n = 5), azathioprine (n = 2) and natalizumab (n = 1)

CI confidence interval, *DMT* disease-modifying therapy, *EDSS* Expanded Disability Status Scale, *Gd+* gadolinium, *MRI* magnetic resonance imaging, *SD* standard deviation

Safety

A total of 299 (92%) patients experienced at least one AE and 19 (5.8%) experienced a serious AE (there were 22 serious AEs in total), two of whom reported a serious pneumonia event that was considered to be related to teriflunomide (Table 2). Sixteen patients showed teriflunomide-related transaminase elevations of mild (eight cases) and moderate intensity (eight cases). None of these transaminase elevations were severe. No AEs were considered of special interest, and no deaths were reported during the study.

DISCUSSION

The TERICARE study suggests that teriflunomide may have a positive effect on psychological aspects of the quality of life of patients with MS in the real-world setting. Following treatment with teriflunomide, we observed that MS patients experienced significant improvements from baseline in the MSIS-29 psychological domain. However, the perceived physical impact of disease remained unchanged over the course of the study. In this respect, we could argue that (1) subjectively perceived improvements in functional limitations may take longer than improvements in emotional well-being; (2) it is more difficult to capture improvements in a 20-item domain (physical domain) than in a 9-item (psychological domain); and (3) our patients had a low level of disability at baseline (mean EDSS 1.7), which was maintained throughout the study. EDSS has been shown to negatively correlate with quality of life in RRMS [22], and the lack of worsening in EDSS may have played a role in the stabilization of physical functioning (in other words, in the absence of deterioration). Although there is evidence that clinical relapses have a measurable effect on the quality of life of people with MS [23], we did not find differences in the changes observed in physical and psychological MSIS-29 scores between patients experiencing relapses and those in remission. This may be due to the well-controlled relapse activity in our study,

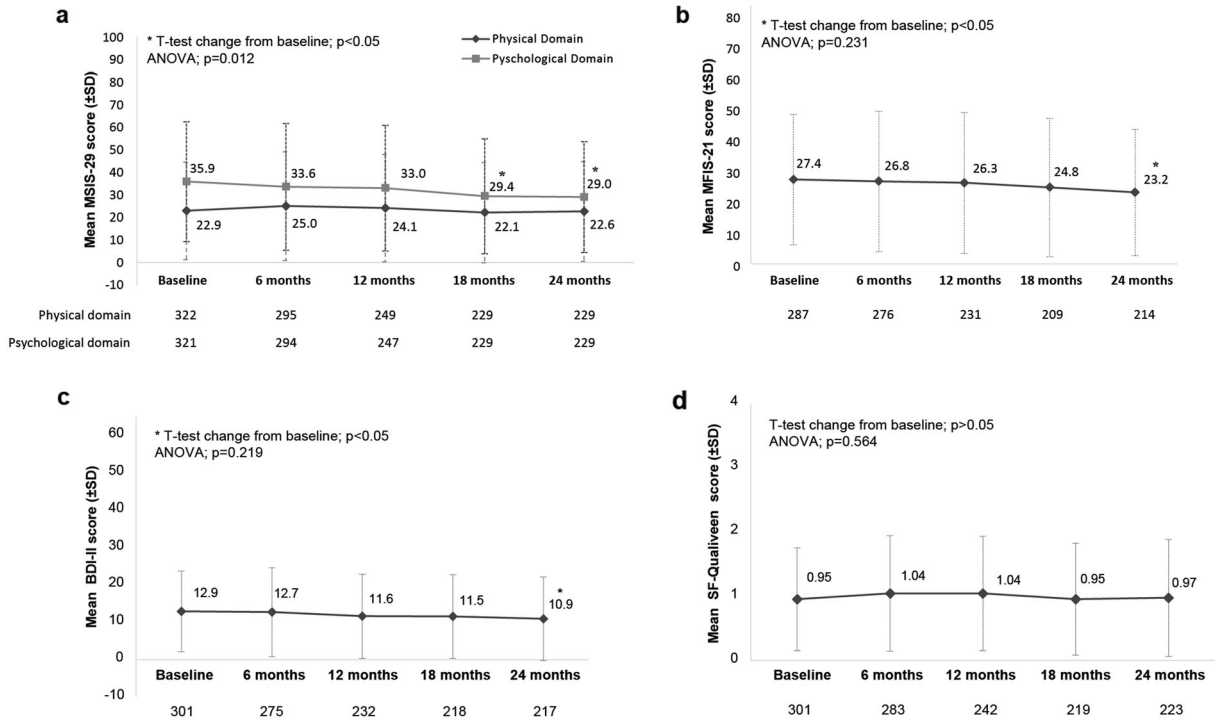


Fig. 1 Patient-reported outcomes over 2 years: (**a**) MSIS-29, (**b**) MFIS-21, (**c**) BDI-II, (**d**) SF-Qualiveen. *BDI-II* Beck Depression Inventory-II, *MFIS-21* 21-item Modified Fatigue Impact Scale, *MSIS-29* 29-item Multiple Sclerosis Impact Scale, *SD* standard deviation. In MSIS-29, MFIS-21, BDI-II and SF-Qualiveen, lower scores are indicative of less impact

although a direct analysis correlating relapses with quality of life was not performed.

When interpreting all these data, it is important to note that quality of life was generally good at inclusion, so the magnitude and meaningfulness of the observed effects on MSIS-29 scores are subject to discussion. While an increase of ≥ 7.5 in the physical MSIS-29 is considered clinically relevant [24], there is no defined threshold for the psychological scale.

Previous real-world studies are consistent with the present study in showing small improvements or stability in the psychological and physical functioning of patients treated with teriflunomide who were similar to our cohort in terms of age, disease duration, disability level and relapse activity [9–11, 13, 14, 25]. Therefore, the effect of teriflunomide on quality of life in different populations needs to be further studied.

Our results on fatigue and depression may help us to understand the data observed on quality of life. Patients in TERICARE were generally mildly affected by fatigue and depression at inclusion. Even so, they showed small yet significant improvements in MFIS-21 and BDI-II scores over 2 years of treatment. Although these improvements do not represent changes in the intensity categories of the scales used, they were maintained over the study and might have aided in enhancing or maintaining the quality of life. In support of this, we have shown that fatigue and depression are strongly correlated with quality of life, and the improvements noticed by patients, however small, may have influenced their perception of their health, as others have suggested [26].

The use of PROs in clinical practice is becoming increasingly important, as they provide information on the impact of a disease and its treatment from the patient's perspective. However, to provide clinicians with a comprehensive assessment of the patient, PRO data should be combined with clinical outcomes.

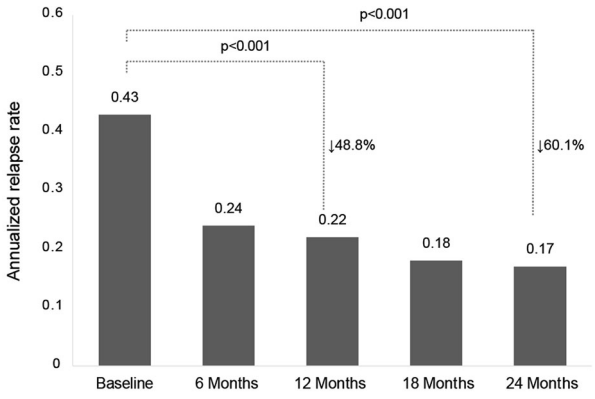


Fig. 2 Annualised relapse rate over 2 years of follow-up

This study showed that teriflunomide significantly reduced the ARR to 0.17 and slowed disability progression in patients with RRMS treated for 2 years. Although our ARR at month 24 seems to be lower than those reported in the phase 3 studies TEMSO, TOWER and TENERE (ranging from 0.26 to 0.37) [1–3, 27], caution is advised when comparing with clinical trials due to differences in methodology and patient populations. These results also appear favourable compared to those from the Teri-PRO and TAURUS-MS observational studies, where patients had a longer disease duration of around 11 years [10, 12]; however, ARR at month 24 in TERICARE was higher than it was in the AURELIO and Teri-REAL cohorts, with fewer relapses prior to teriflunomide [13, 14].

It is of note that most patients were free from relapses (75.6%) and disability progression (80%) during the study. This result is important because teriflunomide was the first DMT used in 36% of patients, suggesting a niche of patients who may benefit from first-line treatment with the drug, but also because it suggests that teriflunomide is an effective switch therapy for previously treated patients with a similar profile to our cohort.

NEDA-3 outcome under teriflunomide has been little explored in the clinical practice setting. Our NEDA-3 results in the first 12 months of treatment with teriflunomide were lower than the 77% and 79% reported in other observational cohorts [28, 29]; however, unlike TERICARE, those studies used a period of 3 months instead of 6 months to confirm disability progression. The increase in NEDA-3 during the following 12 months (months 12–24) reflects that the disease is stabilized on teriflunomide, unconfounded by any disease activity carried over during the time that the medication requires to reach full clinical effect.

The 27% overall study discontinuation rate in TERICARE is within the range of 24.8–41% reported in other observational studies of teriflunomide [12–14, 25, 30, 31]. The low rate of treatment discontinuation due to tolerability issues compared with similar studies [10, 12] may result from the good safety experience with teriflunomide in TERICARE and the substantially lower incidence of serious adverse events

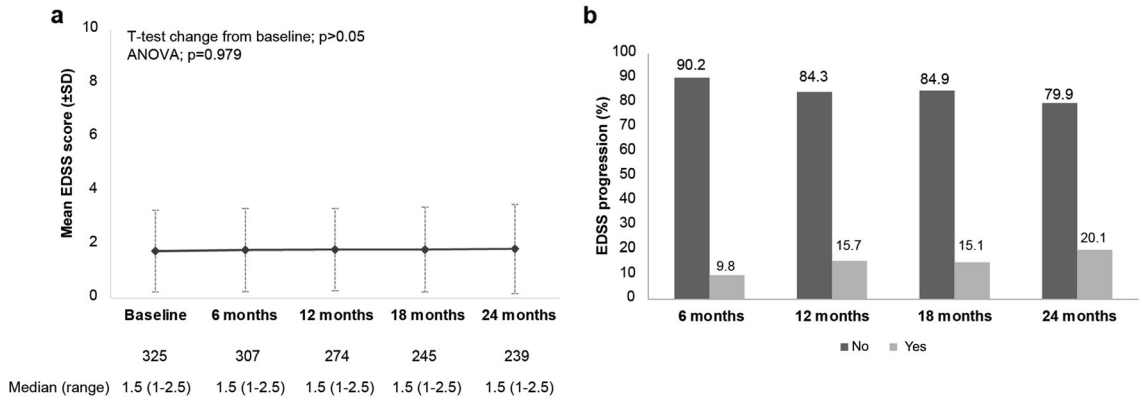


Fig. 3 EDSS change from baseline (**a**) and disability progression (**b**). EDSS progression was measured as an increase of ≥ 1 point (or ≥ 0.5 from a baseline score of ≥ 5.5). *EDSS* Expanded Disability Status Scale, *SD* standard deviation

Table 2 Serious adverse events reported in 19 patients

Event	TERICARE cohort (n = 325)
Multiple sclerosis relapse	4 (1.2)
Syncope	1 (< 1)
Cerebral infarction	1 (< 1)
Asthma	1 (< 1)
Respiratory failure	1 (< 1)
Pulmonary embolism	1 (< 1)
Salpingectomy	1 (< 1)
Cholecystectomy	1 (< 1)
Pancreatitis acute	1 (< 1)
Colitis ischaemic	1 (< 1)
Chest pain	2 (< 1)
Pneumonia	2 (< 1)
Aplastic anaemia	1 (< 1)
Psychotic disorder	1 (< 1)
Back pain	1 (< 1)
Cholelithiasis	1 (< 1)
Obesity	1 (< 1)

Adverse event terminology conforms to the Medical Dictionary for Regulatory Activities, version 23.1

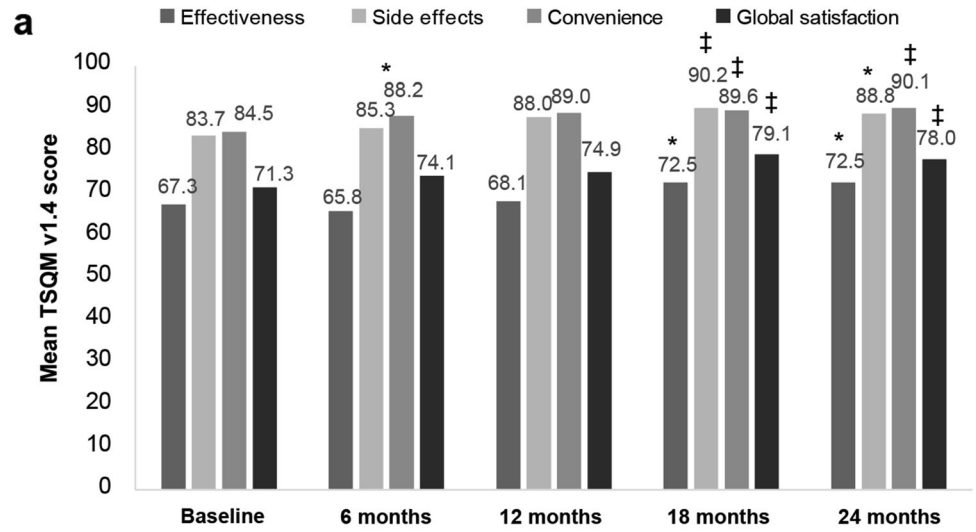
than previously reported (5.8% vs 13%) [10, 12]. It remains to be seen if the low disability level in our cohort and the improvements perceived in their quality of life may have favoured the rate of discontinuation due to a perceived lack of efficacy. What is clear is that the low rates of discontinuation for safety and inefficacy reasons align with the high treatment satisfaction reported by the patients in all four domains of TSQM v1.4. Consistent with other observational studies of teriflunomide, the significant increase in satisfaction following the initiation of therapy persisted over 2 years, regardless of whether patients were DMT-naive or not [9–12].

Fig. 4 Mean TSQM v1.4 global treatment satisfaction, effectiveness, side effects and convenience scores. (**a**) Patients switching to teriflunomide from other DMTs. *t-test change from baseline ($p < 0.05$). ‡t-test change from baseline ($p < 0.01$); ANOVA of effectiveness and side effects ($p < 0.05$). (**b**) DMT-naive patients. *t-test change from baseline ($p < 0.05$); ANOVA of side effects ($p < 0.05$). *DMTs* disease-modifying therapies, *SD* standard deviation, *TSQM* Treatment Satisfaction Questionnaire for Medication

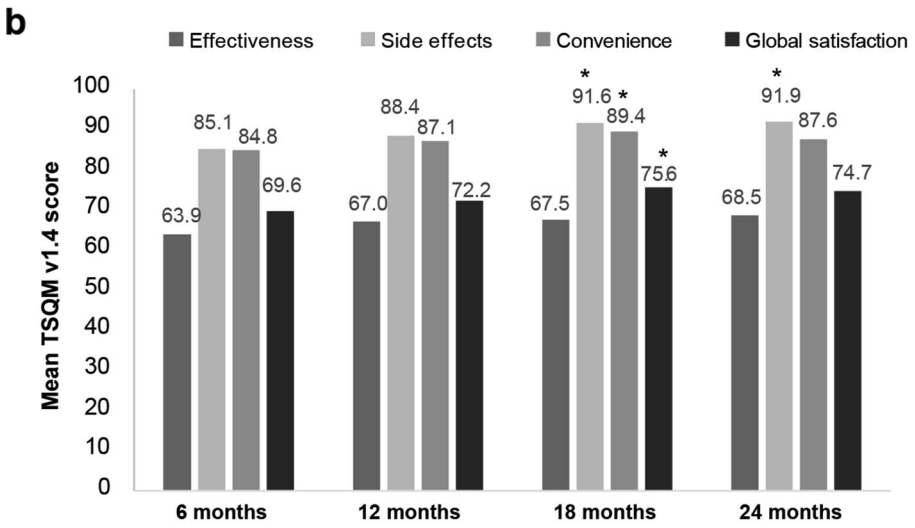
This study had several limitations to consider when interpreting its results, including the observational design, which may have introduced selection bias; the non-collection of symptomatic treatment, which may have favoured some findings; the lack of a comparison group; and the loss to follow-up. Our findings regarding the reduction in relapse rate should be interpreted with caution, as this measure may be biased by the phenomenon of regression to the mean, among other reasons, which may partially explain the observed effect. Further, since patients were treated and followed in a real-world setting, variations in medical practice are possible. Among the strengths of the study are the sample size, with complete representativeness of all regions in Spain; the 2 years of follow-up to allow the detection of changes; and the use of a standardised MS-specific questionnaire for the assessment of HRQoL that accurately identifies the priorities of MS patients.

CONCLUSIONS

The patient-reported benefits in psychological HRQoL and the lack of worsening in fatigue and depression during 2 years of treatment with teriflunomide reflect how MS patients perceived the clinical benefits of the treatment and how it may contribute to their general well-being. In



	Baseline	6 months	12 months	18 months	24 months
Effectiveness	162	184	158	143	142
Side effects	164	182	157	141	138
Convenience	166	184	157	143	142
Global satisfaction	166	184	157	143	142



	6 months	12 months	18 months	24 months
Effectiveness	108	91	85	86
Side effects	107	91	86	86
Convenience	107	92	85	85
Global satisfaction	108	92	85	85

addition, this study shows that teriflunomide is effective at reducing ARR and disability progression in mildly affected relapsing MS patients, reinforcing the importance of proper patient selection in achieving better clinical outcomes. The applicability of the results to wider MS populations warrants further research.

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Declarations

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