**INTRODUCTION**

- Teriflunomide and DMF are oral disease-modifying therapies (DMT) for the treatment of relapsing forms of MS.
- Teriflunomide, a once-daily immunomodulator, was first approved in the U.S. in September 2012, and has since been approved in 80 countries. As of October 2017, over 185,000 patients were being treated with teriflunomide, with a total real-world exposure of approximately 162,000 patient-years since approval.
- DMF, a twice-daily oral DMT, was first approved in the U.S. in March 2010.
- Direct head-to-head clinical trials comparing the efficacy and safety of teriflunomide and DMF have not been conducted. Comparison of treatment outcomes across randomized controlled trials has many challenges, including differences in study populations and designs, as well as definitions of outcome measures.
- An alternative approach that takes into account differences in study populations—number needed to treat—has shown that teriflunomide and DMF have comparable efficacy across clinical trials.
- The Teri-RADAR study was conducted to compare real-world effectiveness of teriflunomide and DMF in patients with relapsing forms of MS (RMS) based on real-world data collected retrospectively in the phase 4 Teri-RADAR study.

**METHODS**

- **Study Design and Patients**
  - Teri-RADAR was a retrospective, phase 4, real-world longitudinal cohort study in patients with RMS receiving oral treatment with teriflunomide or DMF at ≥1 MS centers.
  - Anonymized patient data (including patient demographics, Expanded Disability Status Scale (EDSS) scores, relapses with associated hospitalizations and corticosteroid use, and MRI results) were collected from medical charts and MRI scans from the pictures archiving and communication system for the following periods, as shown in Figure 1:
    - Pre-index visit (V−1): 6–18 months before initiation of teriflunomide or DMF treatment
    - Index visit: time at which teriflunomide or DMF was initiated
    - Follow-up: (V+1) 9–30 months after treatment start (9–24 months for MRI data)
  - Real-world data are increasingly important to support prescribing decisions, and provide a better reflection of patients’ outcomes in real-world clinical practice compared with the highly selected populations and controlled environments of clinical trials.

- **Study Outcomes**
  - The primary study endpoint was the proportion of patients with new and/or enlarging T2 or gadolinium-enhancing (Gd)+ T1 lesions.
  - Secondary endpoints included:
    - Number of new and/or enlarging T2 and Gd+ T1 lesions
    - Whole brain and lateral ventricle volume changes
  - Non-inferiority of teriflunomide compared with DMF was defined as the difference in brain volume loss (BVL) between the two treatment groups being less than 0.25%.

- **Statistical Analysis**
  - Analyses were descriptive, no formal sample-size determination was carried out.
  - Logistic regression was used to compare the proportion of patients with new/lengthening Gd+ lesions between teriflunomide and DMF treatment groups.
  - Baseline and follow-up ARR was calculated using a Poisson regression analysis of the change in number of relapses from baseline to follow-up.
  - Analyses were descriptive; no formal sample-size determination was carried out.

- **MRI Endpoints**
  - The proportion of patients with new and/or enlarging T2 or Gd+ T1 lesions was numerically lower in the teriflunomide group (35.3%) compared with the DMF group (41.1%) (Figure 2A).
  - The difference between the two groups was primarily driven by a difference in the proportion of patients with new and/or enlarging T2 lesions (26.0% vs 40.8%

**RESULTS**

- **Patients**
  - In total, 100 patients were enrolled in the study, 50 receiving teriflunomide 14 mg once daily and 50 receiving DMF 240 mg twice daily.
  - Patient demographics and baseline disease characteristics were generally similar across treatment groups (Table 1), with the following exceptions:
    - Between-group proportions of patients with relapses in the 18 months prior to index date were higher in the teriflunomide group vs the DMF group (22% vs 17%), similarly, ARR in the pre-index period was also higher in the teriflunomide group (0.274 vs 0.083).

- **Safety and Tolerability**
  - Of the 50 patients in each treatment group, 45 (90%) received at least one dose of study medication.
  - Most common treatment-related adverse events were reported in ≥10% of patients in either treatment group.
  - The most common reported adverse events were gastrointestinal disorders, including nausea, vomiting, and dyspepsia.

- **Acknowledgments and Disclosures**

**CONCLUSIONS**

- **From this retrospective study suggest, that in a real-world clinical setting, teriflunomide exhibited similar effectiveness to DMF on a number of MRI and clinical endpoints.
- The incidence of treatment-related AEs was similar between groups, with no unexpected safety signals seen for either teriflunomide or DMF.
- These results reinforce the established real-world effectiveness of teriflunomide 14 mg for the treatment of RMS.

**References**


**Funding provided by Sanofi**

**Acknowledgments and Disclosures**

**OBJECTIVES**

- To compare the effectiveness of teriflunomide and dimethyl fumarate (DMF) in patients with relapsing forms of MS (RMS) based on real-world data collected retrospectively in the phase 4 Teri-RADAR study
- To compare the effectiveness of teriflunomide and dimethyl fumarate (DMF) for the treatment of relapsing forms of MS (RMS) based on real-world data collected retrospectively in the phase 4 Teri-RADAR study.
- The majority of patients had received another DMT prior to initiating teriflunomide or DMF: most commonly intramuscular interferon B-1a (56% and 54% of patients in the teriflunomide and DMF groups, respectively).
- At follow-up, mean (SD) treatment exposure was 15.2 (9) and 15.7 (4) months for the teriflunomide and DMF groups, respectively.

**Clinical Safety and Tolerability**

- Compared with the pre-index treatment period, there was a slight decrease in ARR in the teriflunomide group (0.274 vs 0.259) and a slight increase in the DMF group (0.083 vs 0.110).
- Mean (SD) EDSS scores at follow-up were available for n=53 and n=54 in the teriflunomide and DMF treatment groups, respectively; 3.1 (0.8) for teriflunomide and 3.2 (0.8) for DMF.
- For patients with reported data at both time points (n=37 for teriflunomide, n=34 for DMF), on average, there was no change in EDSS scores between the pre-index period and follow-up in either treatment group (mean SD change: 0.01; for teriflunomide and 0.00; for DMF).

**No Evidence of Disease Activity**

- At follow-up, the proportion of patients with NEDA was the same in both treatment groups.
- The majority of patients had received another DMT prior to initiating teriflunomide or DMF: most commonly intramuscular interferon B-1a (56% and 54% of patients in the teriflunomide and DMF groups, respectively).

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Teriflunomide</th>
<th>DMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>51.7 (11.4)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>39 (78.0)</td>
</tr>
<tr>
<td>Time since first diagnosis of MS, mean (SD), y</td>
<td>11.8 (9.4)</td>
</tr>
<tr>
<td>Time from first diagnosis of MS, mean (SD), y</td>
<td>11.3 (9.5)</td>
</tr>
<tr>
<td>Patients with relapses in the 18 months before</td>
<td>11.2 (22.0)</td>
</tr>
<tr>
<td>ARR (pre-index period, 95% CI)</td>
<td>0.274 (0.040, 0.043)</td>
</tr>
</tbody>
</table>

**Figure 1. Teri-RADAR Study Design**

**Figure 2A. Change in Whole Brain Volumea**

**Figure 2B. Lateral Ventricle Volumeb**

**Figure 3A. No Evidence of Disease Activity**

**Table 2. Most Common Treatment-Related Adverse Events**

<table>
<thead>
<tr>
<th>Teriflunomide</th>
<th>DMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>28 (56.0)</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>9 (18.0)</td>
</tr>
<tr>
<td>Nervous system</td>
<td>6 (12.0)</td>
</tr>
</tbody>
</table>

**References**


**Acknowledgments and Disclosures**

- The authors thank the following investigators for their expertise and contributions to the study:
  - Paul C. Strowger, MD, PhD
  - John H. Tatter, MD
  - Joseph Eraklis, MD
  - Scott S. Kim, MD
  - Mary A. Dunaif, MD
  - James A. Miller, MD
  - David S. Brinton, MD
  - Ronald W. Schupf, MD
  - Robert Zivadinov, MD
  - Jeffrey A. Chover, MD, PhD
  - Brian D. Welsh, MD, PhD
  - Nancy L. Friede, MD
  - Sanofi

**Presented at the American Academy for Treatment and Research in Multiple Sclerosis (AATRMS) Forum, February 1-3, 2018, San Diego, CA**

**Funding provided by Sanofi**