Real-world Effectiveness of Delayed-release Dimethyl Fumarate in Patients With Relapsing-Remitting Multiple Sclerosis: Interim Results From the EFFECT Study

Cohan S,1,2 Chan A,1,2 Callwood J,1,3 Lathii E,1,2 Van der Walt A,1,2 Okwuebenye M,2 Taylor C6
1 Providence Multiple Sclerosis Center, Providence Brain and Spine Institute, Providence Health & Services, Portland, OR, USA; 2 Bern University Hospital, University of Bern, Switzerland; 3 Schapira Center for Multiple Sclerosis, Minneapolis Clinic of Neurology, Golden Valley, MN, USA; 4 MS Center at St. Elizabeth’s, Boston, MA, USA; 5 Royal Melbourne Hospital, Parkville, Victoria, Australia; 6 Addenbrooke’s, Cambridge, UK

Conclusions
- Treatment with DMF was associated with a lower relapse rate in the 12 months after compared with the 12 months before DMF initiation.
- Conclusions should be interpreted cautiously in light of the intrinsic challenges associated with chart reviews, including possible unrecorded confounders.
- This interim analysis suggests that DMF may be effective in the clinical practice setting in patients who are treatment naive or have only received IFN or GA, as well as in patients who are newly diagnosed.

Introduction
- Delayed-release dimethyl fumarate (DMF) has demonstrated a favorable benefit-risk profile in well-controlled clinical trials (DEFENCE, NCT01420212; CONFIRM, NCT00451451S) in patients with relapsing-remitting multiple sclerosis (RRMS).1-3 In a post hoc analysis of newly diagnosed or treatment-naive patients, DMF treatment was associated with strong and sustained efficacy.
- As of January 31, 2017, over 245,000 patients have been treated with DMF worldwide, representing ≥375,000 patient-years of exposure (≤120 patients and ≤9,000 patient-years from clinical trials).
- Evaluation of the effectiveness of DMF in treatment-naive or early stages of the clinical practice can help inform treatment decisions in these specific populations.

Objective
- The retrospective observational EFFECT study (NCT02774072) was undertaken to evaluate the effectiveness of DMF in patients with RRMS in the clinical practice setting, as well as in a subset of newly diagnosed patients.

Methods
- EFFECT is an international, multicenter, retrospective medical record review of patients with RRMS treated with select disease-modifying therapies (DMTs; DMF, glatiramer acetate (GA), interferon beta-1a, or fingolimod).
- Only DMF is reported in this interim analysis; comparative data will be reported in the final analysis.
- The EFFECT study also evaluated rates of DMF discontinuation due to selected gastrointestinal (GI) adverse events (AEs), as well as site mitigation strategies for management of GI AEs during DMF treatment; these results have been reported elsewhere (Min J, et al., LB09).
- To be included in this study, patients had to meet the following criteria:
  - Diagnosis of MS.
  - Initiated DMF treatment after December 2010 and had ≥12 months of follow-up data available after DMF initiation.
  - Treatment naive or have had only 1 prior DMT (IFN or GA). Note: given the observational nature of this study, 2 patients who had received DMTs other than IFN or GA may have been included.
  - The newly diagnosed population was defined as patients who were treatment naive and diagnosed with RRMS within 3 years of DMF initiation.
  - Medical records were reviewed at a single time point for patients who were treated in routine clinical practice. Data collected included:
    - Baseline characteristics, including prior treatment and relapses.
    - Clinical outcomes from date of DMF initiation to ≥12 months after DMF initiation.
    - Selected GI AEs (DMF arm only).

Results
- Study Population
  - As of December 15, 2016, 804 patients were included in the overall analysis population (Figure 1).
  - Baseline characteristics were similar for patients included in the newly diagnosed population: 70% (160/258) were female compared with the overall population (70% [804/1150]; Table 1).
- Relapses and ARR
  - At 12 months after DMF initiation, the KM estimate of the proportion of patients who experienced a relapse was 12% in the overall population (Figure 2).
  - In the overall population, 40% of patients experienced ≥1 relapse in the 12 months after DMF initiation vs. 11% of patients in the 12 months after DMF initiation.
  - In newly diagnosed patients, 62% of patients had experienced ≥1 relapse in the 12 months before DMF initiation vs. 18% of patients in the 12 months after DMF initiation, as calculated by crude estimate of proportion (Table 2).
  - Unadjusted ARR was significantly lower at 12 months after, compared with 12 months before DMF initiation (1.8% [18/1000] vs. 5.6% [26/462]; P < .001).
- Safety
  - No. of patients with ≥1 AEs (DMF arm only).
  - Table 2: Patients with MS relapse within 12 months of DMF initiation

Tables
- Table 1. Baseline characteristics of the overall study population
- Table 2. Patients with MS relapse within 12 months of DMF initiation
- Table 3. DMF discontinuation within 1 year after DMF initiation

Figure 1. Patient disposition

Figure 2. Time to first MS relapse after DMF initiation based on KM method in the overall population

Figure 3. Unadjusted ARR at 12 months before and after DMF initiation

Figure 4. Kaplan-Meier (KM) estimate (overall population, n=804)

Table 1. Baseline characteristics of the overall study population

Table 2. Patients with MS relapse within 12 months of DMF initiation

Table 3. DMF discontinuation within 1 year after DMF initiation