DMT10

Characterizing Early Real-world Experience of NARCOMS Registry Participants Treated With Diroximel Fumarate

Salter A,[1] Lancia S,[1] Marrie RA,[2] Cutter GR,[3] Fox RJ,[4] England SM,[5] Kapadia S,[5*] Shankar SL,[5] Lewin JB[5]

[1]Department of Biostatistics, UT Southwestern Medical Center, Dallas, TX, USA; [2]Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada; [3]Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL, USA; [4]Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland Clinic, Cleveland, OH, USA; [5]Biogen, Cambridge, MA, USA

*At time this work was conducted

OBJECTIVE

- The primary objective of the study is to characterize the persistence of DRF therapy over 1 year in participants with MS from the NARCOMS registry.
  - This preliminary interim analysis reports data in a limited set of participants with at least 6 months of follow-up.

CONCLUSIONS

- In this preliminary analysis of DRF-treated participants from the NARCOMS registry, most participants remained persistent on DRF, and no participants discontinued due to GI side effects.
- Most participants (69.2%) either started on the full maintenance dose of DRF immediately or titrated for 1 week.
  - This finding may be at least partially attributed to the high proportion of DMF-to-DRF switchers in this study population.
- Heterogeneity in dietary practices for DRF was observed, and there was no single predominant practice or strict regimen that participants followed.
- Future analyses of this study will report the effects of DRF on disability progression and patient-reported outcomes.

Consortium of Multiple Sclerosis Centers 2022 Annual Meeting
June 1-4, 2022 | National Harbor, MD

Introduction

- Diroximel fumarate (DRF) is a novel oral fumarate approved for relapsing forms of multiple sclerosis (MS).[1]
- DRF is metabolized to monomethyl fumarate, the same active metabolite of dimethyl fumarate (DMF), and has similar efficacy and safety to DMF.[1-3]
  - However, DRF demonstrated improved gastrointestinal (GI) tolerability in a head-to-head, Phase 3 study compared with DMF.[3]
- Per the US prescribing information, the starting dosage of DRF is 231 mg twice daily, to be increased to 462 mg twice daily after 7 days.[1]
  - However, in real-world practice, dose titration can be variable.
- There is a need for additional data to characterize the persistence of DRF in the real-world setting as well as understanding patient DRF titration regimens and dietary practices.

Methods

Study Design

- North American Research Committee on Multiple Sclerosis (NARCOMS) is a voluntary self-report registry for people with MS.
  - Participants confidentially provide information about their demographic characteristics, medical history, and disease and treatment characteristics at enrollment and every 6 months thereafter, either online or on paper, per their preference.
- This longitudinal study included United States NARCOMS registry participants with relapsing forms of MS reporting DRF initiation between Fall 2020 and Spring 2021.
  - To be included in the analysis, participants had to complete a NARCOMS follow-up survey at least 6 months after the first survey on which the participant indicated taking DRF (index survey); participants who discontinued DRF due solely to financial/insurance reasons were excluded.

Assessments

Assessments made in the interim population at Baseline were:

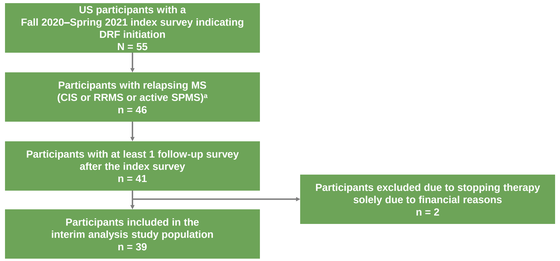
- Demographics.
- Disability status based on the Patient Determined Disease Steps (PDDS).
- MS symptom severity based on the SymptoMScreen (SMSS), which is a concise, self-explanatory, patient-reported outcome that assesses MS-associated symptoms in 12 domains.
  - For each domain, participants report symptom severity level in terms of the effect on daily activities using a 7-point ordinal scale ranging from 0 (not affected at all) to 6 (total limitation).
- Characterization of titration regimens and dietary patterns during treatment with DRF.
- Persistence, discontinuation rate, and discontinuations due to GI side effects.

Results

Baseline Demographics and Clinical Characteristics

- Overall, 55 NARCOMS participants initiated DRF, of whom 39 met the inclusion criteria (Figure 1).

Figure 1. Patient Disposition



CIS = clinically isolated syndrome; DRF = diroximel fumarate; MS = multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary-progressive multiple sclerosis
[a]Active SPMS was defined as patient reporting SPMS along with at least 1 relapse in the year prior to index survey.

- Participants had mean (SD) age of 57.5 (10.0) years and mean (SD) body mass index of 27.7 (7.2; Table 1).
  - Most participants were female (94.9%) and White (89.7%).
  - Mean (SD) disease duration was 19.8 (9.4) years and mean (SD) age at MS diagnosis was 36.6 (10.6) years.

Table 1. Baseline Demographics and Characteristics

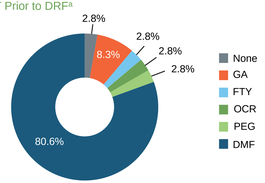
Characteristic	Interim Population n = 39
Age at DRF initiation, mean (SD), y	57.5 (10.0)
Female, n (%)	37 (94.9)
Race, n (%)	
White	35 (89.7)
Non-white	4 (10.3)
Education level,[a] n (%)	
High school diploma/GED	6 (17.6)
Associate's degree	3 (8.8)
Bachelor's degree	12 (35.3)
Post-bachelor's degree	13 (38.2)
Age at symptom onset, mean (SD), y	27.5 (16.8)
Age at MS diagnosis, mean (SD), y	36.6 (10.6)
Duration since MS diagnosis, mean (SD), y	19.8 (9.4)
MS subtype,[b] n (%)	
RRMS	34 (87.2)
Unknown	3 (7.7)
BMI, mean (SD)	27.7 (7.2)
Relapse in prior 6 months,[c] n (%)	5 (12.8)

BMI = body mass index; DRF = diroximel fumarate; GED = General Educational Development; MS = multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis
[a]Data missing for 5 participants.
[b]Data not reportable for 2 participants.
[c]Not sure/not answered for 2 participants.

Baseline Demographics and Clinical Characteristics (cont.)

- Most participants (80.6%) had switched to DRF from DMF (Figure 2).

Figure 2. DMT Prior to DRF[a]

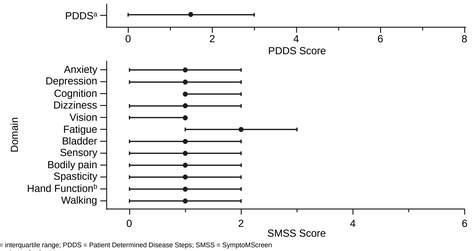


DMF = dimethyl fumarate; DMT = disease-modifying therapy; DRF = diroximel fumarate; FTY = fingolimod; GA = glatiramer acetate; OCR = ocrelizumab; PEG = peginterferon beta-1a
[a]Data missing for 3 out of 39 patients.

Baseline Disability Status and MS Symptom Severity

- Median PDDS score indicated moderate disability at Baseline in this population (Figure 3); however, 48.7% of patients had none to mild disability (PDDS score ≤1).
  - Most patients rated their MS symptoms as mild or very mild based on SMSS scores.

Figure 3. Median (IQR) PDDS and SMSS Scores at Baseline

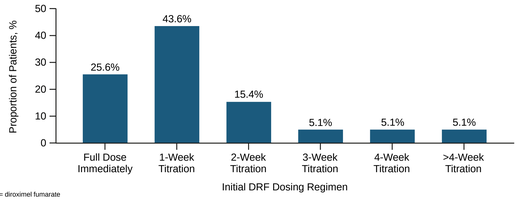


IQR = interquartile range; PDDS = Patient Determined Disease Steps; SMSS = SymptoMScreen
[a]Data missing for 1 patient.
[b]Data missing for 1 patient.

DRF Dosing Regimen

- Most patients (69.2%) either started on the full maintenance dose of DRF immediately or titrated for 1 week (Figure 4).

Figure 4. Initial DRF Dosing Regimen



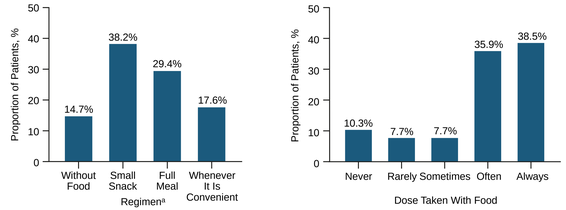
DRF = diroximel fumarate

Dietary Information

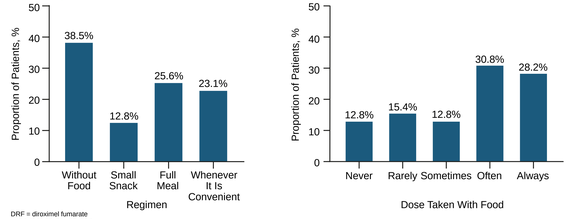
- Based on the 5-point Likert scale question, most participants indicated that they at least "sometimes" take their medication with food (Figure 5).
  - However, based on the other questions, many participants do not make a conscious effort to take their medication with food; there does not appear to be one predominant practice or any strict food-related regimen that participants follow:
    - Among the participants, 32.3% take their morning DRF dose without food or whenever is convenient for them; other participants take DRF with a small snack (38.2%) or with a full meal (29.4%; Figure 5A).
    - Responses showed 61.6% of participants take their evening DRF dose without food or whenever is convenient for them; other participants take DRF with a small snack (12.8%) or with a full meal (25.6%; Figure 5B).

Figure 5. (A) Morning and **(B)** Evening Dietary Habits for DRF Dosing, n = 39

(A) Morning



(B) Evening



DRF = diroximel fumarate
[a]Data missing for 7 patients.

Persistence Rate and Reasons for Discontinuation

- The median (range) DRF treatment duration was 6 (0–12) months.
- Most patients (84.6%) remained persistent on DRF at the time of this analysis (Table 2).
  - No patients discontinued due to GI side effects.

Table 2. Persistence on DRF and Reasons for Discontinuation

	Interim Population n = 39
Persistence, n (%)	
Remaining on DRF at time of analysis	33 (84.6)
Discontinued	6 (15.4)
Reasons for discontinuation, n (%)	
Progressive MS	1 (2.6)
GI side effect	0 (0)
Other non-GI related side effect[a]	5 (12.8)

DRF = diroximel fumarate; GI = gastrointestinal; HSV-1 = herpes simplex virus 1; MS = multiple sclerosis
[a]Other non-GI related side effects included: recurrent intraoral HSV-1 (n = 1), hysterectomy (n = 1), excessive sleeping (n = 1), incontinence/balance worse (n = 1), and low lymphocyte count (n = 1).

References 1. Vumerity [prescribing information]. Cambridge, MA: Biogen; 2021. 2. Tecfidera [prescribing information]. Cambridge, MA: Biogen; 2021. 3. Naismith RT, et al. EVOLVE-MS-2 Study Group. *CNS Drugs*. 2020;34(2):185-196.

Disclosures AS: research funding from the Consortium for Multiple Sclerosis Centers. MS Society of Canada, National MS Society, and US Department of Defense; editorial board member for *Neurology*; SL: journal editor/editorial board member for *Multiple Sclerosis Journal*-*Multiple Sclerosis Journal*-*Experimental*, *Translational and Clinical* and *Neurology*; RAM: co-investigator on a study funded by Biogen and Roche (no funds to her/her institution); GRC: data/safety monitoring committees for AMO, BioLineRx, BrainStorm Cell Therapeutics, Galmed, Hisun, Horizon, Merck, Merck/Pfizer, OPKO Biologics, Neurim, Novartis, Orphazyme, Reata, Receptos/Celgene, Sanofi, Teva, the National Heart, Lung, and Blood Institute (Protocol Review Committee), and the National Institute of Child Health and Human Development (OPRU oversight committee); consulting/advisory boards for Biogen, Click Therapeutics, Genentech, Genzyme, GW Pharmaceuticals, Klein Buendel, MedDay, MedImmune, Novartis, Osmotica, Perception Neuroscience, Recursion, Roche, Somahlution, and TG Therapeutics; RJF: consulting fees from AB Science, Biogen, Celgene, EMD Serono, Genentech, Genzyme, Greenwich Biosciences, Immunic, Janssen, Novartis, Sanofi, and TG Therapeutics; advisory committees for AB Science, Biogen, Genzyme, Immunic, Janssen, Novartis, Sanofi, and TG Therapeutics; clinical trial contract and research grant funding from Biogen, Novartis, and Sanofi; editorial board member for *Neurology* and *Multiple Sclerosis Journal*; SME, SLS, and JBL: employees of and hold stock/stock options in Biogen; SK: employee of and stockholder in Biogen at the time of this work.

Acknowledgments This study was sponsored by Biogen (Cambridge, MA, USA). Writing and editorial support for the preparation of this poster was provided by Excel Scientific Solutions (Glasgow, UK); funding was provided by Biogen.