Patient Perspectives on Factors Related to Medication Persistence in MS Patients Experiencing DMF-Associated Gastrointestinal Events

5487

Hendin B,[1] Mayer L,[2] Namey M,[3] Edwards MR,[4] Jordan B,[4] Herbert LB,[5] Koulinska I[4]

[1]Phoenix Neurological Associates, Phoenix, AZ, USA; [2]Central Texas Neurology Consultants, Round Rock, TX, USA; [3]Cleveland Clinic, Cleveland, OH, USA; [4]Biogen, Cambridge, MA, USA; [5]Health Union, LLC, Philadelphia, PA, USA

Conclusions

- Persistence on DMF when experiencing DMF-associated GI AEs can be improved by effective communication between patients and HCPs, including a rationale for therapy selection, expectation setting on the intensity and duration of GI events, written instructions that include food recommendations, and appropriate symptomatic management.

Introduction

- As of January 31, 2018, >311,000 patients have chosen delayed-release dimethyl fumarate (DMF) treatment worldwide, representing >544,000 patient-years of exposure. Of these, ~6252 patients (and ~12,631 patient-years) were from clinical trials.
- Gastrointestinal (GI) symptoms, mostly mild or moderate in severity, are common adverse events (AEs) associated with DMF.[1] The incidence of GI AEs is more frequent during the first month of treatment and usually decreases over time.[1,2]
- Successful strategies for managing common side effects of therapies for relapsing-remitting multiple sclerosis (RRMS) are important to optimize clinical outcomes.
- Health care providers (HCPs) employ different strategies in an attempt to mitigate GI symptoms, including taking DMF with food, gradual dose increase, and a variety of symptomatic therapies.[3] Setting patient expectations about the nature of GI symptoms at therapy initiation also has been found to be helpful.[3] However, there are limited patient-reported data on the effectiveness of and adherence to different GI management recommendations.

Objective

- The primary objective of the study was to identify patient-reported approaches to improve persistence on DMF among patients with DMF-associated GI AEs.

Methods

- An online survey using Health Union's proprietary platform MultipleSclerosis.net was conducted June 30, 2017–August 25, 2017 with 3 groups of adult patients with RRMS:
  - DMF users without GI AEs who were treated with DMF for ≥3 months (n=195);
  - DMF users with GI AEs who persisted on DMF despite GI symptoms (n=103); and
  - Previous DMF users (who discontinued DMF due to GI symptoms; n=88).
- This online survey platform was selected to reach an extensive MS population across the United States, enabling the inclusion of 3 distinct groups of DMF-treated patients, and minimizing the risk of incorrect self-reports of MS diagnosis.
- The questionnaire was pretested with patients with MS before study initiation. Because strategies for mitigation of GI AEs have evolved since the launch of DMF in the United States, and to minimize recall bias, only patients who initiated DMF after January 1, 2015 were included in the survey.
- Patients who reported concurrent chronic irritable bowel syndrome (IBS), Crohn's disease (CD), or ulcerative colitis (UC) were excluded.
- Questions were designed to compare patient demographics, medical history, AE type/severity, mitigation strategies, and HCP recommendations across patient study groups.
- Responses were evaluated using descriptive statistics, chi-square test, and analysis of variance.

Results

Patient Demographics and MS History

- There were no significant differences among study groups in gender, ethnicity, body mass index, prior treatment status, and time since MS diagnosis or DMF initiation (Table).
- Overall, DMF-treated patients with GI AEs (both those who persisted and those who discontinued) tended to be younger than those without GI AEs (mean 46.5 vs. 49.3 years, respectively).
  - Patient groups were similar in their type of health insurance, type of prescribing HCP, and type of health care facility where they receive MS care (not shown).
- Patients who persisted on DMF despite GI AEs were more likely to be employed than those who discontinued therapy (*P*=.006).
- Most patients were exposed to other MS therapies before DMF.

Medical History and Comorbidities

- When asked about specific comorbidities, DMF-treated patients with GI AEs were more likely to report seasonal allergies (*P*=.04) and acid reflux/gastric reflux/gastroesophageal reflux disease (*P*=.02) than those without GI AEs (Figure 1).
- History of other GI diseases, including gastritis and ulcers, did not differ among study groups; patients with IBS, CD, and UC were not included in the study.

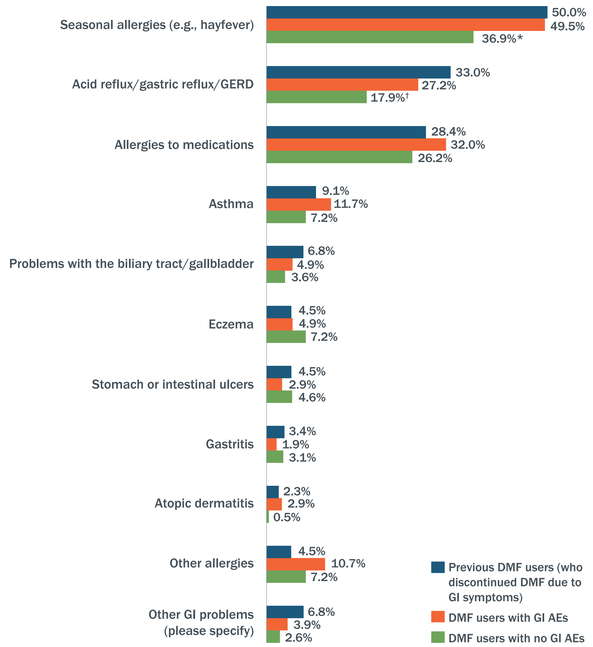
Characteristics of GI AEs

- The incidence of GI AEs was the highest within the first 3 weeks (80–93% of patients) and decreased over time.
- Among patients with GI AEs, a higher proportion of those who discontinued DMF reported severe symptoms (17–59% vs. 8–13% across symptoms) and a higher number of symptoms vs. those who persisted on DMF (mean 3.1 [1–4] vs. 2. 8 [1–4]; *P*=.01).

GI AE Management

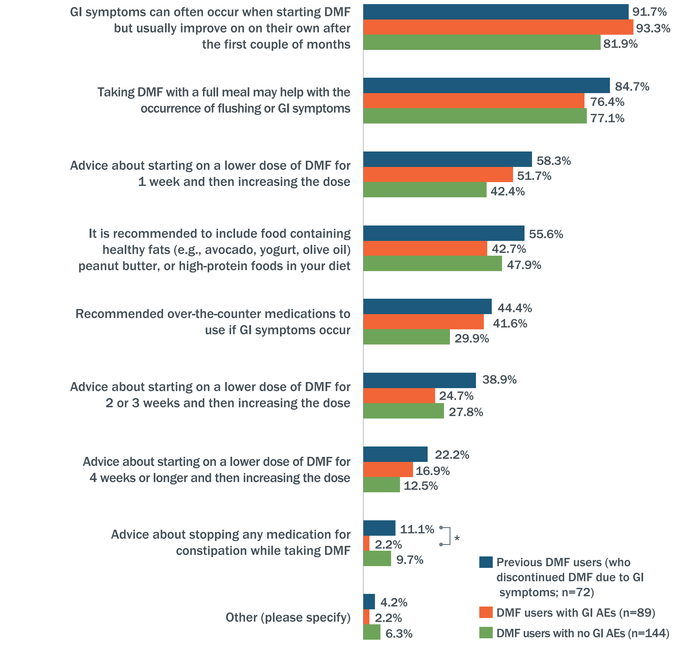
- Over half of patients across study groups (57–64%) did not recall receiving written instructions for taking DMF and managing GI AEs. Among those receiving written instructions, a higher proportion of patients who persisted on DMF found written instructions helpful than those who discontinued (93% vs. 75%, respectively; *P*=.04).
- At DMF initiation, only 42–44% of DMF users with GI AEs received recommendations for over-the-counter symptomatic therapies and only 43–56% of patients recalled receiving guidance on specific types of food to incorporate in their diet (Figure 2).
- Key influencers for staying on DMF despite GI AEs were:
  - Identifying successful symptomatic management strategies;
  - Being informed about the likely transient nature of GI AEs; and
  - Being advised that DMF is the best choice for them at the time (Figure 3).

Figure 1. Medical history and current comorbidities before starting DMF, stratified by subgroup



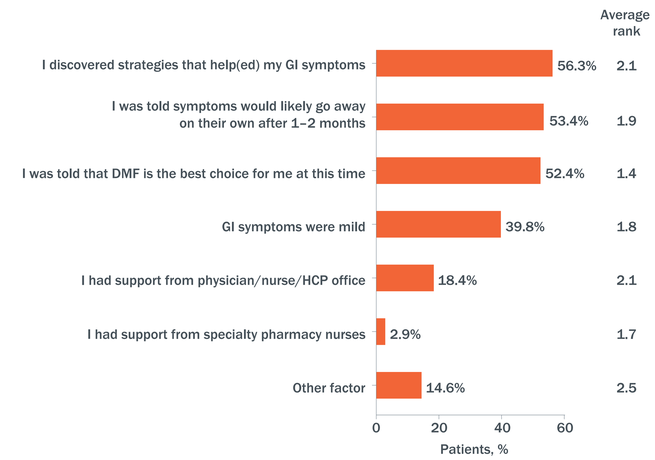
AE = adverse event; DMF = delayed-release dimethyl fumarate; GERD = gastroesophageal reflux disease; GI = gastrointestinal
Patients responded to the question, "Please indicate if you have had any of the following conditions before starting DMF. (Select all that apply)"
* indicates *P*=.04 and † indicates *P*=.02 for DMF users with no GI AEs compared with DMF users with GI AEs (combined group of all patients with GI AEs, whether or not they discontinued DMF)

Figure 2. HCP recommendations related to DMF tolerability stratified by subgroup



AE = adverse event; DMF = delayed-release dimethyl fumarate; GI = gastrointestinal; HCP = health care provider
Patients responded to the question, "Which of the following do you recall being told by your health care provider? (Select all that apply)." Other responses included taking medications, that GI history may result in GI issues, and return to a lower dose
* indicates *P*=.02 for DMF users with GI AEs who persisted on DMF compared with previous DMF users (who discontinued DMF due to GI symptoms)

Figure 3. Top 3 factors that impacted decision to stay on DMF



DMF = delayed-release dimethyl fumarate; GI = gastrointestinal; HCP = health care provider
Patients responded to the questions, "Select the top 3 factors that most impacted your decision to continue taking DMF once you developed gastrointestinal symptoms (n=103). Rank these factors from 1 to 3; 1 is most important to 3 is least important to you. Drag and drop into the desired order (n=103)." Other factors included: preference for an oral therapy vs. injectable, effectiveness/reduction of lesions, benefits outweighed side effects, awareness of side effects upon starting DMF, and side effects fewer/less severe than with other disease-modifying therapies

Table. Patient demographics and MS disease history

Characteristic	Previous DMF users (who discontinued DMF due to GI symptoms) n=88	DMF users with GI AEs who persisted on DMF despite GI symptoms n=103	DMF users without GI AEs n=195
Age, y			
Mean (SD)*	47.8 (11.4)	45.5 (11.3)	49.3 (9.5)
Median	46.5	46.0	49.0
Female, n (%)†	83 (94.3)	94 (91.3)	160 (82.1)
Ethnicity, %			
White	86.4	84.5	81.0
Black or African American	3.4	4.9	7.7
Latino or Hispanic	3.4	4.9	6.7
Asian	0	0	0.5
Other	3.4	3.9	1.0
No answer	3.4	1.9	3.1
BMI, kg/m²			
Mean (SD)	30.2 (7.7)	30.9 (7.9)	29.6 (6.7)
Median	29.0	30.4	28.8
Employment level, %†			
Employed or self-employed, %	34.1	54.4	44.1
On disability	37.5	23.3	39.5
Other	28.4	22.3	16.4
Time since DMF initiation, d			
Mean (SD)	646.4 (241.6)	584.4 (233.6)	616.8 (228.7)
Median	710.0	608.5	668.3
Prior treatment status, %			
DMT naive	18.2	20.4	22.6
DMT taken before DMF	81.8	79.6	77.4
Time since MS diagnosis, y			
Mean (SD)	8.4 (7.2)	8.3 (7.3)	10.2 (8.3)
Median	6.0	6.0	9.0

AE = adverse event; BMI = body mass index; DMF = delayed-release dimethyl fumarate; DMT = disease-modifying therapy; GI = gastrointestinal; MS = multiple sclerosis
Other includes: fully retired, unemployed (unable to work or waiting for disability), homemaker/stay-at-home parent, and unemployed (looking for work). Significant testing was conducted across the 3 subgroups
*P=.01; †P=.006

References 1. Phillips J, *et al. Int J MS Care*. 2017;19(2):74-83. 2. Fox EJ, *et al. Int J MS Care*. 2016;18(1):9-18. 3. Phillips JT, *et al. Mult Scler Relat Disord*. 2014;3(4):513-519. **Disclosures** BH: speaker bureaus for Biogen; LM: consulting fees from and speaker bureaus for Biogen, EMD Serono, Genentech, Genzyme, and Novartis; MN: consulting fees from Biogen, Genentech, and Sanofi-Genzyme; speaker bureaus for Acorda, Avanir, Biogen, EMD Serono, Genentech, Novartis, Sanofi-Genzyme, and Teva Neuroscience; MRE, BJ, and IK: employees of and hold stock/stock options in Biogen; LBH: employee of Health Union, LLC. **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 (Southport, CT, USA); funding was provided by Biogen.