A Delphi Panel to Address Management of Gastrointestinal Side Effects Observed With Use of Delayed-Release Dimethyl Fumarate

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INTRODUCTION

During clinical development of delayed-release dimethyl fumarate (DMF) for the treatment of multiple sclerosis (MS), gastrointestinal (GI) side effects were observed in a small number of patients treated at very high doses of DMF. The presence of GI side effects led to uncertainty in the clinical management of GI symptoms during treatment with delayed-release DMF.

METHODS

A Delphi Panel was convened to provide guidance on the management of GI side effects in the clinic. The Delphi process was based on the method of collecting data that elicits the opinions of a panel of experts. The Delphi process is a structured, repeated survey method used for reaching consensus from a larger group of experienced clinicians on the most effective strategies to manage side effects and to develop consensus statements.

Participants were invited to participate if they were practicing neurologists or nurses who had experience managing GI side effects with delayed-release DMF. Prior to the Delphi process, participants had the opportunity to provide open-ended comments on the management of GI side effects and to review a series of evidence summaries and case studies. Participants were not paid for their response to the questionnaire.

RESULTS

The Delphi process involved three rounds of surveys that were completed by 60% (n=36) of the 60 respondents. Three rounds of surveys were completed over a 3-month period.

In Round 1, respondents were asked to describe their most effective and least effective strategies for managing GI side effects. For instance, respondents were asked to list the most effective strategies for managing nausea, vomiting, abdominal pain, and diarrhea.

Table 1: Characteristics of respondents

- Country of practice
  - USA
  - Canada
  - Other
- Sample size
  - 1
  - 2
  - 3
  - 4
  - 5
  - 6
- Role
  - Physician
  - Nurse
  - Other
- Experience with delayed-release DMF
  - >1 year
  - 1 year
  - No experience

Figure 1: Structure of the questionnaire

- Patients were instructed to take delayed-release DMF with food; however, some patients reported GI symptoms when taking delayed-release DMF without food.
- Forty-four (70%) respondents reported nausea as a GI side effect, 16 (25%) vomiting, 26 (41%) abdominal pain, and 8 (13%) diarrhea in their patients. The most common strategies prescribed to manage nausea were antiemetics, such as ondansetron and promethazine.
- Forty-one (67%) respondents reported that nausea was somewhat more frequent than other side effects, while 17 (27%) reported that nausea was more frequent than other side effects.
- Table 2: GI side effects reported by respondents

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- When asked about how they set expectations of their typical patients about the GI side effects of delayed-release DMF, 46/63 (73%) respondents indicated that they had tried slow titration of initial dose with respect to food, on the frequency, or timing of delayed-release DMF dose with respect to food.
- Between 70% and 81% of respondents were more confident or much more confident in their ability to manage GI side effects in their patients when compared with a typical patient.
- Based on their expectations, respondents provided their current strategies for managing GI side effects. For instance, respondents indicated that they used a combination of strategies to manage nausea, such as antiemetics, antacids, and proton-pump inhibitors.

Figure 2

- No. of responses

- Number of respondents who had patients that had reported severe side effects (ie, nausea, vomiting, abdominal pain, or diarrhea) to you while being treated with Tecfidera?

Figure 3

- No. of patients with MS in practice

- Figure 2

- Figure 3

- Table 1: Characteristics of respondents

- Table 2: GI side effects reported by respondents

- Table 3: Strategies for managing GI side effects

- Figure 4

- Chart 1

Figure 4

- No. of respondents

- Figure 4

- Chart 1

- Chart 2

- Chart 3

Figure 5

- Figure 5

- Chart 4

- Chart 5

- Chart 6

CONCLUSIONS

- Each of the GI side effects encountered by respondents is in 90%–95% of patients and severe side effects were typically observed in 0%–10% of patients.
- Although nausea was somewhat more frequent than other side effects, nausea was managed effectively in most patients (60%–90%).
- Most respondents who had tried slow titration attempted a range of prescription medications, nonprescription medications, and/or dietary/nutritional changes to manage GI side effects in their patients.
- The majority of respondents provided a range of suggestions regarding setting patient expectations and managing GI side effects in their patients.
- Between 70% and 81% of respondents were more confident or much more confident in their ability to manage GI side effects in their patients when compared with a typical patient.
- Based on their expectations, respondents indicated that they would use the strategies they reported to manage GI side effects in their patients.

Table 3: Strategies for managing GI side effects

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- Chart 1

- Chart 2

- Chart 3

- Chart 4

- Chart 5

- Chart 6

Disclosures

All authors disclosed funding for the design and implementation of the survey. Among participants, no one reported having a financial relationship with a wealth management company or drug maker. Two authors disclosed funding from Biogen Idec for participation in multidisciplinary groups related to the development of the treatment of multiple sclerosis.

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