Strategies to Reduce Adverse Events Related to Oral dimethyl fumarate

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BACKGROUND:

Oral dimethyl fumarate (DMF) is approved in the United States for the treatment of relapsing forms of multiple sclerosis (MS). In the Phase 3 DEFINE and CONFIRM studies, the most common adverse events associated with DMF included flushing and gastrointestinal (GI) events. For most patients, these events were mild or moderate in severity and decreased in incidence after the first month of treatment. In clinical practice, DMF-associated adverse events have been largely related to medication tolerability rather than serious safety concerns. Tolerability of a medication may affect adherence, which in turn may affect efficacy of the drug. However, tolerability-related adverse events of DMF can often be overcome with time. If adverse events due to tolerability are not managed early, appropriate patients may discontinue therapy prematurely.

OBJECTIVES:

To investigate the impact of a structured nursing initiation protocol (IP) on DMF adverse effects and adherence.

	DEFINE			CONFIRM			
Adverse Event	Placebo N=408	DMF BID N=410	DMF TID N=416	Placebo N=363	DMF BID N=359	DMF TID N=344	GA N=351
Flushing	5%	38%	32%	13%	31%	24%	2%
Diarrhea	13%	15%	19%	8%	13%	15%	4%
Nausea	9%	13%	13%	8%	11%	15%	4%

NYU Initiation Protocol

- 120 mg once daily for 14 days
- 240 mg once daily for 14 days
- 240 mg twice daily

METHODS:

Immediately following introduction of DMF to the U.S. market, we initiated patients on DMF utilizing the standard pharmaceutical recommendations (PR-IP). Thereafter we developed a DMF Initiation Protocol (NYU-IP) that includes a modified titration schedule, pre-medication recommendations, specific dietary instructions consisting of a high fat healthy diet, regular follow-up encounters and a variety of other educational measures to help patients manage DMF adverse effects. We conducted a retrospective review comparing DMF adherence following drug initiation utilizing NYU-IP and PR-IP.

RESULTS:

A total of 329 patients were initiated on DMF from March 2013 to January 2014, 124 patients using PR-IP (group 1) and 205 patients using the NYU-IP (group 2). After six weeks, total discontinuations were 14 (12%) and 5 (2.5%) for groups 1 and 2, respectively (p = 0.0029). Discontinuations attributed to GI side effects were 10 (8%) and 4 (1.9%; p = 0.0215) respectively, and discontinuations due to flushing were 4 (3.2%) and 1 (0.5%; p=0.0733) respectively.

	Biogen Protocol	NYU Protocol
# of patients enrolled	124	205
GI Discontinuations	8% (10)	1.9% (4)
Flushing Discontinuations	3.2% (4)	0.5% (1)
Total Discontinuations	12% (14)	2.5% (5)

CONCLUSIONS:

A structured nursing protocol for initiation of DMF was highly effective in reducing adverse effects and maintaining adherence to DMF treatment. Effective nursing strategies are key to optimizing treatment adherence and outcomes with DMF.

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Presented at the 2014 ACTRIMS-ECTRIMS Meeting: September 10 – 13, 2014, Boston, MA

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