Management of Reported Side Effects of Patients Initiating Therapy on dimethyl fumarate

Jaspreet Abraham, RN, BSN, MSCS, Victoria Stokes, RN, BSN, Gina Remington, RN, BSN, MSCN, Diana Logan, RN, FNP-C, BC, MSCN, Teresa Frohman, MPAS, PA-C, Elliot Frohman, MD, PhD, FAAN

University of Texas Southwestern Medical Center at Dallas, Department of Neurology and Neurotherapeutics

Objective

To characterize patient-reported side effects in multiple sclerosis (MS), patients treated with dimethyl fumarate, and to ascertain whether pre-emptive symptom management strategies could impact upon these side effects and ultimately on treatment adherence

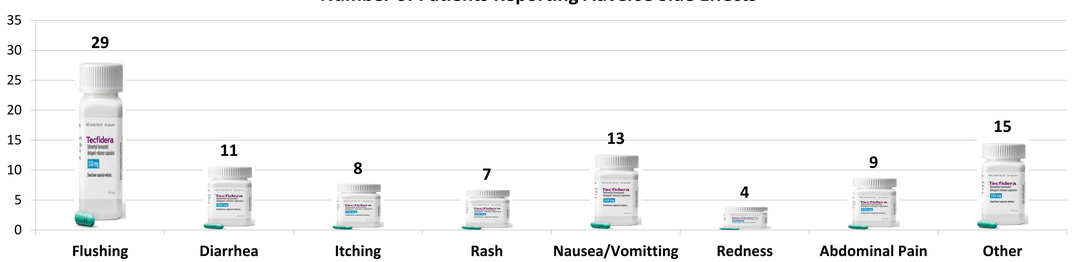
Background

Dimethyl fumarate is an oral medication approved by the FDA in April 2013 for the treatment of relapsing-remitting Multiple Sclerosis (RRMS). Phase III pivotal clinical trials revealed common adverse events related to dimethyl fumarate (previously designated as BG-12), including flushing, diarrhea, nausea, abdominal pain, and itching. In an attempt to proactively manage these well-recognized, and not infrequently limiting side effects, providers recommended pre-treatment with a variety of medications including aspirin, anti-histamine agents, anti-cholinergic (e.g. glycopyrrolate) agents, and bismuth subsalicylate.

Design/Methods

In our large, academic, Clinical Center for MS at UT Southwestern Medical Center, 66 MS patients treated with dimethyl fumarate were systematically evaluated for treatment-associated symptoms, and their potential management. Patients were transitioned from various disease modifying therapies such as interferon beta-1a, interferon beta-1b, glatiramer acetate, azathioprine, fingolimod, nataluzimab, or rituximab. Patients were followed via telephone and secure EMR messages. Additionally, data was collected at a clinical follow-up visit 3 months after initiating treatment with the new disease modifying therapy. Providers requested surveillance laboratory studies including complete baseline blood work (CBC and CMPL) as well as follow-up studies with CBC and CMPL repeated monthly for the first 3 months.

Number of Patients Reporting Adverse Side Effects



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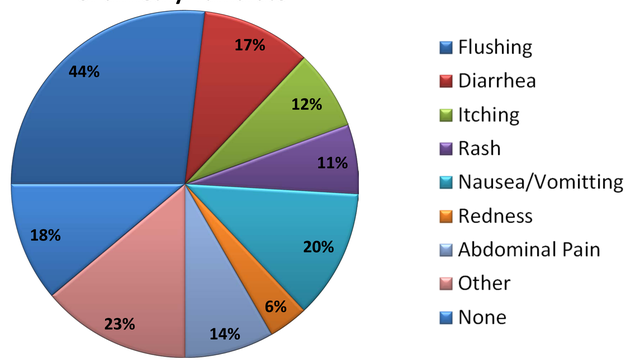
Patient Reported Adverse Side Effects of dimethyl fumarate



Side effect treatment

Results

Regardless of the symptom being reported, patients most commonly reported side effects as they titrated from the starting dose of 120 mg twice daily, to the maintenance dose of 240 mg twice daily. Similar to the Phase III clinical findings, patients most commonly reported flushing, abdominal pain, diarrhea, nausea, vomiting, and itching. Low dose aspirin (81mg BID) was recommended for flushing. Diphenhydramine or cetirizine was recommended for patients who experienced itching or rash. In some cases we prescribed montelukast for flushing. For diarrhea and abdominal discomfort, loperamide or bismuth subsalicylate was recommended. If over the counter therapies were not sufficient then we prescribed glycopyrrolate for GI issues. In rare instances, providers extended the length of time for the initial dose of 120 mg twice daily to a month and then transitioned to maintenance dose of 240 mg twice daily. A majority of patients experienced adverse side effects for a period lasting up to 3 months. Patients were educated to take the medication with food (yogurt, apple sauce, peanut butter). Regardless of prophylactic treatments, 26% of the patients stopped taking the medication due to one or more adverse side effects.

Conclusions

66 patients transitioned to dimethyl fumarate following final FDA approval and were monitored for reported adverse side effects. In a real-world environment, patients experienced symptoms including flushing, abdominal pain, diarrhea, and itching. These common side effects can be managed in the majority of patients if pre-treated with aspirin, diphenhydramine, cetirizine, loperamide or bismuth subsalicylate or with prescription medicines montelukast and glycopyrrolate.

Disclosures:
J. Abraham has received speaker fees from Genzyme.
V. Stokes has nothing to disclose.
G. Remington has consulted for IOMSN, NMSS, Genzyme, Biogen Idec, and Teva Neuroscience.
D. Logan has received speaker fees from Teva Neuroscience.
T. Frohman has received speaker and consultant fees from Biogen Idec, Novartis and Acorda and consulting fees from Genzyme.
Dr. E. Frohman has received speaking and consulting fees from Biogen Idec, Teva Neuroscience, Acorda, Novartis and consulting fees from Genzyme and Abbott.