27th Annual Meeting of the European Charcot Foundation (ECF)
EVOLVE-MS-2 End of Study
Submission deadline: 18 September 2019; 11:59pm CEST

Title:
Diroximel Fumarate Demonstrates Improved Gastrointestinal Tolerability Profile Compared to Dimethyl Fumarate in Patients with Relapsing-Remitting Multiple Sclerosis: Results from the Randomized, Double-Blind, Phase 3 EVOLVE-MS-2 Study

Short Title: (45 characters maximum; required for the Annual Meeting Mobile Application)

EVOLVE-MS-2: GI Tolerability of DRF vs DMF

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Abstract (300/300 words maximum)

Introduction: Diroximel fumarate (DRF) is an investigational, novel, oral fumarate in development for relapsing forms of multiple sclerosis (MS). DRF is rapidly converted to monomethyl fumarate (MMF), the same active metabolite of dimethyl fumarate (DMF). DRF 462 mg and DMF 240 mg produce bioequivalent levels of systemic MMF and are expected to have similar efficacy/safety profiles. However, the distinct chemical structure of DRF may elicit less irritation to the gastrointestinal (GI) system. Well-tolerated treatment options are important for long-term adherence.

Objective: To evaluate tolerability of DRF versus DMF in patients with relapsing-remitting MS.

Methods: EVOLVE-MS-2 (NCT03093324) was a phase 3, randomized, 5-week study utilizing an adaptive trial design to evaluate the tolerability of DRF 462 mg twice-daily and DMF 240 mg twice-daily using two patient-reported GI symptom scales: Individual Gastrointestinal Symptom Impact Scale (IGISIS) and Global Gastrointestinal Symptom Impact Scale (GGISIS). Primary endpoint was number of days with an IGISIS intensity score ≥2 relative to exposure. Severity of GI symptoms as measured by IGISIS, investigator-reported adverse events (AEs), and AEs leading to discontinuation were also collected.

Results: Overall, 504 patients received ≥1 dose of study drug. DRF patients (n=253) experienced a significant reduction (46%) in number of days with an IGISIS intensity score ≥2 versus DMF patients (n=249; adjusted rate ratio 0.54 (95% confidence interval, 0.39-0.75), p=0.0003). Lower rates of GI AEs (including diarrhea, nausea, vomiting, and abdominal pain) were seen with DRF versus DMF (34.8% vs 49%). Treatment discontinuation due to AEs and GI AEs was lower for DRF versus DMF (1.6% vs 5.6%; 0.8% vs 4.8%).

Conclusions: DRF demonstrated improved tolerability versus DMF, with significantly reduced duration and severity of patient-reported GI symptoms. Investigator-reported GI AEs and discontinuation due to GI AEs were lower with DRF.

Support: Alkermes/Biogen

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Author Disclosures

Krzysztof Selmaj reports receiving consulting fees from Genzyme, Novartis, Ono, Roche, Synthon, and Teva, and speaker fees from Biogen

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Anthony J. Lembo reports fees for participation in scientific advisory boards from Bayer, Biogen Idec, Ironwood, Takeda, Shire, and Salix

Ilda Bidollari reports being a full-time employee of and holding stock/stock options in Alkermes.

Hailu Chen reports being a full-time employee of and holding stock/stock options in Biogen.

Jerome Hanna reports being a full-time employee of and holding stock/stock options in Biogen.

Richard Leigh-Pemberton reports being a full-time employee of and holding stock/stock options in Alkermes.

Maria Lopez-Bresnahan reports being a full-time employee of and holding stock/stock options in Alkermes.

Jennifer Lyons reports being a full-time employee of and holding stock/stock options in Biogen.

Jordan Messer reports being a full-time employee of and holding stock/stock options in Biogen.

Catherine Miller reports being a full-time employee of and holding stock/stock options in Biogen.

David Rezendes reports being a full-time employee of and holding stock/stock options in Alkermes.

Jerry S. Wolinsky reports compensation for consulting, scientific advisory boards, or other activities with Alkermes, AbbVie, Actelion, Acorda, Bayer, Celgene, Forward Pharma, EMD Serono, GeNeuro, GW Pharma, MedDay, Novartis, Otsuka, PTC, Roche/Genentech, Sanofi Genzyme, Takeda, and Teva, and royalties for out-licensed monoclonal antibodies through UTHealth from Millipore Corporation

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