Onset of Action of Ozanimod for MRI Outcomes in Patients With RMS

Short title: Onset of Action of Ozanimod for MRI Outcomes

Patrick Vermersch,[1] Douglas L. Arnold,[2] Jeffrey A. Cohen,[3] Giancarlo Comi,[4] Amit Bar-Or,[5] Chahin Pachai,[6] Hongjuan Liu,[6] James K. Sheffield,[6] Diego Silva,[6] Krzysztof W. Selmaj[7]

[1]Univ. Lille, Inserm UMR 1172, CHU Lille, FHU Precise, Lille, France; [2]NeuroRx Research and Montréal Neurological Institute, McGill University, Montréal, Quebec, Canada; [3]Mellen Center for MS Treatment and Research, Cleveland Clinic, Cleveland, Ohio; [4]Vita-Salute San Raffaele University, Milan, Italy; [5]Center for Neuroinflammation and Experimental Therapeutics, and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; [6]Bristol Myers Squibb, Princeton, New Jersey; [7]Center for Neurology, Łódz, Poland and Collegium Medicum, Department of Neurology, University of Warmia and Mazury, Olsztyn, Poland

Introduction:
Knowledge of the onset of action by magnetic resonance imaging (MRI) for disease-modifying therapies in relapsing multiple sclerosis (RMS) is important for treatment monitoring. To estimate the onset of action of ozanimod, we analysed monthly MRI scans in a 24-week, phase 2, randomised, double-blind, placebo-controlled study (RADIANCE [NCT01628393]) of ozanimod 0.46 and 0.92 mg/day in RMS (N=258).

Methods:
MRI scans were acquired at baseline, W8, W12, W16, W20, and W24. In this post hoc analysis, onset of action was estimated for reduction in number of gadolinium-enhancing (GdE) lesions (primary outcome), number of new/enlarging T2 lesions, T2 lesion volume, number of new un-enhancing T1 lesions (black holes), and whole brain atrophy rate (all secondary outcomes). Onset of action was defined as the earliest time point at which a nominally significant difference (P<0.05) in the rate ratio of the least square means (LSM) and 95% confidence intervals (CIs) between ozanimod 0.92 mg and placebo occurred and was sustained.

Results:
Nominally significant reductions in number of GdE and new/enlarging T2 lesions were observed beginning at W8 for ozanimod 0.92 mg vs placebo; CIs for LSM number of GdE and new/enlarging T2 lesions did not overlap from W12 onward. For new black holes, a nominally significant difference was observed beginning at W12 for ozanimod 0.92 mg vs placebo;

however, CIs for LSMs, which were wide in the placebo group, overlapped at all time points except W20. No obvious changes were observed for T2 lesion volume or whole brain atrophy over 24 weeks in this small sample.

Conclusions:

Onset of action of ozanimod 0.92 mg based on GdE and new/enlarging T2 MRI lesion activity in this phase 2 study was detected as early as W8, the earliest available MRI time point, with complete separation from placebo beginning at W12.

Presented at AAN 2021.

Funding: This study was supported by Bristol Myers Squibb, Princeton, NJ.

Disclosures

PV: honoraria and consulting fees from Biogen, Celgene, Merck, Novartis, Roche, Sanofi Genzyme and Teva; research support from Novartis, Roche and Sanofi Genzyme.

DLA: personal fees for consulting and/or grants from Albert Charitable Trust, Biogen, Celgene, F. Hoffmann-La Roche, Frequency Therapeutics, MedDay, Merck Serono, Novartis, Population Council, and Sanofi-Aventis; grants from Biogen, Immunotec, and Novartis; and an equity interest in NeuroRx Research.

JAC: personal compensation for consulting for Adamas, Atara, Bristol Myers Squibb, Convelo, MedDay, and Mylan; and serving as an Editor of *Multiple Sclerosis Journal.*

GC: compensation for consulting and/or speaking activities from Almirall, Biogen, Celgene, EXCEMED, Forward Pharma, Genzyme, Merck, Novartis, Roche, Sanofi, and Teva.

ABO: participated as a speaker in meetings sponsored by and received consulting fees and/or grant support from: Atara Biotherapeutics, Biogen, BMS-Celgene, EMD Serono, Sanofi Genzyme, Novartis, and Roche-Genentech.

CP, HL, JKS, DS: employees and shareholders of Bristol Myers Squibb.

KWS: consulting for Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, and Teva.