Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis: results from the DAYBREAK open-label extension study

Authors: Lawrence Steinman,[1] Giancarlo Comi,[2] Amit Bar-Or,[3] Krzysztof W. Selmaj,[4] Douglas L. Arnold,[5] Hans-Peter Hartung,[6] Xavier Montalban,[7] Eva Kubala Havrdová,[8] James K. Sheffield,[9] Neil Minton,[9] Anne Janjua,[9] Vivian Huang,[9] Diego Silva,[9] Ludwig Kappos,[10] Jeffrey A. Cohen,[11] Bruce A. C. Cree[12]

Affiliations: [1]Department of Neurology and Neurological Sciences, Beckman Center for Molecular Medicine, Stanford University Medical Center, Stanford, California, USA; [2]Department of Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; [3]Center for Neuroinflammation and Experimental Therapeutics, and Multiple Sclerosis Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [4]Center for Neurology, Łódz, Poland and Collegium Medicum, Department of Neurology, University of Warmia and Mazury, Olsztyn, Poland; [5]NeuroRx Research and Montréal Neurological Institute, McGill University, Montréal, Quebec, Canada; [6]Department of Neurology, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany; [7]Division of Neurology, St Michael's Hospital, University of Toronto, Toronto, Canada, and Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitario Vall d'Hebron, Barcelona, Spain; [8]Department of Neurology and Center for Clinical Neuroscience, First Medical Faculty, Charles University, Prague, Czech Republic; [9]Celgene Corporation, Summit, New Jersey, USA; [10]Neurologic Clinic and Policlinic, University Hospital and University of Basel, Basel, Switzerland; [11]Mellen Center for MS Treatment and Research, Cleveland Clinic, Cleveland, Ohio, USA;

[12]Weill Institute for Neurosciences, Department of Neurology, UCSF University of California San Francisco, San Francisco, California, USA.

Introduction: Ozanimod, a sphingosine 1-phosphate receptor modulator, has been evaluated for relapsing multiple sclerosis (RMS) treatment in clinical pharmacology and in phase 2/3 efficacy and safety studies. This ongoing open-label extension (OLE) study characterised ozanimod's long-term safety and efficacy.

Methods: RMS participants who completed 1 of 4 parent trials were eligible for the OLE, where they received ozanimod HCl 1 mg. The primary efficacy endpoint, annualised relapse rate (ARR), was calculated via negative binomial regression. Efficacy data were summarised by pooled parent-trial treatment group (ITT population): placebo followed by ozanimod HCl 0.5 mg/d (n=37) or 1 mg/d (n=35), intramuscular interferon β-1a (IFN) 30 µg/wk (n=740), or ozanimod HCl 0.5 mg/d (n=838) or 1 mg/d (n=844). Treatment-emergent adverse events (TEAEs) were monitored.

Results: This interim analysis included 2,494 participants with mean (range) ozanimod exposure of 19.0 (0.03–32.5) mo in the OLE. In phase 3 parent trials (12–24 mo), mean ARR was 0.153 (95% CI, 0.125–0.187) with ozanimod HCl 1 mg and 0.246 (0.204–0.297) with IFN. Among participants who received ozanimod HCl 1 mg in parent trials, ARR with continued ozanimod HCl 1 mg (additional 19.2 mo) was 0.126 (0.099–0.161). Among those who received IFN in parent trials, mean ARR was reduced to 0.123 (0.095–0.158) after switching to ozanimod HCl 1 mg (mean exposure 18.3 mo). In the OLE, 1,704 participants (68.3%) had any TEAE, 144 (5.8%) had a serious TEAE, and

30 (1.2%) discontinued due to a TEAE. TEAEs and serious TEAEs were similar in the parent trials. The most common TEAE was nasopharyngitis (11.7%).

Conclusions: Ozanimod HCl 1 mg was associated with a low ARR. Ozanimod was generally well tolerated, with no new safety concerns. These data support ozanimod as a potential safe and effective therapy for RMS patients.

Data were presented at ECTRIMS, September 11–13, 2019.