Suggested title:

Safety and tolerability of conversion to siponimod in patients with relapsing multiple sclerosis: interim results of the EXCHANGE study

Authors

Amit Bar-Or[1], Bianca Weinstock-Guttman[2], Yang Mao-Draayer[3], Gina Mavrikis Cox[4], Linda-Ali Cruz[4], Xiangyi Meng[4], Wendy Su[4] and Stanley L Cohan[5]

Affiliations

[1]Center for Neuroinflammation and Experimental Therapeutics, and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [2]Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, The State University of New York, Buffalo, NY, USA; [3]Autoimmunity Center of Excellence, Multiple Sclerosis Center, University of Michigan, Ann Arbor, MI, USA; [4]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [5]Providence Multiple Sclerosis Center, Providence Brain and Spine Institute, Portland, OR, USA

Abstract

Background: In the USA, siponimod is approved in adults for the treatment of relapsing multiple sclerosis (RMS), including active secondary progressive MS (SPMS). Understanding washout requirements when converting from other disease-modifying treatments (DMTs) to siponimod is important in clinical practice and should be assessed prospectively.

Objectives: To report results from an interim analysis of EXCHANGE (NCT03623243), a prospective, 6 month, multicenter, open-label, single-arm study evaluating safety and tolerability of overlapping effects when converting to siponimod from other DMTs.

Methods: Patients aged 18-65 years with advancing RMS, Expanded Disability Status Scale (EDSS) score of >2.0 to 6.5, and on continuous oral/injectable DMTs for ≥3 months at time of consent were included in the analysis. Patients were immediately converted to siponimod, except those previously on teriflunomide who required 11-14 days' washout (with cholestyramine or activated charcoal). During days 1-6, siponimod was titrated from 0.25 mg to 2 mg. Primary endpoint was incidence of drug-related adverse events (AEs). About 100 patients are being enrolled in a parallel, novel virtual cohort, with telemedicine tools.

Results: 112 patients (1 in the virtual arm; 70.5% female) from 42 centers in the USA were enrolled, completed screening and were eligible for safety analysis (33.9% ongoing; 20.5% discontinued; 45.5% completed). At screening, 74.1% (n=83) of patients had relapsing-remitting MS, 21.4% (n=24) had SPMS, 3.6% (n=4) had primary progressive MS and 0.9% (n=1) had a single demyelinating event; 42.0% (n=47) had ≥1 relapse in the prior 12 months. At baseline, median age was 45.5 years, median time since MS diagnosis was 11.2 years and median EDSS score was 3.5. In the safety analysis set, ≥1 drug-related AE was reported in 34.8% of patients (n=39) (95% confidence interval [CI]: 26.2-44.5); 4.5% (n=5) had ≥1 serious AE and 5.4% (n=6) had ≥1 AE leading to drug discontinuation. In the subgroup of patients who had completed or discontinued from the study (n=74), 40.5% (n=30) (95% CI: 29.5-52.6) had ≥1 drug-related AE. Change from baseline in heart rate to 6 hours post first dose and AEs by prior DMT will be presented.

Conclusions: Conversion from oral/injectable DMTs to siponimod without washout had a good safety and tolerability profile with no unexpected findings. Subsequent analyses will include data on conversion to siponimod from infusible (natalizumab/ocrelizumab) DMTs.

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Suggested topic: Disease Modifying Therapies – Risk Management or Clinical Trials

Available topics:

- Biomarkers and Bioinformatics
- Biosensors
- Biostatistical Methods
- Clinical Outcome Measures
- **Clinical Trials**
- Comorbidities
- Diagnostic Criteria and Differential Diagnosis
- Disease Modifying Therapies – Mechanism of Action
- **Disease Modifying Therapies – Risk Management**
- Epidemiology
- Experimental Models
- Gender Differences, Hormones and Sex Chromosomes
- Genetics and Epigenetics
- Imaging
- Internet and Social Media
- Machine Learning/Network Science
- Microbiome
- Metabolomics
- Neuromyelitis Optica and Anti-MOG Disease
- Neuro-Ophthalmology
- Neuroprotection, Regeneration and/or Remyelination
- Neuropsychology and Cognition
- Observational Studies
- Pathogenesis – Immunology
- Pathogenesis – Neurodegeneration

- Pathogenesis – Role of Glia
- Pathogenesis – the Blood-Brain Barrier
- Pediatric MS
- Prognostic Factors
- Patient-Reported Outcomes and Quality of Life
- Rehabilitation and Comprehensive Care
- Reproductive Aspects and Pregnancy
- Symptom Management