P604

Longer-term Safety with Siponimod Treatment in Multiple Sclerosis: Pooled Analysis of Data from the Bold and Expand Trials and their Extensions

L. Kappos[1], P. Vermersch[2], R. Fox[3], A. Bar-or[4], B. Cree[5], G. Giovannoni[6], R. Gold[7], T. Masior[8], D. P. Meier[8], D. Tomic[8], N. Rouyrre[8]

[1]Neurologic Clinic and Policlinic, Departments of Medicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital and University of Basel, Basel, Switzerland
[2]Universityof Chu Lille, L/ric-inserm U995, Lille, France
[3]Mellen Centre for Treatment and Research in Multiple Sclerosis, Neurological Institute, Cleveland Clinic, Cleveland, Oh, United States of America
[4]Center for Neuroinflammation and Experimental Therapeutics and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pa, United States of America
[5]UCSF Weill Institute for Neurosciences, Department of Neurology, University of California San Francisco, San Francisco, Ca, United States of America
[6]Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom
[7]Department of Neurology, St. Josef-hospital/ruhr-university Bochum, Bochum, Germany
[8]Novartis Pharma Ag, Basel, Switzerland

Background: Siponimod, an oral, selective sphingosine-1-phosphate (S1P15) receptor modulator, showed efficacy/safety recently in secondary progressive MS (phase 3 expand) and previously in relapsing MS (phase 2 bold) populations. Objective: To assess the longer-term safety of siponimod treatment for up to 6 years in MS patients (PTs) using pooled data from the bold and expand core/extensions trials.
Methods: Pooled safety data were evaluated in 2 groups: A controlled pool (CP) of pts who received siponimod 2mg (n=1148) and placebo (PBO; n=607) during the core phase of PBO-controlled studies; a long-term pool (LP) of pts who received ≥1 dose of siponimod 2 or 10mg in core/extension phases (n=1737)- data collected includes pts on any siponimod dose 0.25, 0.5, 1.25, 2, or 10mg in core phase bold and switched to 2mg in extension phase. Analysis included adverse events (AEs), serious AEs (SAES), and AEs of special interest with S1P modulators. The relation of infections and lymphocyte counts was analysed in the expand trial. All safety outcomes are presented as incidences or incidence rates (IRS)/100 patient-years (PYS).
Results: In the CP, mean exposure to siponimod 2 mg was 17.7 months (1696 PYS) and 16.5 months (835 PYS) for PBO. As of may 2017, mean exposure in the LP was 27.8 months (4018 PYS); 127 pts were exposed for ≥5 years. In the LP, AEs were reported in 90% of pts, SAES in 20.7%, and AEs that led to study discontinuation in 9.6%. IRS of the most common AEs (incidence ≥10%) in the LP were consistent with those reported with siponimod 2mg in the CP: Nasopharyngitis (9.1 vs 9.7), headache (7.9 vs 11.3), urinary tract infection (uti; 6.9 vs 8.3), fall (5.5 vs 7.9), and hypertension (4.9 vs 7.4). IRS of infections were 43.2 in the LP and 48.9 for siponimod 2mg and 53.8 for PBO in the CP; nasopharyngitis and uti were the most common infections. No increase in IRS of oral herpes (1.2 vs 1.1), herpes simplex (0.2 vs 0.2), and varicella zoster virus infections (1.8 vs 1.9) was observed in LP versus CP. Among pts with ≥1 measured lymphocyte count< 0.4x109 /l at any time, 53% had any infection, 44.7% in the 0.4-0.6x 109/l and 42.3% in the >0.6x109/l categories similar/lower to the rate in the PBO (49.8%). IRS of malignancies were similar in CP and LP (1.2).
Conclusions: Longer-term follow-up treatment with siponimod 2 mg did not reveal any increase in ir of AEs or new safety findings versus the CP. Low lymphocyte counts were not associated with an increased infection rate.