Safety and Tolerability of Conversion to Siponimod With and Without Titration in Patients with Advancing Forms of Relapsing Multiple Sclerosis: Interim Results of the Phase 3b EXCHANGE Study

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OBJECTIVE

Report interim analyses of EXCHANGE (NCT03623243).

BACKGROUND

EXCHANGE is assessing conversion to siponimod with/without dose titration, and completed 50% subject enrollment.

DESIGN/METHODS

Analysis included patients aged 18-65 years with advancing forms of RMS, EDSS 2.0–6.5, and on continuous oral/injectable DMTs for ≥3 months at time of consent. Patients previously on teriflunomide required 11-14 days' accelerated washout. Those converting from fingolimod immediately switched to siponimod 2mg, without dose-titration. All other patients initiating siponimod were titrated from 0.25 to 2mg over 6 days. Primary endpoint was incidence of AEs possibly related to siponimod treatment.

RESULTS

163 patients (74.2% female; mean age 46.6 years; mean baseline EDSS 3.9) from 42 US centers were eligible for safety analysis (16.6% ongoing; 18.4% discontinued; 65.0% completed). At screening, 76.7% had RRMS, 20.2% SPMS, 2.5% PPMS, and 0.6% single demyelinating event. Most patients (54%) had no relapses in the year prior to screening. Most common prior DMTs were oral/injection therapies: 30.7% fingolimod, 27.6% glatiramer acetate/IFNβ, 20.9% dimethyl fumarate, and 17.2% teriflunomide. 31.3% of patients reported ≥1 AE possibly related to siponimod treatment. Most common AEs by preferred term were headache (8.0%), dizziness (4.3%), nausea (3.7%), bradycardia (3.1%), and fatigue (3.1%). There was no decrease in heart rate at 6-hours post-1st dose from baseline in the overall or any of the prior DMT groups. In the subgroup of fingolimod patients (n=7) who were switched to

siponimod without dose titration, mean heart rate (SD) was 73.1 bpm (18.1) at 6 hours post 1st dose vs 68.4 bpm (10.8) at baseline.

CONCLUSIONS

Immediate conversion from other DMTs to siponimod had an acceptable safety/tolerability profile, with no unexpected findings. There was no evidence of a meaningful reduction in heart rate when initiating siponimod in the overall group or in subgroups stratified by prior DMTs, including subjects transitioning from fingolimod to siponimod without dose titration.