Background

- Siponimod (Mayzent®) is an oral S1P receptor type 1, 5 modulator that reduces relapses and disability progression in patients with SPMS.
- Approved by the USA for adults with RMS, including CIS, RRMS and active SPMS
- Indicated in EU for adults with SPMS as shown by reduction in disease activity.
- Indicated in Japan and Australia for SPMS.

Objective

- To report interim analyses of EXCHANGE, evaluating safety and tolerability of converting from other DMTs with and without dose titration.

Study design and patient population

- This 6-month, prospective, multicenter, open-label, single arm trial (Figure 1) has completed 50% of expected enrollment.
- Analysis included patients aged 18-65 years with advancing forms of RMS, EDSS 2.0-6.5, and on continuous or recent-active DMTs for 3 months at time of consent.
- Uniquely, some patients participated in a virtual cohort, which enabled certain visits to be conducted virtually, allowing for flexible participation during the COVID-19 pandemic.
- Most patients initiating siponimod were titrated from 0.25 to 2 mg over 6 days.
- Patients transitioning from teriflunomide required 11-14 days accelerated washout with cholestyramine or activated charcoal.
- Patients transitioning from natalizumab or occluzumab required 24- or 34-week washout period, respectively.
- Those converting from fingolimod immediately switched to siponimod 2 mg, with no dose titration.

Results

Patient disposition and demographics

- 163 patients from 42 US centers were eligible for inclusion in the safety analysis.
- 65.0% completed the study phase, 16.6% were receiving other DMTs at trial endpoint.

Effect of siponimod conversion on heart rate

- There was no decrease in heart rate at 6 hours post first dose from baseline in the overall group or in subgroups stratified by prior DMTs, including subjects transitioning from fingolimod to siponimod without dose titration.
- EXCHANGE will provide clinically relevant data to HCPS in providing management guidelines for switching patients to siponimod from other DMTs.

Conclusions

- In this interim analysis, immediate conversion over 6 days from other DMTs to siponimod was generally well tolerated, with no unexpected findings.
- Furthermore, there was no evidence of a meaningful reduction in heart rate when switching to siponimod in the overall group or in subgroups stratified by prior DMTs, including subjects transitioning from fingolimod to siponimod without dose titration.
- EXCHANGE will provide clinically relevant data to HCPS in providing management guidelines for switching patients to siponimod from other DMTs.

References


Abbreviations

AE, adverse event; bpm, beats per minute; CL, confidence interval; CIS, clinically isolated syndrome; DMT, disease modifying therapy; EDSS, Expanded Disability Status Scale; EDSS, end of study; EOT, end of treatment; GA, glatiramer acetate; HCP, healthcare professional; IFN, interferon; IRRS, interrelated sclerosis; MS, multiple sclerosis; N, number of patients; n, number of observations; PI, principal investigator; PPMS, primary progressive multiple sclerosis; RMS, relapsing remitting multiple sclerosis; RMS, relapsing-remitting multiple sclerosis; S1P, sphingosine 1 phosphate; SAE, serious adverse event; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

Disclosures

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