Introduction

• For patients with relapsing multiple sclerosis (MS), risk of transitioning to secondary progressive MS (SPMS) remains high, despite treatment availability.

• Siponimod (Mayzent®) is a selective sphingosine 1-phosphate receptor (S1P1 and S1P5) modulator, approved in the USA for the treatment of adults with clinically isolated syndrome, relapsing-remitting MS and active SPMS.

• Increasing age is associated with disability accumulation, independent of MS duration, and may negatively affect treatment outcomes.

• In EXPAND, a phase 3 trial examining the efficacy and safety of siponimod in an SPMS population, siponimod significantly reduced risk of confirmed disability progression (CDP) versus placebo.

• We investigated efficacy and safety of siponimod, by age subgroups, in the subpopulation of patients from EXPAND with active SPMS (relapse in 2 years before screening and/or ≥1 T1 gadolinium-enhancing lesion at baseline), in line with approved indication of siponimod.

Objective

• Assess efficacy and safety of siponimod in patients with active SPMS in subgroups of patients aged <50 and ≥50 years at Baseline from the EXPAND study.

Methods

Study design

• EXPAND was a phase 3, 36 month, randomized, placebo-controlled trial of siponimod 2 mg/day in adults (18-60 years) with SPMS, Expanded Disability Status Scale (EDSS) score ≥3.0-6.5, and EDSS progression in the 2 years before study.

Results

Patient Disposition

• EXPAND included 1651 patients (siponimod, n=1105; placebo, n=546).

• Of these, 779 patients had active SPMS and were stratified by median baseline age:
  – <50 years: 471 patients (siponimod, n=326; placebo, n=145)
  – ≥50 years: 308 patients (siponimod, n=190; placebo, n=118)

Efficacy

• In the phase 3 EXPAND trial, for patients with active SPMS, siponimod reduced risk of (Figure 1): – 3-month CDP by 31% (p=0.0054)
  – 6-month CDP by 37% (p=0.0034)

• In patients <50 years, siponimod reduced risk of (Figure 1): – 3-month CDP by 31% versus placebo (siponimod, 27%; placebo, 36%; p=0.0365)
  – 6-month CDP by 38% (siponimod, 21%; placebo, 32%; p=0.126)

• In those ≥50 years, siponimod reduced the risk of (Figure 1): – 3-month CDP by 38% versus placebo (siponimod, 22%; placebo, 33%; p=0.0332)
  – 6-month CDP by 37% (siponimod, 16%; placebo, 24%; p=0.0749)

Safety

• The safety profile of siponimod in EXPAND was generally similar in the overall population and among baseline age subgroups.

• Siponimod was generally well tolerated in both age subgroups (Figure 2): – <50 years: rates of any AE were similar for siponimod and placebo (85.6% vs. 80.0%)
  – ≥50 years: rates of any AE were slightly higher for siponimod than placebo (88.9% vs. 76.3%)

• In both age subgroups, rates of serious AEs were slightly lower for siponimod than placebo.

• These results are consistent with the overall active SPMS cohort in EXPAND.

References


Conclusions

• Siponimod provided similar clinical benefits in reducing CD risk in patients aged <50 years and ≥50 years with active SPMS.

• Siponimod was generally well tolerated by patients with active SPMS, regardless of baseline age.

• These results are consistent with the overall active SPMS cohort in EXPAND®.

Table 1. AEs associated with siponimod in the overall EXPAND population, and baseline age subgroups

<table>
<thead>
<tr>
<th>Event</th>
<th>Overall Population</th>
<th>&lt;50 years</th>
<th>≥50 years</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Siponimod (n=1099)</td>
<td>Siponimod (n=546)</td>
<td>Placebo (n=546)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>48 (4.4)</td>
<td>14 (2.6)</td>
<td>30 (5.9)</td>
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<tr>
<td>Hypertension</td>
<td>137 (12.5)</td>
<td>50 (9.2)</td>
<td>32 (9.8)</td>
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<tr>
<td>Lymphopenia</td>
<td>9 (0.8)</td>
<td>0</td>
<td>4 (1.2)</td>
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<tr>
<td>Macular edema</td>
<td>18 (1.6)</td>
<td>1 (0.2)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>25 (2.3)</td>
<td>4 (0.7)</td>
<td>5 (1.5)</td>
</tr>
</tbody>
</table>

Data are number of patients (%)