Maralixibat Improves Cholestatic Pruritus and Bile Acids in Children With FIC1: Data From the MARCH Trial

Introduction

• Progressive familial intrahepatic cholestasis (PFIC) is a group of genetic disorders that result in disrupted bile composition and cholestasis.1

• PFIC1 is characterized by defective pruritus, impaired growth, reduced quality of life (QoL), and with most children undergoing liver transplants.2-3

• MARCH (the largest phase 3 trial conducted in children with PFIC):4-5

• Key criteria: patients with Alagille syndrome ≥3 months of age in the US and ≥2 months of age in Europe

• Diagnosis of PFIC

• Persistent, moderate pruritus and bile acid accumulation

• ItchRO (Obs): The Itch-Reported Outcome (Observer) score measures parent/caregiver-reported pruritus.6-7,a

• MARCH, the largest phase 3 trial conducted in children with PFIC9:

• Persistent, moderate pruritus and bile acid accumulation

• ItchRO (Obs): The Itch-Reported Outcome (Observer) score measures parent/caregiver-reported pruritus.6-7,a

Objective

• To report efficacy and safety data from the FIC1 cohort in MARCH, a 26-week, randomized, phase 3 clinical trial, evaluating maralixibat for the treatment of PFIC patients

• Maralixibat (MRX) was generally well tolerated:

Methods

Baseline Characteristics

Table 1: MARCH: Key Demographics and Baseline Characteristics of Patients With FIC1 Deficiency

<table>
<thead>
<tr>
<th>Variable</th>
<th>MRX (n=7)</th>
<th>Placebo (n=6)</th>
<th>Overall (N=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>6.6 ± 1.8</td>
<td>8.2 ± 4.9</td>
<td>7.4 ± 3.7</td>
</tr>
<tr>
<td>Male, %</td>
<td>57.1</td>
<td>50.0</td>
<td>58.5</td>
</tr>
<tr>
<td>Overall bilirubin, mg/dL</td>
<td>3.8 ± 2.2</td>
<td>7.3 ± 2.9</td>
<td>5.4 ± 1.3</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>5.3 ± 2.9</td>
<td>9.7 ± 3.8</td>
<td>7.3 ± 2.0</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>61 ± 31</td>
<td>90 ± 51</td>
<td>75 ± 41</td>
</tr>
<tr>
<td>Direct bilirubin, mg/dL</td>
<td>3.2 ± 1.7</td>
<td>6.1 ± 4.0</td>
<td>4.6 ± 2.4</td>
</tr>
<tr>
<td>Total bile acid, nmol/L</td>
<td>996 ± 365</td>
<td>1230 ± 573</td>
<td>1098 ± 482</td>
</tr>
</tbody>
</table>

Results

Figure 1. MARCH Phase 3 Study Design

Figure 2. Weekly Average ItchRO(Obs) Score Over Time

Figure 3. Average sBA Over Time

Figure 4. Pruritus Score (ItchRO[Obs]) by Patient

Figure 5. sBA Levels by Patient

Figure 6. Total Biliirubin by Patient

Figure 7. Direct Biliirubin in FIC1 Deficiency Cohort

Conclusions

• Maralixibat resulted in improvements in pruritus and statistically significant improvements in sBA levels compared to placebo.

• Statistically and clinically significant improvements were observed in sBA in the BSEP and All-PFIC cohorts.

• The study was not powered to identify differences in the FIC1 subpopulation, but the magnitude of treatment effect changes in pruritus and sBA were consistent with MARCH for the BSEP cohort and the all-PFIC cohort.

• Maralixibat was generally well tolerated.

• No significant changes in ALT levels from baseline were observed following maralixibat treatment.

Disclosures

References

Acknowledgments

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