Pruritus intensity is associated with cholestasis biomarkers and quality of life measures after maralixibat treatment in children with Alagille syndrome

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Introduction

- Alagille syndrome (ALGS) is a rare, genetic, multisystem disorder that commonly presents in infancy.1
- Patients with ALGS experience severe cholestatic pruritus due to the accumulation of serum bile acids (sBA).2
- ALGS-associated pruritus can be extremely debilitating, resulting in bleeding, scarring, sleep disturbance, fatigue, and decreased quality of life, which negatively impacts the patient and their family.3

Methods

- Study design: ICONIC is a long-term, Phase 2b, double-blind study assessing the effect of maralixibat treatment in children with ALGS, with a placebo-controlled, randomized, withdrawal period (Figure 1). Participants continued to receive maralixibat in an ongoing, follow-up extension study.
- Baseline characteristics: Twenty-nine of the 31 enrolled participants completed 48 weeks of treatment, with 27 evaluated for this analysis.

Results

- Baseline characteristics: Table 1 presents baseline characteristics for the analysis population.

Table 1. Baseline characteristics for the analysis population.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>Median (Q1–Q3)</th>
<th>Min–Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10.5 (3.8)</td>
<td>10.2 (9.7)</td>
<td>4.5–18.0</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 24, Female 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus intensity</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ItchRO score (0–4)</td>
<td>3.4 (0.7)</td>
<td>3.2–3.7</td>
<td>2.0–5.0</td>
</tr>
<tr>
<td>CSS score (0–7)</td>
<td>3.3 (1.0)</td>
<td>3.0–4.0</td>
<td>0.0–7.0</td>
</tr>
</tbody>
</table>

- Pruritus measurements: Pruritus intensity was assessed using the validated ItchRO and CSS scores.
- ItchRO and CSS scores were statistically significant at baseline and week 48.
- Significant results were also observed for ATX and height z-score.

Statistical methods

- Post hoc analysis: Twenty-nine of the 31 enrolled participants completed 48 weeks of treatment, with 27 evaluated for this analysis.
- Results: Pruritus intensity was assessed at baseline and week 48 using the ItchRO tool.
- Significant results were observed for ItchRO and CSS scores.

Conclusion

- Significant correlations were observed between pruritus and cholestasis biomarkers.
- Pruritus intensity was significantly reduced with maralixibat treatment.

References

5. El-Serag HB, Shneider BL, Teeny L, Spino C, Kamath BM, et al. Pruritus in Alagille syndrome: a phase 2, randomised, double-blind, placebo-controlled trial. Alagille Syndrome Association Research Conference; 2018 Dec 12–14; Santa Clara, CA. The authors would like to thank the clinical trial participants, their families, and site staff for their participation and support. This work was supported by Mirum Pharmaceuticals, Inc. No other relationships or activities described are relevant to this poster. Presented at the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) Annual Meeting (Virtual); 2021 (in press).