Real-World Safety Experience in Patients With Alagille Syndrome Treated With Maralixibat

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Introduction
• Maralixibat (MRX; NBI-2761) is a minimally absorbed bile acid transport inhibitor (BAT) that prevents enterohepatic bile acid recycling and is approved for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 23 months of age in the US and 22 months of age in the EU.¹
• Rare disease clinical trials are often limited by narrowly selected populations, small sample sizes, and evaluation of treatment emergent adverse events (TEAEs) that may not reflect real-world experience.
• In September 2020, a global Expanded Access Program was opened to facilitate access to maralixibat for eligible patients with ALGS who were unable to participate in clinical trials.²

Objective
• To report real-world safety observations from the initial Expanded Access Program of maralixibat.

Methods

Registration

Enrollment period: September 2020 to February 2022

All patients who received maralixibat through the Expanded Access Program, following the commercial dosing regimen with a target dose of 380 mg/kg daily, were included in this analysis

Physicians prescribing maralixibat, as part of the Expanded Access Program, reported patient baseline characteristics and all TEAEs to a central database

Results

Expanded Access Program Safety Population (N=37) Included Participants From 6 Countries

- USA (19 [51%])
- Australia (6 [16%])
- Canada (4 [11%])
- Germany (4 [11%])
- Netherlands (4 [11%])
- Norway (2 [5%])

Lost to follow-up=3 (8.1%)

Table 1. Proportion of Participants Who Experienced TEAEs Following Treatment With MRX

<table>
<thead>
<tr>
<th>TEAE Category</th>
<th>N=37</th>
<th>TEAE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAE*</td>
<td>16</td>
<td>43.2%</td>
</tr>
<tr>
<td>TEAE: potentially related to MRX</td>
<td>16 (43.2%)</td>
<td></td>
</tr>
<tr>
<td>Treatment-emergent SAE</td>
<td>2 (5.4%)</td>
<td></td>
</tr>
<tr>
<td>TEAE leading to dose modification</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TEAE leading to MRX interruption</td>
<td>1 (2.7%)</td>
<td></td>
</tr>
<tr>
<td>TEAE leading to MRX discontinuation</td>
<td>1 (2.7%)</td>
<td></td>
</tr>
<tr>
<td>TEAE leading to death</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Notes:
• *Includes all adverse events.
• TEAEs are adverse events (AEs) and/or serious adverse events (SAEs) that occurred in the Expanded Access Program and that were considered by investigators as being related to MRX.
• TEAEs leading to dose modification included dose reduction and dose interruption.
• TEAEs leading to MRX interruption included MRX suspension.
• TEAEs leading to MRX discontinuation included MRX discontinuation.

Patients Dispositions

- Registered N=37
- Safety assessed in m=37
- Under observation n=28
- SAE under observation m=29

Discussion

Maralixibat is a minimally absorbed BAT that prevents enterohepatic bile acid recycling and is approved for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS). In the Expanded Access Program, 37 patients with ALGS were treated with maralixibat following the commercial dosing regimen with a target dose of 380 mg/kg daily. Of these patients, 16 (43.2%) experienced any TEAE, 2 (5.4%) of which were SAEs. TEAEs leading to dose modification, MRX interruption, or discontinuation were rare, occurring in only 1 (2.7%) patient. No safety concerns were noted in the Expanded Access Program that were not previously reported in clinical trials.

SAE under observation n=28

- GI disorders (3 [10%])

- Liver/serum abnormalities (3 [10%])

- SAEs under observation n=29

Conclusions

• Safety and tolerability experience in a real-world setting is reflective of real-life clinical practice.

- In this real-world analysis of maralixibat, treatment-related GI AEs were mild and observed in only 3 patients (8.1%). There were no discontinuations due to GI AEs.

- There were no serious AEs or deaths related to maralixibat treatment, and no reports of GI bleeding, fat-soluble vitamin deficiency events, or fractures.

- Maralixibat appears to be well tolerated in patients with ALGS in the real-world setting, with a lower rate of AEs than described in clinical trials.

Abbreviations
ALGS: Alagille syndrome; GI: gastrointestinal; BAT: bile acid transport

Disclosures
The sponsor funded the study, collected the data, and prepared the manuscript. The sponsor had full access to all the data in the study and final responsibility for the decision to submit for publication.

References

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