Real-world safety experience in patients with Alagille syndrome treated with maralixibat

Ryan W Himes,[1] Douglas B Mogul,[2] Marshall Baek,[2] Regino P Gonzalez-Peralta[3]

[1]Pediatric Hepatology, Ochsner Hospital for Children, New Orleans, LA, USA; [2]Mirum Pharmaceuticals, Inc., Foster City, CA, USA; [3]Pediatric Gastroenterology, Hepatology, and Liver Transplant, AdventHealth for Children and AdventHealth Transplant Institute, Orlando, FL, USA

4807

Introduction

- Maralixibat (MRX) is an ileal bile acid transporter inhibitor (IBATi) approved by the US Food and Drug Administration (FDA) to treat cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older.[1]
- The MRX label includes 5 years of safety data, capturing all reported adverse events (AEs), regardless of whether they were thought to be related to MRX.[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 (EAP) was opened to facilitate access to MRX for eligible patients with ALGS who were unable to participate in clinical trials.[2]

Aim

- To report real-world safety observations from the initial EAP of MRX.

Methods

Registration

Enrollment period:
September 2020 to February 2022

All patients who received MRX through the EAP, following the commercial dosing regimen with a target dose of 380 µg/kg daily, were included in this analysis

Physicians prescribing MRX, as part of the EAP, reported patient baseline characteristics and all TEAEs to a central database

TEAEs were defined as those occurring on or after the first dose of MRX and within 7 days from the last medication dose

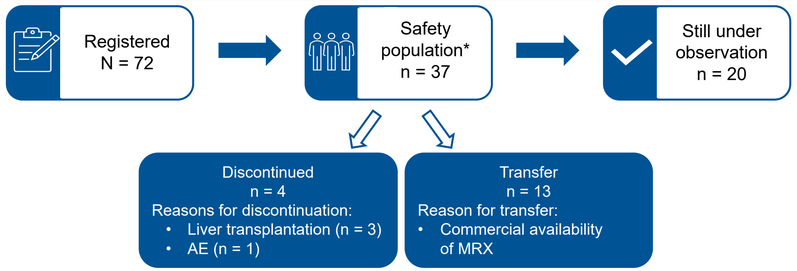
Results

EAP safety population (N = 37) included participants from six countries

Percentages represent the country of origin for the safety population (N = 37). The EAP safety population includes all participants who were enrolled, consented, and received at least one dose of MRX.
EAP, Expanded Access Program; MRX, maralixibat.

- At baseline, median (range) age was 6 years (1–27), median height was 103 cm (48–162), median weight was 16 kg (7–60), and 20 patients (54%) were male.
- Median (range) duration of follow-up was 243 days (52–385).

Patient dispositions



*The safety population includes all participants who were enrolled, consented to provide RWD, and received at least one dose of MRX.
AE, adverse event; MRX, maralixibat; RWD, real-world data.

Proportion of participants who experienced TEAEs following treatment with MRX

Subjects experiencing ≥1 of each AE category, n (%)	N = 37
TEAE*	16 (43.2)
TEAE potentially related to MRX	6 (16.2)
Treatment-emergent SAE†	2 (5.4)
Treatment-emergent SAE potentially related to MRX	0
TEAE leading to dose modification‡	3 (8.1)
TEAE leading to MRX interruption§	1 (2.7)
TEAE leading to MRX discontinuation‖	1 (2.7)
TEAE leading to death	0

*TEAEs are AEs with a start date on or after the first dose of MRX and started prior to the last dose of MRX plus 7 days.
†Treatment-emergent SAEs included viral infection (n = 1) and fever (n = 1).
‡TEAEs leading to dose modification included diarrhea (n = 2) and incorrect initial dosing (n = 1).
§TEAEs leading to MRX interruption included mild liver enzyme elevation (n = 1; grade 1).
‖TEAEs leading to MRX discontinuation included liver enzyme elevation (n = 1; grade 3).
AE, adverse event; MRX, maralixibat; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

TEAEs in the EAP

- The majority of TEAEs observed were mild in severity and not related to MRX.
- Three patients (8.1%) experienced gastrointestinal (GI) TEAEs that were considered possibly related to MRX. All were mild in severity, and there were no dose interruptions or discontinuations.
- Overall, there was only one treatment discontinuation possibly related to MRX due to transaminase elevation (grade 3) of unknown clinical significance.
- Infections and other TEAEs were not considered related to MRX treatment.*

Proportion of participants in the EAP with drug-related TEAEs

System Organ Class	n (%)
GI Disorders	3 (8.1)
Liver Test Abnormalities	3 (8.1)

*TEAEs unrelated to MRX: infections of any attribution included; COVID-19 (n = 2), otitis media (n = 2), Coxsackie viral infection (n = 1), acute otitis media (n = 1), respiratory tract infection (n = 1), urinary tract infection (n = 1), and viral infection (n = 1; grade ≥3). Other TEAEs, all unrelated to MRX, were reported in the following system organ classes: general disorders and administration-site conditions (n = 3; including one case of grade ≥3 pyrexia); injury, poisoning, and procedural complications (n = 1); musculoskeletal and connective tissue disorders (n = 1); psychiatric disorders (n = 2); and respiratory, thoracic, and mediastinal disorders (n = 2).
EAP, Expanded Access Program; GI, gastrointestinal; MRX, maralixibat; TEAE, treatment-emergent adverse event.

Conclusions

- **Safety and tolerability experience in a real-world setting is representative of real-life clinical practice and is important for prescribing physicians.**
- **In this real-world analysis of MRX, treatment-related GI AEs were mild and observed in only three patients (8.1%). There were no discontinuations due to GI AEs.**
- **There were no serious AEs related to the use of MRX, and no reports of GI bleeding, fat-soluble vitamin deficiency events, or fractures.**
- **MRX 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.[1]**

Contact information

Ryan Himes, ryan.himes@ochsner.org

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References

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