Real-World Use of Maralixibat in Biliary Atresia: A Case Series

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Introduction

- Biliary atresia (BA) is a progressive disorder of intrahepatic and extrahepatic bile ducts; it is the most common indication for pediatric liver transplantation worldwide.[1-3]
  - BA is the most common cause of cholestasis in infants and presents in the first few weeks of life with persistent jaundice, clay-colored stools, dark urine, and hepatomegaly.[2-4]
  - If left untreated, BA can cause fibrosis, cirrhosis, end-stage liver disease, and death, with survival at <10% at 3 years of age.[2-5]
- A Kasai procedure is the primary surgical management strategy for BA to restore bile flow in the first months of life, but many patients subsequently require liver transplantation.[2,4,5]
- Even after a Kasai, patients with BA may experience pruritus that substantially impairs quality of life.[6]
  - Pruritus is a common complication in most cholestatic disorders, including BA, and is thought to result in part from accumulation of toxic bile acids.[7,8]
- Maralixibat (MRX) is a minimally absorbed ileal bile acid transporter inhibitor that prevents enterohepatic bile acid recirculation and is approved for[9,10]:
  - Treatment of cholestatic pruritus in patients with Alagille syndrome ≥3 months of age in the US and ≥2 months of age in the EU
  - Treatment of cholestatic pruritus in patients with progressive familial intrahepatic cholestasis (PFIC) ≥12 months of age in the US and treatment of PFIC in patients ≥3 months of age in the EU
- Several patients with BA have received maralixibat for the treatment of cholestatic pruritus as part of a compassionate use program.

Objective

- To report on the use of maralixibat for the treatment of cholestatic pruritus in patients with BA.

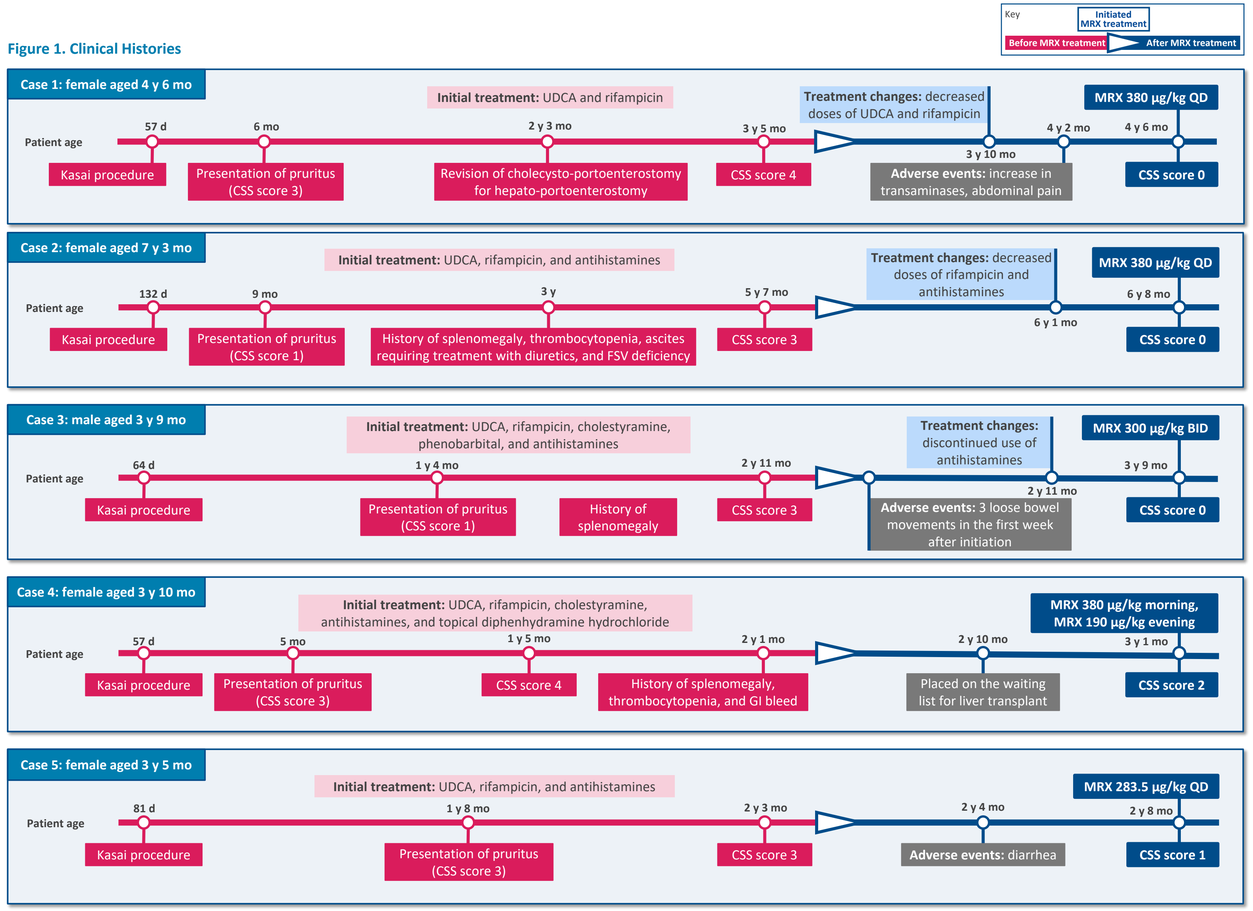
Methods

- A retrospective review of patient records was performed for children with BA, from 5 tertiary hospitals, who received maralixibat for at least 3 months through the compassionate use program.
- Treating physicians were provided a standardized form to collect key clinical variables, including demographics, past medical history, laboratory markers, and medications.
- Pruritus was assessed using the clinician scratch scale (CSS) at Baseline and last clinical follow-up.
  - CSS is a 5-point scale, where 0 = none, 1 = rubbing or mild scratching when undistracted, 2 = active scratching without abrasions, 3 = abrasions, and 4 = cutaneous mutilations, hemorrhage, scarring.[11]

Results

Clinically Significant Reduction in Pruritus (≥1-Point Decrease) Was Observed in All Patients, Including Complete Resolution in 3 Patients

Figure 1. Clinical Histories



All Patients Underwent a Kasai Procedure Before 4 Months of Age

Table 1. Key Baseline Demographics and Characteristics

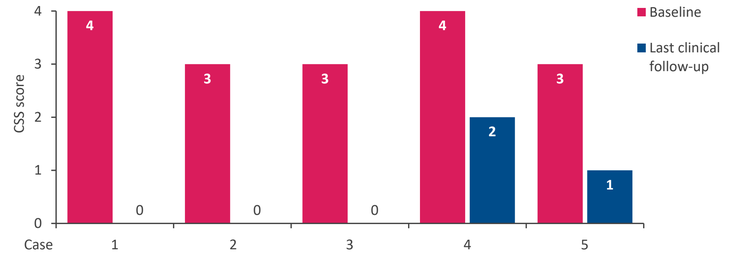
Parameter[a]	All cases (N=5)
Age at initiation of maralixibat, y	2.9 (1.8, 4.3)
Sex, female, %	80
CSS score	3 (3, 4)
Age at Kasai procedure, d	64 (57, 81)
sBA, µmol/L	86 (76, 188)
Total bilirubin, mg/dL	1 (0.8, 2.2)
ALT, U/L	133 (109, 156)
AST, U/L	127 (98, 159)
GGT, U/L	97 (89, 300)
Height Z-score[b]	-0.3 (-1.0, 0.4)
Weight Z-score[b]	0.2 (-0.1, 0.4)

[a]All values are median (Q1, Q3) unless otherwise specified. [b]Based on 4 cases for which data were available.

- The median (range) age at presentation of pruritus was 9 (5-20) months.
- Prior to initiation of maralixibat, all patients were taking at least 2 antipruritic medications.
- At maralixibat initiation, none of the patients were undergoing evaluation for liver transplantation.

Complete Resolution of Pruritus Was Observed in 3 of 5 Cases

Figure 2. CSS Scores at Baseline and Last Clinical Follow-Up



Conclusions

- These real-world cases provide evidence that maralixibat may be effective for the management of cholestatic pruritus in patients with BA.
- These data highlight the need for larger studies to systematically evaluate the potential of maralixibat for the treatment of cholestatic pruritus in patients with BA.

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BA, biliary atresia; BID, twice daily; CFB, change from Baseline; CSS, clinician scratch scale; FSV, fat-soluble vitamin; GGT, gamma-glutamyl transferase; GI, gastrointestinal; MRX, maralixibat; PFIC, progressive familial intrahepatic cholestasis; QD, once daily; sBA, serum bile acid; UDCA, ursodeoxycholic acid.

Disclosures

ND, CAC, JF, and RR have nothing to disclose. BK is an advisor for Mirum Pharmaceuticals, Inc. BR is consultant at IPSEN and an advisor for Mirum Pharmaceuticals, Inc.

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