Maralixibat, an Ileal Bile Acid Transporter Inhibitor, Delays the Need for Liver Transplant in Patients With Alagille Syndrome: Real-World Experience

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Background

- Alagille syndrome (ALGS) is a rare, debilitating, autosomal dominant disorder that presents with a broad range of clinical manifestations.[1]
  - The key clinical manifestations include cholestasis, failure to thrive, xanthomas, and progressive liver disease, all of which can lead to liver transplant or death.[1]
- Cholestatic pruritus is the most debilitating symptom of ALGS and among the most severe of any chronic liver disease.[2]
- Patients with ALGS frequently require a liver transplant before adulthood, with transplant-free survival ranging from 24%-40.3% by approximately 18 years of age.[3,4]
  - In patients with ALGS who received a liver transplant, refractory pruritus was an indication for 69%-81.8%.[4,5]
- Maralixibat (MRX), an ileal bile acid transporter (IBAT) inhibitor, is approved for the treatment of cholestatic pruritus in patients with ALGS ≥2 months of age in the EU, and ≥3 months of age in the US (Fig.1).[6,7]
- In a retrospective study of patients with ALGS, MRX treatment was associated with statistically significant improvement in event-free survival (*P*<.0001) and transplant-free survival (*P*<.0001).[8]

Objective

- To report real-world experience of delaying the need for liver transplant following treatment with MRX in 2 children with ALGS

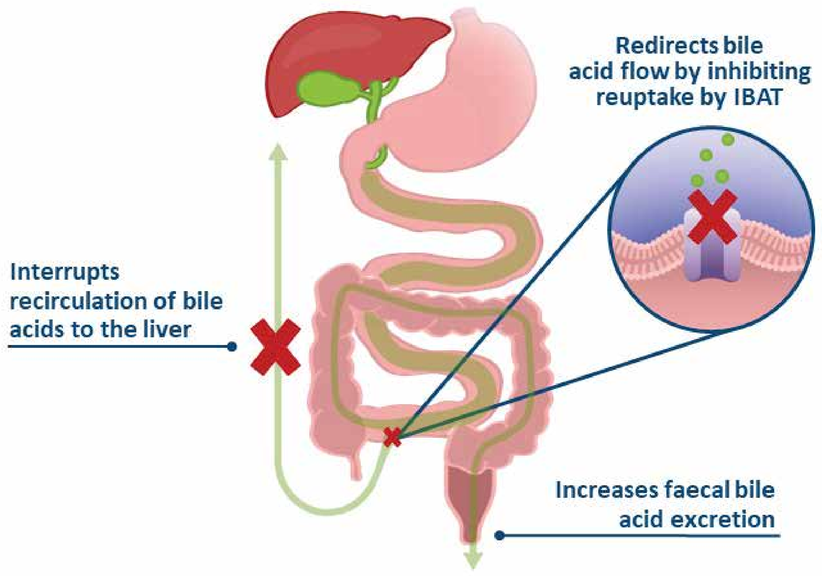
Methods

- Chart reviews were performed for 2 patients with ALGS listed for liver transplant due to cholestatic pruritus whose treatment with MRX led to delay of liver transplant

MRX is a novel, minimally absorbed, orally administered IBAT inhibitor that interrupts the enterohepatic circulation of bile acids to improve cholestatic pruritus.[6,9]

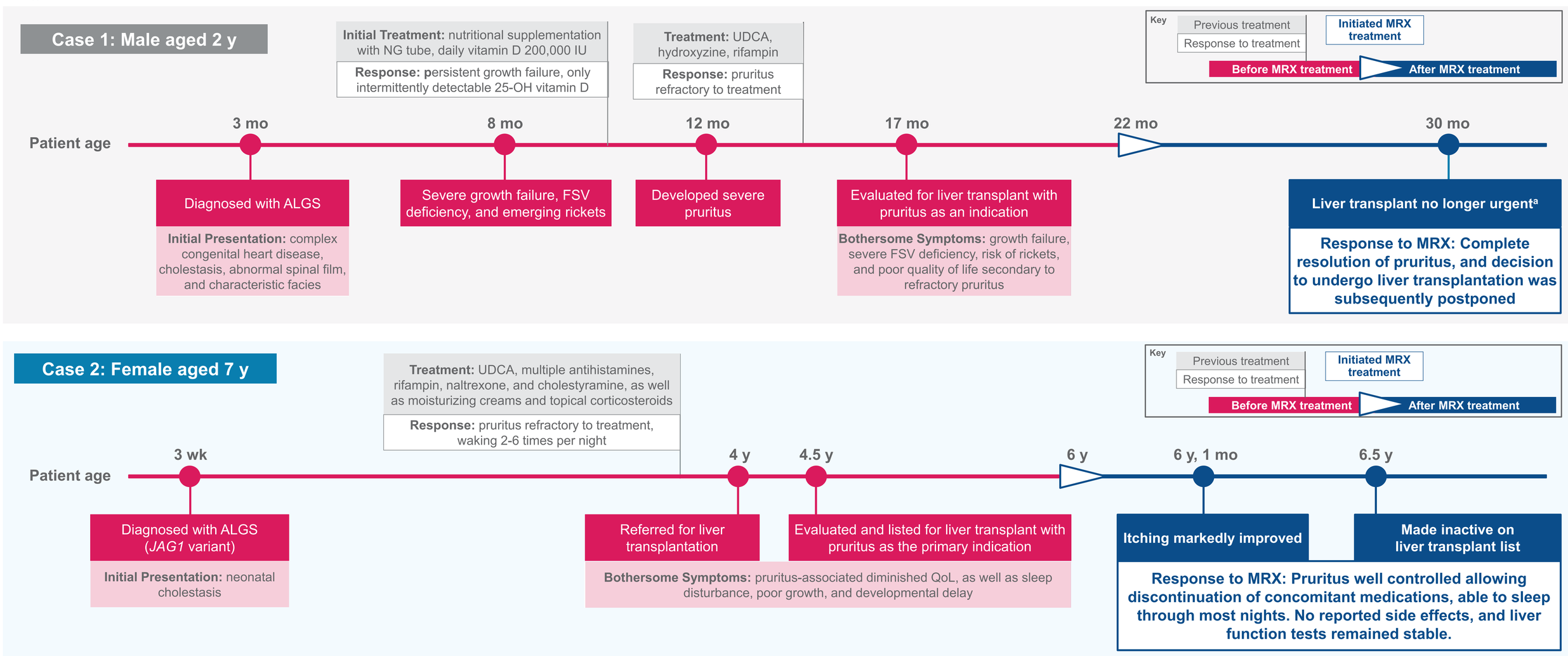
Figure reprinted from *The Lancet*, 398, Gonzales E, et al., 'Efficacy and safety of maralixibat treatment in patients with Alagille syndrome and cholestatic pruritus (ICONIC): a randomised phase 2 study', 1581–1592, Copyright (2021), with permission from Elsevier.

Figure 1. MRX Mechanism of Action



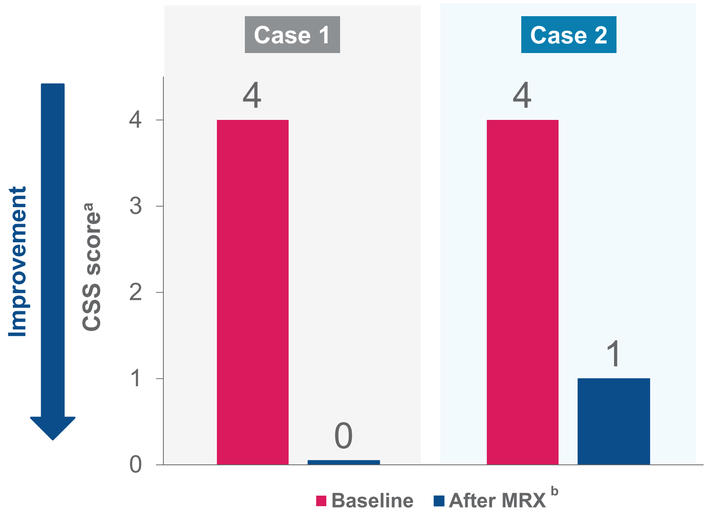
Results

Figure 2. Clinical Histories



FSV, fat-soluble vitamin; MRX, maralixibat; NG, nasogastric; QoL, quality of life; UDCA, ursodeoxycholic acid. [a]The patient is still anticipated to need a liver transplant given growth failure and persistent FSV deficiency.

Figure 3. Improvement of CSS Scores Upon Treatment With MRX



CSS, Clinician Scratch Scale; MRX, maralixibat. [a]CSS, 0 = none, 1 = rubbing or mild scratching when undistracted, 2 = active scratching without abrasions, 3 = abrasions, and 4 = cutaneous mutilations, hemorrhage, scarring.[9] [b]At the time of reporting, these patients had received 8 and 12 months of treatment with MRX, respectively.

Table 1. Laboratory Values for Each Patient at Baseline and After MRX Treatment

Case	Laboratory assessments	Baseline values	Last visit after MRX treatment[a]
1	Height *z* score	-2.52	-2.72
	Weight *z* score	-4.14	-2.43
	Total bilirubin (mg/dL)	11.4	10.6
	ALT (U/L)	148	166
	AST (U/L)	156	168
	GGT (U/L)	1321	808
2	Height *z* score	-2.9	-2.5
	Weight *z* score	-1.7	-1.7
	Total bilirubin (mg/dL)	1.3	1.6
	ALT (U/L)	126	138
	AST (U/L)	108	101
	GGT (U/L)	375	408

ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; MRX, maralixibat. [a]At the time of reporting, the MRX treatment duration was 8 months for case 1 and 12 months for case 2.

Conclusions

- The 2 cases presented provide real-world evidence of the effectiveness of MRX in delaying the need for liver transplant in patients with ALGS due to significant and rapid improvements in pruritus and QoL.
  - In Case 1, pruritus control with MRX enabled liver transplant evaluation to be postponed, allowing for ongoing optimization of his nutrition and cardiac disease.
  - In Case 2, after 6 months of MRX treatment, the patient is now inactive on the transplant list (status 7), discontinued several concomitant medications, and is able to sleep through most nights.
- These real-world cases highlight the impact that MRX has on improving transplant-free survival in patients with ALGS.

Acknowledgments

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Disclosures

ND, KS, and RV report no conflicts of interest. DBM is a full-time employee of and shareholder in Mirum Pharmaceuticals, Inc.

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