Significant improvement in cholestatic pruritus in patients with Alagille syndrome treated with maralixibat, an ileal bile acid transporter inhibitor: Real-world experience

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Introduction

- Maralixibat (MRX) is an ileal bile acid transporter inhibitor (IBATi) recently approved by the US Food and Drug Administration (FDA) for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older.[1]
- MRX is an oral medication that blocks intestinal reabsorption of bile acids, increasing faecal bile acid excretion and lowering endogenous bile acids, thereby improving cholestasis and associated symptoms.[2,3]
- The restrictiveness of inclusion/exclusion criteria for clinical trials make it difficult to generalise the effectiveness of the study drug in a wider population.
- Three case studies from the MRX Expanded Access Program (EAP) for children with ALGS provide insights into the real-world application of MRX outside of clinical trials.[4]

Aim

- To assess the real-world application of MRX in children with ALGS and cholestatic pruritus.

Methods

- Three children with ALGS were enrolled in the MRX EAP, presenting with a variety of clinical manifestations (**Figure 1**).
- Clinicians rated pruritus using the Clinician Scratch Scale, on a scale of 0–4, where 0 = none and 4 = cutaneous mutilation, haemorrhage and scarring evident.[3]
- Laboratory parameters, including total bilirubin, alanine aminotransferase and alkaline phosphatase, were monitored at varying time intervals in the months prior to and after starting MRX treatment.

Results

Figure 1. Clinical presentation of the three patients in the MRX Expanded Access Program.

Patient 1
Age: 11 years old

- **Facies:** yes
- **Evidence of heart abnormalities:** mild peripheral pulmonic stenosis
- **Vertebral anomalies:** no
- **Presence of posterior embryotoxon:** yes
- **Liver biopsy results:**, giant cell transformation
- **Genetics:** testing not performed
- **Age at initiation of itching:** 6 months old

Patient 2
Age: 7 years old

- **Facies:** yes
- **Evidence of heart abnormalities:** coarctation of aorta, branch pulmonary artery stenosis
- **Vertebral anomalies:** no
- **Presence of posterior embryotoxon:** yes
- **Liver biopsy results:** unavailable
- **Genetics:** *JAG1* mutation
- **Age at initiation of itching:** 3 months old

Patient 3
Age: 2 years old

- **Facies:** yes
- **Evidence of heart abnormalities:** peripheral pulmonic stenosis, persistent patent foramen ovale
- **Vertebral anomalies:** no
- **Presence of posterior embryotoxon:** no
- **Liver biopsy results:** giant cell transformation
- **Genetics:** *JAG1* mutation
- **Age at initiation of itching:** soon after birth

Figure 2. Patient clinical information.

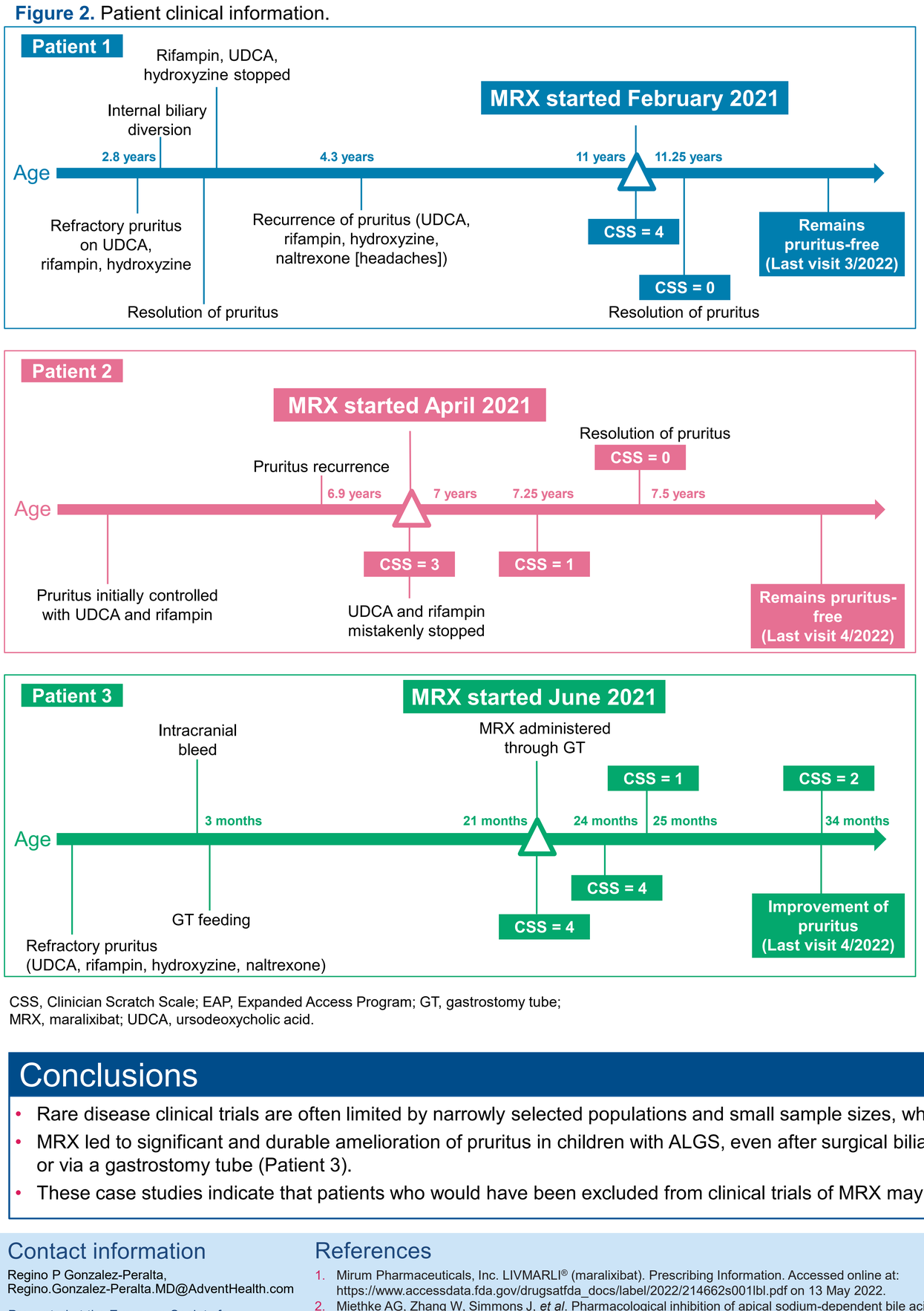
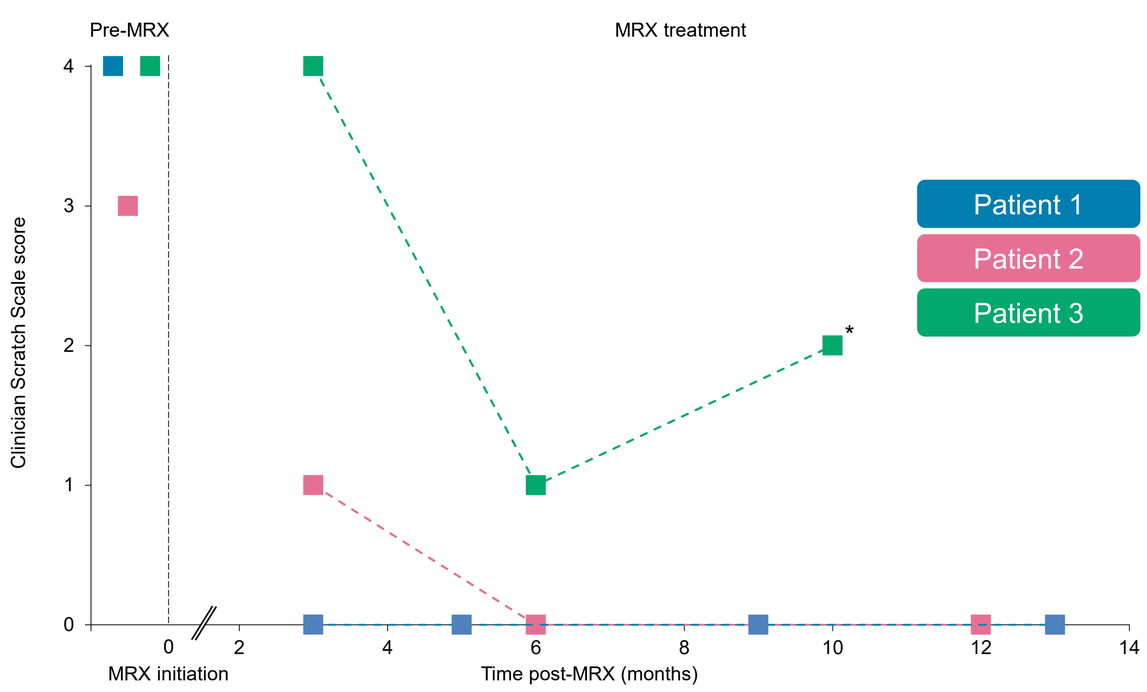
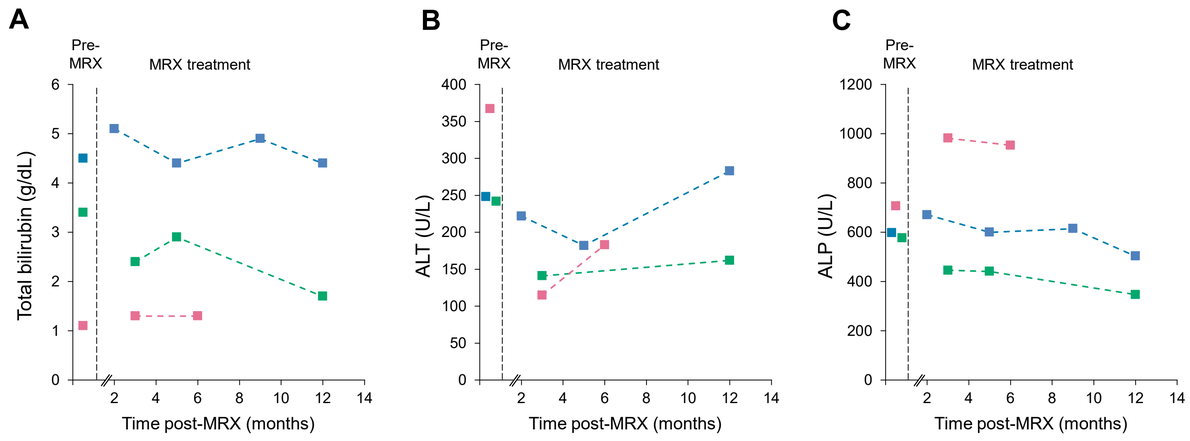


Figure 3. Clinician Scratch Scale scores for the three patients.



MRX, maralixibat.
*Increase in CSS likely due to MRX weight based dosing not being adjusted when patients' weight increased – MRX dose has since been adjusted to match the new weight.

Figure 4. Laboratory parameters for the three patients: (A) total bilirubin, (B) ALT and (C) ALP.



CSS, Clinician Scratch Scale; EAP, Expanded Access Program; GT, gastrostomy tube; MRX, maralixibat; UDCA, ursodeoxycholic acid.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; MRX, maralixibat.

Conclusions

- Rare disease clinical trials are often limited by narrowly selected populations and small sample sizes, which may not reflect real-word experience.
- MRX led to significant and durable amelioration of pruritus in children with ALGS, even after surgical biliary diversion (Patient 1), administered as monotherapy (Patient 2), or via a gastrostomy tube (Patient 3).
- These case studies indicate that patients who would have been excluded from clinical trials of MRX may have meaningful reductions in pruritus.

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