Introduction

• Alagille syndrome (ALGS) is a rare, lifelong, multisystem disorder characterized by intrahepatic bile duct paucity, growth retardation, ocular, cardiac, and renal defects.
• Cholestatic pruritus is a symptom of this disorder, often extreme and debilitating, and lead to sleep deprivation.
• ItchRO (Observer), a subjective assessment of itch severity, has been approved by the FDA to assess itch in patients with ALGS ≥1 year of age.
• Maralixibat (MRX), the ileal bile acid transporter inhibitor, has been approved by the US FDA for the treatment of cholestatic pruritus in patients with ALGS ≥1 year of age.

Methods

Study design

• Patients from Study LUM001-301-B (Phase 3) continued on this extension study (NCT02057692) that was a 13-week, randomized, placebo-controlled study.
• Patients from Study LUM001-302 (Phase 3) continued on this extension study (NCT01903460) that was a 13-week, randomized, placebo-controlled study.
• Patients from Study LUM001-304 (Phase 3) continued on this extension study (NCT02160782) that was a 48-week, randomized, placebo-controlled study.

Study population

• 10% of patients enrolled in Studies LUM001-301 and LUM001-302 up to 266 µg/kg/day.

Statistical analysis

• Treatment-emergent AEs of diarrhea and abdominal pain were analyzed for reported rates, including by severity and seriousness, actions taken with the study drug, and discontinuations due to AEs.
• Treatment-emergent AEs of diarrhea and abdominal pain were analyzed in all patients, irrespective of relatedness.

Results

• Overall, 10% of patients treated with MRX at any dose were included in this integrated MRX safety population.
• The median duration of exposure was 22.2 months, with up to 68.8 months of treatment with MRX (up to >5 years).
• The overall incidence of diarrhea with >5 years of MRX treatment was 31.0%.
• There were no discontinuations for diarrhea with up to >5 years of MRX treatment.

Conclusions

• Maralixibat is well tolerated for up to 5 years, with no new safety signals identified.
• Treatment-emergent AEs of diarrhea and abdominal pain are manageable and do not result in discontinuations or study withdrawals.
• MRX-treated patients have reduced rates of AEs compared to placebo.

Incidence and prevalence of diarrhea in the integrated MRX safety population.

Figure 1. Incidence and prevalence of diarrhea in the integrated MRX safety population.