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Abstract

TITLE: LONG-TERM MAINTENANCE OF RESPONSE AND IMPROVED LIVER HEALTH WITH MARALIXIBAT IN PATIENTS WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS (PFIC): DATA FROM THE MARCH-ON STUDY

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ABSTRACT BODY:

Abstract Body : Background: Progressive familial intrahepatic cholestasis (PFIC) is a group of genetic disorders resulting in disrupted bile composition, cholestasis, and pruritus. Maralixibat (MRX) is a minimally absorbed ileal bile acid transporter (IBAT) inhibitor which prevents enterohepatic bile acid recirculation. In the 26-week placebo-controlled MARCH Phase 3 study, MRX at 570 µg/kg BID demonstrated significant improvements in pruritus, serum bile acid (sBA), bilirubin and growth in patients across the broadest range of PFIC types studied to date. MARCH-ON is an open-label, long-term extension study for patients who completed the MARCH study. Here, we report on long-term maintenance of effect from MARCH-ON.
Methods: Long-term maintenance of response was assessed for patients who were originally randomized to receive MRX in MARCH and continued with treatment in MARCH-ON (MRX-MRX group; n=33). MRX response was assessed for patients who received PBO in the MARCH study and switched to open-label MRX in MARCH-ON (PBO-MRX group; n=24). Assessments included: pruritus measured by 0-4 scale of ItchRO[Obs]), sBA, bilirubin, and growth z-scores, as well as incidence of treatment-emergent adverse events (TEAEs). Baseline (BL) was defined as the start of MRX for each group.
Results: For the MRX-MRX group, the median (min, max) time on MRX was 394 days (108, 836). In total, 20 of 33 patients reached Week 52 at time of analysis. Significant improvements observed in the first 26 weeks of the MARCH study were sustained from BL through Week 52 in MARCH-ON for pruritus severity (-2.13, $p<0.0001$), sBA (-200 µmol/L, $p=0.0004$), bilirubin (-2.64 mg/dL, $p=0.0084$), height z-score (+0.54, $p<0.0001$), and weight z-score (+0.44, $p=0.0010$). In the PBO-MRX group, the median time on MRX was 256 days (29, 569). In total, 15 of 24 patients reached Week 26 at time of analysis. Newly gained statistically significant reductions in pruritus and sBA levels were observed in the key efficacy endpoints from BL through Week 26 for pruritus (-1.05, $p=0.0017$) and sBA (-141 µmol/L, $p=0.0003$), in line with observations from the initial MARCH MRX group. Overall, there were no new safety signals identified. The most frequent TEAEs were GI-related with early onset of diarrhea (44%) in line with the mechanism of IBAT inhibition, mostly mild and transient. In the MRX-MRX sub-group, fewer patients experienced diarrhea in MARCH-ON supporting these effects are early and transient in nature.
Conclusions: Significant and sustained responses in pruritus, sBA, bilirubin as well as growth are observed with 52 weeks of MRX treatment across the broadest range of genetic PFIC types studied to date. These data suggest overall improved liver health with MRX treatment which can be maintained over time.

(No Image Selected)

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DISCLOSURE STATEMENT: Study conforms to the principles of the Declaration of Helsinki.

DISCLOSURE STATEMENT: Study conforms to the "Guiding Principles in the Care and Use of Animals" of the American Physiological Society.

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