Background

- Primary sclerosing cholangitis (PSC) is a chronic liver disease characterized by progressive cholestasis.
- Cholestasis can often lead to severe pruritus, which significantly impacts quality of life.
- Maralixibat (formerly SHP624, LUNAR) is a minimally absorbed, selective inhibitor of the apical sodium-dependent bile acid transporter (ASBT).
- Maralixibat interrupts enterohepatic circulation of bile acids.
- Maralixibat may control pruritus in patients with PSC.

Methods

- Design: CAMEO (ClinicalTrials.gov: NCT02061540) was a 14-week, single-arm, open-label, phase 2a, proof-of-concept study of maralixibat in PSC.
- A 4-week dose-escalation period (maralixibat 0.5 mg, 1 mg, 2.5 mg, 5 mg and 7.5 mg/day) was followed by an 8-week dose-maintenance period (maralixibat 10 mg/day) and a 4-week follow-up period.

Participants

- Eligible patients were adults aged 18–80 years with a diagnosis of PSC as defined: history of alkaline phosphatase (ALP) levels >1.5×ULN, biopsy obstruction and histological findings consistent with PSC (if previously biopsied).
- Patients were excluded if they had a history of premalignant or malignant gastrointestinal conditions.

Study Assessments

- Treatment-emergent adverse events (TEAEs) were assessed regularly.
- Pruritus was assessed using Adult Itch Reported Outcome (ItchRO) weekly scores and average daily scores (mean score over 7-day period).
- Other efficacy assessments included change from baseline in levels of sBA, total bilirubin, aminotransferase, alkaline phosphatase, ALT, and total cholesterol.

Additional Outcomes

- Mean autotaxin and LDL-C levels decreased from baseline overall and in participants with an ItchRO daily score ≥ 4 at baseline.
- Total cholesterol levels decreased and conjugated bilirubin levels increased significantly from baseline, changes in total bilirubin, alkaline phosphatase, creatinine, and LDL-C were not statistically significant (Table 2).

Conclusions

- In this proof-of-concept trial including 27 adults with PSC who received maralixibat for 14 weeks:
  - Statistically significant reductions from baseline in pruritus levels of ≥8 and autotaxin were observed.
  - These improvements appeared to be greater in participants with an ItchRO daily score ≥ 4 at baseline than in the overall population.
  - Changes in LDL-C and total cholesterol were consistent with ASBT inhibition.
  - TEAEs were generally mild or moderate and were mostly gastrointestinal.
  - These findings warrant further Investigation of ASBT inhibition for the treatment of adults with PSC.