Long-term Efficacy and Safety of Open-Label Seladelpar Treatment in Patients With Primary Biliary Cholangitis (PBC): Interim Results for 2 Years From the ASSURE Study

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Background
- Seladelpar is a first-in-class, potent, and selective PPARα agonist, or delpar, with anti-inflammatory and anti-pruritic activities.
- In the pivotal placebo-controlled, double-blind, Phase 3 RESPONSE (NCT04620733) study, seladelpar was safe and well-tolerated, achieving significantly greater improvements in liver biochemistry parameters and pruritus compared with placebo. The ASSURE (NCT03301506) study was a Phase 3 open-label study of the long-term safety and efficacy of seladelpar 10 mg in patients with PBC.
- Patients could enter ASSURE through 2 pathways:
  - Direct rollover from the RESPONSE study
  - Participation in a previous seladelpar PBC study ("Legacy studies")
- Interim 2-year efficacy and safety results through January 31, 2024, are reported for 337 patients enrolled in the ongoing ASSURE study.

Study Design
- The Primary Analysis Population is defined as those patients who were administered the 10 mg dose of seladelpar.

Patient Disposition
- 179 patients enrolled in the ongoing ASSURE study.
- Of these, 132 patients were from the Legacy studies.
- Legacy studies:
  - Participation in a previous seladelpar PBC study
  - Direct rollover from the RESPONSE study
- 44 patients enrolled in the ongoing ASSURE study.
- Of these, 28 patients were from the Legacy studies.
- Legacy studies:
  - Participation in a previous seladelpar PBC study
  - Direct rollover from the RESPONSE study

Demographics and Characteristics at ASSURE Baseline
- Median (range) values:
  - Age: 57.9 (18.8–82.9) years
  - BMI: 27.0 (15.1–53.3) kg/m²
  - MELD score: 10 (6–16)
  - Race or ethnicity:
    - Caucasian: 33 (24.8%)
    - Hispanic or Latino: 100 (74.4%)
    - Asian: 5 (3.7%)
  - Child-Pugh Class:
    - Class A: 47 (34.5%)
    - Class B: 52 (38.6%)
    - Class C: 38 (28.0%)
  - Liver-related comorbidities:
    - Ascites: 2 (1.5%)
    - Oesophageal varices: 2 (1.5%)
    - Ocular icterus: 2 (1.5%)
    - Peripheral edema: 2 (1.5%)
    - Variceal bleed: 1 (0.7%)
    - Hsp velocity grade ≥3: 2 (1.5%)
  - Charted laboratory values:
    - Total bilirubin: 2.9 (0.4–14.1) mg/dL
    - AST: 54 (4–330) U/L
    - ALT: 44 (6–330) U/L
    - ALP: 314.6 (117.7–123.0) U/L
    - Pruritus: NRS ≥4: 65 (48.4%)

Composite Response
- Total Bilirubin Percentage Change From Baseline
- ALP Percentage Change From Baseline
- AST Percentage Change From Baseline
- GGT Percentage Change From Baseline
- Change in Pruritus NRS

AST Percentage Change From Baseline
- In Patients With NRS 24 at Baseline
- In Patients With Elevated ALT at Baseline

ALT Normalization
- In Patients With Elevated ALT at Baseline
- Total Bilirubin Normalization
- In Patients With Elevated Bilirubin at Baseline

Safety Overview
- Clinical Outcomes
  - Total bilirubin and AST are measured in mg/dL.
  - ALT is measured in U/L.
  - ALP is measured in U/L.
  - Pruritus is measured on a NRS scale.
  - TEAEs are reported as treatment-emergent, serious, or leading to discontinuation.
  - TEAEs are categorized by MedDRA System organ class and preferred term.

CONCLUSIONS
- 2-year results from the ASSURE long-term extension study of seladelpar for the treatment of PBC demonstrated:
  - Durable effect on markers of cholestasis and liver injury was maintained for up to 2 years.
  - Sustained reduction in pruritus in patients with baseline NRS 24 was observed.
  - Safety profile appears safe and well tolerated.
  - Results are consistent with the pivotal Phase 3 RESPONSE study.

REFERENCE

DISCLOSURES
- The authors declare no conflicts of interest.

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AE, adverse event; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; BMI, body mass index; DILI, drug-induced liver injury; GGT, gamma-glutamyltransferase; M, month; MELD, Model for End-Stage Liver Disease; NRS, numerical rating scale; PPAR, peroxisome proliferator-activated receptor; SAE, serious adverse event; TEAE, treatment-emergent adverse event. 

* Early terminated. † Patients were eligible to enroll in ASSURE after completing the study, but they had to meet screening criteria and had variable time to entry. § Mean ALP values are from ASSURE entry. At RESPONSE entry, the mean (SD) for placebo patients (N=65) was 313.8 (117.7) U/L and for seladelpar patients (N=128) it was 314.6 (123.0) U/L. ¶ RESPONSE entry for patients with NRS ≥4, mean (SD) baseline NRS was 6.1 (1.4) for seladelpar patients and 6.6 (1.4) for placebo patients. mean (SD) baseline NRS  in Legacy patients with NRS ≥4 (at ASSURE baseline) was 6.4 (1.7).