Long-Term Efficacy and Safety of Open-Label Seladelpar Treatment in Patients With Primary Biliary Cholangitis: Pooled Interim Results for up to 3 Years From the ASSURE Study

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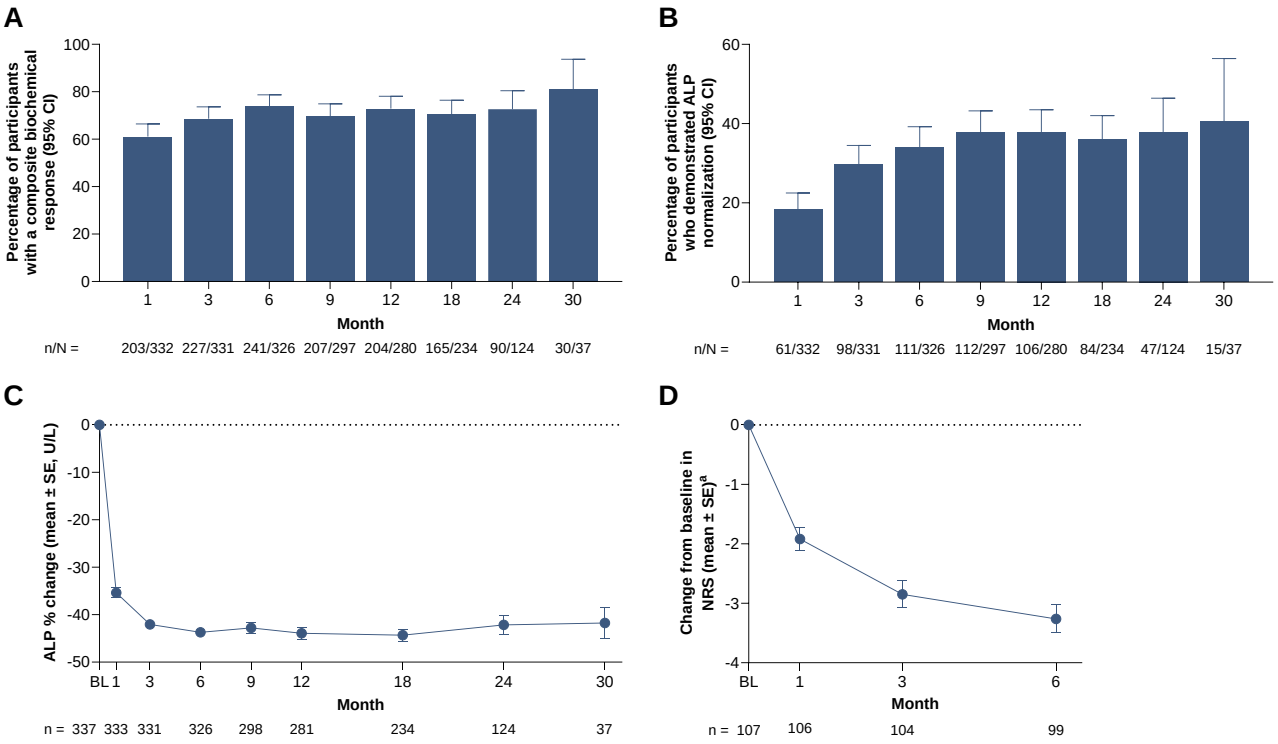
Background: ASSURE (NCT03301506) is an ongoing, open-label, long-term, Phase 3 trial of seladelpar—a novel delpar (selective PPARδ agonist)—in patients (pts) with primary biliary cholangitis rolling over from the Phase 3, placebo-controlled, registrational RESPONSE trial (NCT04620733) or with prior participation in legacy trials (Phase 3 ENHANCE [NCT03602560], CB8025-21629 [NCT02955602], CB8025-31731 [NCT03301506], CB8025-21838 [NCT04950764]). The parent studies required an inadequate response or intolerance to first-line ursodeoxycholic acid. Here, we report pooled interim efficacy and safety for all pts in ASSURE.

Material and Methods: Using a data cutoff of January 31, 2024, pt exposure to seladelpar in ASSURE (including exposure in pts who were randomized to the active treatment arm in RESPONSE) was analyzed. Key efficacy endpoints included composite biochemical response (CBR; alkaline phosphatase [ALP] <1.67× upper limit of normal [ULN], ALP decrease ≥15%, and total bilirubin [TB] ≤ULN) and ALP normalization. Pruritus was recorded using a numeric rating scale (NRS; 0–10) collected daily through month (M) 6; change from baseline (BL) was assessed through M6 in pts with moderate-to-severe pruritus (NRS ≥4) at BL. Exposure-adjusted adverse events (AEs) were calculated for each year on study as incidence per 100 pt-years. BL was based on first exposure to seladelpar in ASSURE or RESPONSE.

Results: 337 pts received 10-mg seladelpar daily. 34 pts reached 30M on study; 90 pts had ≥24M of seladelpar exposure. At BL, the mean (SD) age was 58.1 (9.7) years, 318/337 (94%) pts were female, mean (SD) ALP was 287.5 (128.4) U/L, mean (SD) TB was 0.75 (0.34) mg/dL, and 55/337 (16%) had cirrhosis. At M12, M24, and M30, 204/280 evaluable pts (73%), 90/124 (73%), and 30/37 (81%) met the CBR endpoint, respectively, and ALP normalized in 106/280 (38%), 47/124 (38%), and 15/37 (41%) pts, respectively. In the pruritus NRS, mean (SE) change from BL at 6M was –3.3 (0.24) among 99 evaluable pts. Outcomes are in **Figure 1**. Exposure-adjusted AEs were observed in 86, 70, and 63 pts per 100 pt-years at M12, M24, and M36, respectively. There were no treatment-related serious AEs.

Conclusions: By M30 of the long-term ASSURE study, seladelpar resulted in a durable and sustained biochemical response in 81% of pts, with an ALP normalization rate of 41%, and robust improvement in pruritus. Seladelpar continues to appear safe and well tolerated, with no new safety signals or change in frequency of AEs with up to 3 years of exposure.

Figure 1. (A) Composite Biochemical Response Rate Through Month 30, **(B)** ALP Normalization Through Month 30, **(C)** ALP Percentage Change From BL Through Month 30, and **(D)** Pruritus NRS Change From BL Through Month 6



Data cutoff: January 31, 2024.

ALP, alkaline phosphatase; BL, baseline; NRS, numeric rating scale.

[a]The pruritus NRS ranged from 0 (no itch) to 10 (worst itch imaginable).