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

Poster ST-13

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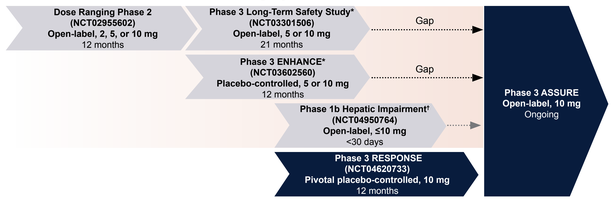
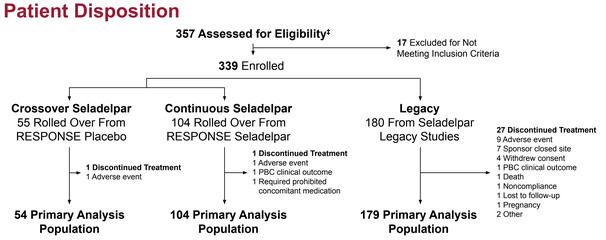
Background

- Seladelpar is a first-in-class, potent, and selective PPARδ agonist, or delpar, with anti-cholestatic, 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 is 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
  - The Primary Analysis Population is defined as those patients who were administered the 10 mg dose of seladelpar

Study Design



Patient Disposition



ONGOING STUDY

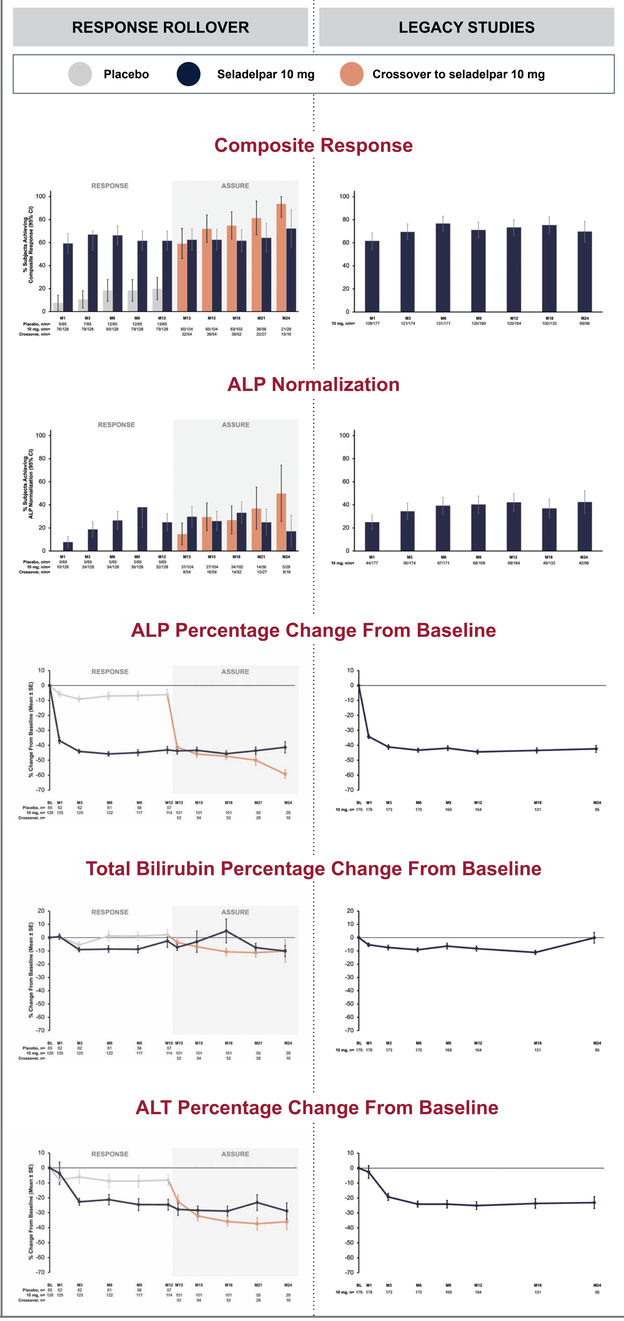
Patients as of January 31, 2024

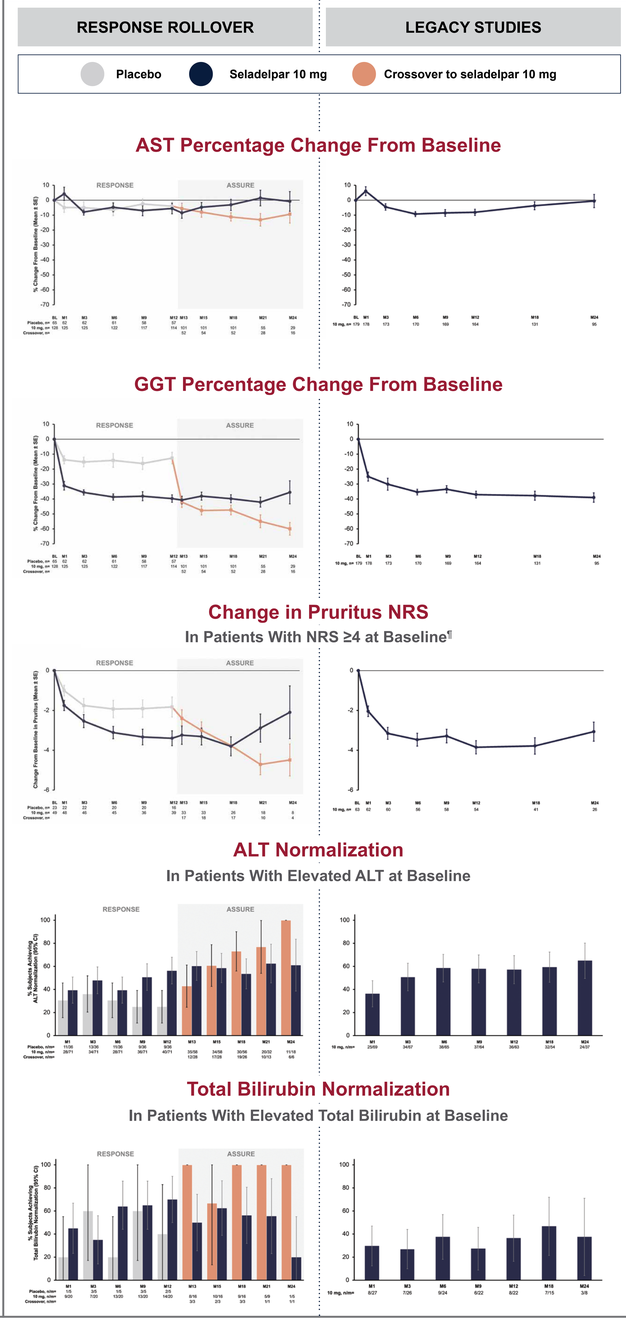
Time Point		≥26 Weeks	≥12 Months	≥18 Months	≥24 Months
Number of Patients in Each Arm	Crossover Seladelpar	52	14	2	0
	Continuous Seladelpar	123	116	103	28
	Legacy	172	165	133	97

Time points for Crossover Seladelpar and Legacy groups indicate time in ASSURE. Time points for Continuous Seladelpar indicate time in both RESPONSE and ASSURE.

Demographics and Characteristics at ASSURE Baseline

Category	RESPONSE Rollover Patients		Legacy Patients
	Crossover Seladelpar (N=54)	Continuous Seladelpar (N=104)	Seladelpar 10 mg (N=179)
Age, years, mean (SD)	57.9 (9.3)	58.0 (10.1)	58.8 (9.6)
Female sex, n (%)	50 (92.6)	99 (95.2)	169 (94.4)
Race or ethnicity, n (%)			
American Indian or Alaska Native	3 (5.6)	2 (1.9)	6 (3.4)
Asian	4 (7.4)	6 (5.8)	14 (7.8)
Black or African American	2 (3.7)	2 (1.9)	3 (1.7)
White	45 (83.3)	93 (89.4)	153 (85.5)
Hispanic or Latino	23 (42.6)	24 (23.1)	24 (13.4)
BMI, kg/m², mean (SD)	26.9 (5.1)	27.8 (6.1)	27.4 (6.0)
Patients with cirrhosis at baseline, n (%)	7 (13.0)	16 (15.4)	35 (19.6)
Child-Pugh Class A, n (%)	7 (100)	15 (93.8)	31 (88.6)
Child-Pugh Class B, n (%)	0	1 (6.3)	4 (11.4)
Patients with cirrhosis at baseline and portal hypertension, n (% of cirrhotics)	1 (14.3)	0	8 (22.9)
MELD score ≥12, n (%)	0	2 (1.9)	1 (0.6)
ALP,§ U/L, mean (SD)	288.7 (125.5)	183.1 (112.1)	274.2 (133.1)
Total bilirubin, mg/dL, mean (SD)	0.7 (0.3)	0.7 (0.5)	0.8 (0.4)





Safety Overview

TEAE Category, n (%)	RESPONSE Rollover Patients		Legacy Patients
	Crossover Seladelpar (N=54)	Continuous Seladelpar (N=104)	(N=179)
Subjects with ≥1 TEAE	42 (77.8)	73 (70.2)	149 (83.2)
Treatment-emergent SAE	7 (13.0)	6 (5.8)	24 (13.4)
Grade ≥3 TEAE	5 (9.3)	9 (8.7)	27 (15.1)
Treatment-related treatment-emergent SAE	0	0	0
TEAE with action taken as permanent withdrawal of study drug	1 (1.9)	2 (1.9)	11 (6.1)
TEAE leading to study discontinuation	1 (1.9)	1 (1.0)	7 (3.9)
TEAE with fatal outcome	0	0	1 (0.6)

- 1 fatal outcome was due to autoimmune hemolytic anemia
  - Assessed to be unrelated to seladelpar by both the investigator and the sponsor

Common AEs (≥5% of Overall Patient Population)

TEAEs by Preferred Term, n (%)	RESPONSE Rollover Patients		Legacy Patients
	Crossover Seladelpar (N=54)	Continuous Seladelpar (N=104)	(N=179)
COVID-19	5 (9.3)	5 (4.8)	38 (21.2)
Pruritus	0	10 (9.6)	24 (13.4)
Urinary tract infection	2 (3.7)	7 (6.7)	17 (9.5)
Nausea	2 (3.7)	5 (4.8)	16 (8.9)
Diarrhea	5 (9.3)	2 (1.9)	15 (8.4)
Fatigue	1 (1.9)	5 (4.8)	14 (7.8)
Nasopharyngitis	0	5 (4.8)	15 (8.4)
Abdominal pain upper	1 (1.9)	5 (4.8)	12 (6.7)
Arthralgia	4 (7.4)	3 (2.9)	11 (6.1)

Liver-Related AEs (Overall, Occurring in >1 Patient)‖

TEAEs Overall & by Preferred Term, n (%)	RESPONSE Rollover Patients		Legacy Patients
	Crossover Seladelpar (N=54) n (%)	Continuous Seladelpar (N=104) n (%)	(N=179) n (%)
Subjects with ≥1 liver-related TEAE	0	7 (6.7)	18 (10.1)
AST increased	0	0	6 (3.4)
ALT increased	0	0	5 (2.8)
Blood bilirubin increased	0	0	4 (2.2)
Hyperbilirubinemia	0	2 (1.9)	2 (1.1)
Ascites	0	1 (1.0)	2 (1.1)
Hepatic cyst	0	2 (1.9)	1 (0.6)
Portal hypertension	0	2 (1.9)	1 (0.6)
Oesophageal varices	0	1 (1.0)	2 (1.1)
Ocular icterus	0	0	2 (1.1)

- 7.4% of subjects overall had liver-related AEs by predefined search strategy
  - Most were Grade 1 or 2
  - 5 subjects had events that led to discontinuation (events of blood bilirubin increased, hepatorenal syndrome, hyperbilirubinemia, jaundice, and oesophageal varices haemorrhage)
    - 3 events (2 SAEs) were adjudicated by the CERC as PBC clinical outcomes (variceal bleed in 1 patient [186 days on study], ascites requiring treatment in 2 patients [309 and 473 days on study])
    - 3 subjects were reviewed by the CERC and none were adjudicated as positive for DILI
- All muscle-related AEs were Grade 1 or 2
  - None led to discontinuation
- There was 1 proteinuria renal event of Grade 1

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 ≥4 was observed
  - Seladelpar appears safe and well tolerated
  - Results are consistent with the pivotal Phase 3 RESPONSE study

REFERENCE

Hirschfield GM, et al. *N Engl J Med*. 2024;390(9):783-794.

DISCLOSURES

DBC, CH, SP, SZ, and CAM are employees of CymaBay Therapeutics, Inc.

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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. ‡1 patient of the total patient population (N=357) was eligible but did not receive seladelpar and thus was not formally enrolled. §Mean ALP values are from ASSURE entry. At RESPONSE entry, the mean ALP (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. ¶At 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). ‖By predefined MedDRA search strategy.