Seladelpar Leads to Long-Term Efficacy and Safety in Patients with Prior OCA and/or Fibrate Exposure

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Conclusions

- Seladelpar led to marked and sustained biochemical response with up to 4 years of treatment in ASSURE, with clinically meaningful pruritus improvement, regardless of prior obeticholic acid (OCA) and/or fibrate exposure
- Seladelpar was well tolerated in patients with and without prior OCA/fibrate use for up to 5 years of treatment

Plain Language Summary

- Some people with primary biliary cholangitis (PBC) receive fibrates or obeticholic acid (OCA) if first-choice treatment does not work for them, but OCA is no longer widely available and fibrates can have worrisome side effects
- In this study, seladelpar helped to improve disease measures of PBC similarly in people who had previously used fibrates or OCA and people who had not
- Safety results were similar between people who had previously used fibrates or OCA and those who had not, up to 5 years after starting seladelpar

References: **1.** Lindor KD, et al. *Hepatology.* 2019;69(1):394–419. **2.** Intercept. Intercept announces voluntary withdrawal of OCALIVA® for primary biliary cholangitis (PBC) from the US market; US clinical trials involving obeticholic acid placed on clinical hold. September 11, 2025. Accessed September 15, 2025. https://www.interceptpharma.com/about-us/news/?id=3148535. **3.** Ocaliva. https://www.ema.europa.eu/en/medicines/human/EPAR/ocaliva. Accessed August 4, 2026. **4.** Schattenberg JM, et al. *Aliment Pharmacol Ther.* 2026;63(9):1215–1235. **5.** Hirschfield GM, et al. *N Engl J Med.* 2024:390(9):783–794. **6.** Livdelzi. US prescribing information. Gilead Sciences, Inc.; 2026. **7.** Livdelzi. UK Summary of Product Characteristics. Gilead Sciences, Inc.; 2025. **8.** Lyvdelzi. EU Summary of Product Characteristics. Gilead Sciences, Inc.; 2026. **9.** NCT04620733. https://clinicaltrials.gov/study/NCT04620733. Accessed August 4, 2026. **10.** European Association for the Study of the Liver; American Association for the Study of Liver Diseases. *J Hepatol.* 2026;85(3):583–602. **11.** Supplement for Hirschfield GM, et al. *N Engl J Med.* 2024;390(9):783–794. **12.** NCT03301506. https://clinicaltrials.gov/study/NCT03301506. Accessed August 4, 2026. **13.** Villamil AM, et al. EASL 2025. Poster THU-274. **14.** Gordon SC, et al. *Clin Gastroenterol Hepatol.* 2026:S1542-3565(26)00039-X. **15.** Levy C, et al. *Am J Gastroenterol.* 2026;121(5):1140–1153.

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Introduction

- Primary biliary cholangitis (PBC) is a chronic, progressive, cholestatic liver disease[1]
- The approved second-line treatment obeticholic acid (OCA) was withdrawn from European and United States markets in 2024 and 2025, respectively;[2,3] fibrates are used (off-label in some geographies) with variable efficacy and safety data[4]
- Given the withdrawal of OCA and safety concerns associated with fibrates, efficacy and safety data from patients on seladelpar who were previously treated with these agents are timely and relevant to inform clinical practice
- Seladelpar is a first-in-class delpar (selective peroxisome proliferator-activated receptor delta [PPARδ] agonist) indicated for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA or as monotherapy in patients who are unable to tolerate UDCA[5–8]
- In the Phase 3, placebo-controlled RESPONSE trial (NCT04620733),[9] seladelpar significantly reduced alkaline phosphatase (ALP), a key marker of disease progression in PBC, and pruritus, a predominant PBC symptom[10,11]
- In RESPONSE and an interim analysis of the ongoing, open-label, long-term, Phase 3 ASSURE study (NCT03301506),[12] seladelpar has demonstrated consistent efficacy and safety regardless of prior OCA/fibrate use with up to 18 months of treatment[13,14]

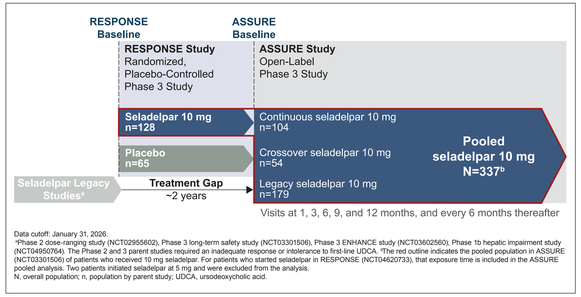
Objective

- To evaluate updated long-term efficacy and safety up to 5 years in patients with or without prior OCA/fibrate use in the ongoing ASSURE study

Methods

- Patients rolled over directly from RESPONSE or enrolled after prior participation in a legacy study and received open label seladelpar 10 mg daily in ASSURE (**Figure 1**)
  - OCA and fibrates were prohibited, and a 6-week washout was required prior to study entry
- This analysis is based on a pooled population of all patients enrolled in ASSURE where baseline was defined as the time of seladelpar initiation in RESPONSE or ASSURE. The data cutoff for this interim analysis was January 31, 2026
- Analyses were conducted in patients with a history of prior OCA and/or fibrate use versus no history of prior use
- Efficacy endpoints for this analysis included ALP normalization, composite biochemical response (ALP <1.67 × upper limit of normal [ULN], ≥15% reduction in ALP, and total bilirubin [TB] ≤ULN), and change from baseline in key cholestatic and liver injury markers through Month 48
  - Patients with prior fibrate use (with or without prior OCA use) were also summarized separately; data are presented through Month 36 due to smaller sample sizes beyond that time point in this ongoing study
- Clinically meaningful pruritus improvement (≥3-point reduction[10]) was evaluated in patients with baseline moderate to severe pruritus (numerical rating scale [NRS] score ≥4); similarly, data are presented through Month 36 due to smaller sample sizes beyond the Month 36 time point
- Safety was assessed using all available data through Month 60 in this interim analysis
- All analyses were descriptive in nature and were not powered to detect statistically significant differences

Figure 1. Study Design



Data cutoff: January 31, 2026.
[a]Phase 2 dose-ranging study (NCT02955602), Phase 3 long-term safety study (NCT03301506), Phase 3 ENHANCE study (NCT03602560), Phase 1b hepatic impairment study (NCT04950764). The Phase 2 and 3 parent studies required an inadequate response or intolerance to first-line UDCA. [b]The red outline indicates the pooled population in ASSURE (NCT03301506) of patients who received 10 mg seladelpar. For patients who started seladelpar in RESPONSE (NCT04620733), that exposure time is included in the ASSURE pooled analysis. Two patients initiated seladelpar at 5 mg and were excluded from the analysis.
N, overall population; n, population by parent study; UDCA, ursodeoxycholic acid.

Seladelpar Treatment Duration at Data Cutoff

	Year 1	Year 2	Year 3	Year 4	Year 5
Patients who completed treatment through time point, n (%)	325 (96)	298 (88)	243 (72)	116 (34)	2 (<1)

Results

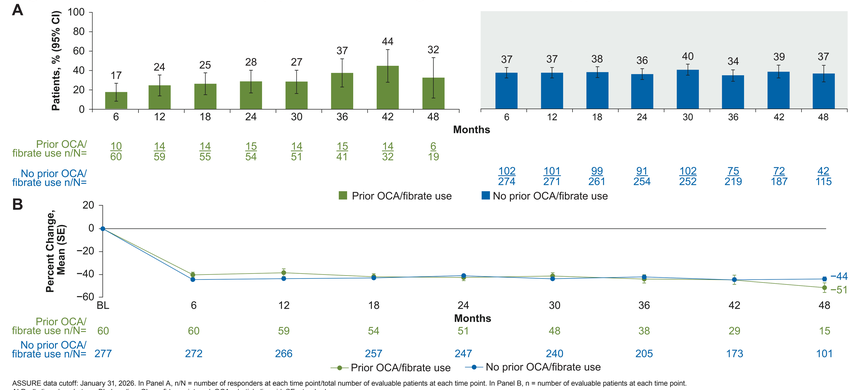
Table 1. Demographics and Baseline Characteristics

	SEL 10 mg		
	Prior OCA/Fibrate Use (N=60)	Prior Fibrate Use[a] (N=19)	No Prior OCA/Fibrate Use (N=277)
Age, years, mean (SD)	59.2 (10.2)	55.9 (10.1)	57.8 (9.6)
Sex, female, n (%)	53 (88.3)	18 (94.7)	265 (95.7)
Prior use of OCA and/or fibrates, n (%)			
Prior OCA	47 (78.3)	6 (31.6)	0
Prior fibrates[a]	19 (31.7)	19 (100.0)	0
Bezafibrate	14 (23.3)	14 (73.7)	0
Fenofibrate	5 (8.3)	5 (26.3)	0
Gap from OCA and/or fibrate use, weeks, mean (SD)	76.9 (69.3)	77.1 (65.3)	—
Cirrhosis, n (%)	6 (10.0)	1 (5.3)	46 (16.6)
Child-Pugh A, n (%)[b]	6 (100.0)	1 (100.0)	42 (91.3)
Liver stiffness, kPa, mean (SD)	9.5 (6.1)	9.4 (3.8)	10.2 (8.5)
ALP, U/L,[c] mean (SD)	331 (160.3)	368 (219.0)	278 (118.5)
ALT, U/L,[c] mean (SD)	50 (32.5)	49 (24.3)	41 (20.1)
AST, U/L,[c] mean (SD)	42 (22.7)	42 (17.5)	37 (14.4)
GGT, U/L,[c] mean (SD)	300 (300.3)	303 (322.4)	221 (184.6)
TB, mg/dL,[c] mean (SD)	0.76 (0.28)	0.80 (0.31)	0.75 (0.35)
Albumin, g/dL, mean (SD)	4.1 (0.3)	4.1 (0.2)	4.1 (0.3)
Platelet count, 10^3/µL, mean (SD)	238 (68.8)	247 (49.8)	239 (80.2)
Pruritus NRS, mean (SD)	2.9 (2.9)	3.6 (3.0)	2.7 (2.8)
Patients with moderate to severe pruritus,[d] n (%)	20 (33.3)	9 (47.4)	88 (31.8)
Pruritus NRS, mean (SD)	6.4 (1.3)	6.2 (1.5)	6.3 (1.6)

ASSURE data cutoff: January 31, 2026. [a]No patients used more than one type of fibrate. [b]Percentage out of patients with cirrhosis. [c]ALP ULN=116 U/L; ALT ULN=41 U/L; AST ULN=34 U/L; GGT ULN=52 U/L for male patients and 38 U/L for female patients; TB ULN=1.10 mg/dL.[15] [d]Defined as pruritus NRS ≥4. [e]Patients with prior fibrate use could have also had prior OCA use.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; NRS, numerical rating scale; OCA, obeticholic acid; SD, standard deviation; SEL, seladelpar; TB, total bilirubin; ULN, upper limit of normal.

- Among 337 seladelpar-treated patients, 60 had prior OCA/fibrate use and 277 had no prior use
- Baseline mean (standard deviation) ALP was numerically higher in patients with prior versus no prior use (331 [160.3] U/L and 278 [118.5] U/L, respectively; **Table 1**)
- Among patients with prior fibrate use (n=19), baseline ALP level and percentage of patients with moderate to severe pruritus were numerically higher, and the percentage of patients with cirrhosis was numerically lower, than in the prior OCA/fibrate and no prior OCA/fibrate use groups

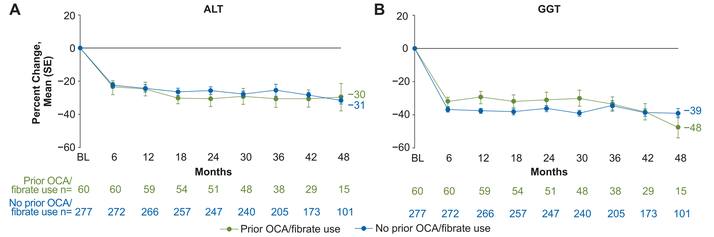
Figure 2. ALP Normalization (A) and ALP Change from Baseline (B) by Prior OCA/Fibrate Use



ASSURE data cutoff: January 31, 2026. In Panel A, n/N = number of responders at each time point/total number of evaluable patients at each time point. In Panel B, n = number of evaluable patients at each time point.
ALP, alkaline phosphatase; BL, baseline; CI, confidence interval; OCA, obeticholic acid; SE, standard error.

- At Month 48, patients with versus without prior OCA/fibrate use achieved similar rates of ALP normalization (**Figure 2A**) and had similarly rapid and sustained changes in ALP (**Figure 2B**)
- Similar proportions of patients with versus without prior OCA/fibrate use achieved sustained composite biochemical response over time; at Month 48, rates of composite biochemical response were 63.2% (12/19) versus 67.0% (77/115), respectively

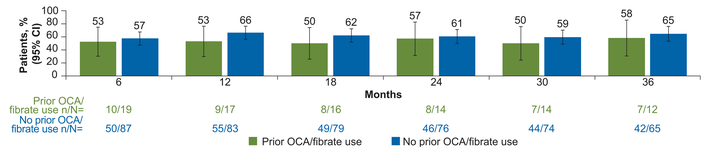
Figure 3. Change from Baseline in ALT (A) and GGT (B) by Prior OCA/Fibrate Use



ASSURE data cutoff: January 31, 2026. n = number of evaluable patients at each time point.
ALT, alanine aminotransferase; BL, baseline; GGT, gamma-glutamyl transferase; OCA, obeticholic acid; SE, standard error.

- At Month 48, patients with and without prior OCA/fibrate use demonstrated similar mean [SE] changes in alanine aminotransferase (ALT; −29.5% [8.3] and −31.0% [2.7]) and gamma-glutamyl transferase (GGT; −47.8% [6.7] and −39.3% [3.1]; **Figure 3A and 3B**)
  - Aspartate aminotransferase (AST) and TB remained stable overall in both groups
- Similar trends of rapid and sustained biochemical response were observed in patients with prior fibrate use (regardless of prior OCA use)
  - At Month 36, mean (SE) changes from baseline in ALP, ALT, and GGT for patients with prior fibrate use were −44.9% (5.3), −20.5% (12.6), and −31.2% (9.1), respectively; TB and AST remained stable and 44.4% (4/9) achieved ALP normalization

Figure 4. Clinically Meaningful Reduction in Pruritus NRS Score Among Patients with Baseline Moderate to Severe Pruritus by Prior OCA/Fibrate Use



ASSURE data cutoff: January 31, 2026. n/N = number of responders at each time point/number of evaluable patients with moderate to severe pruritus at each time point. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4. Clinically meaningful reduction in pruritus was defined as ≥3-point improvement in pruritus NRS score.[10]
CI, confidence interval; NRS, numerical rating scale; OCA, obeticholic acid.

- In patients with baseline moderate to severe pruritus, similar proportions of patients with versus without prior OCA/fibrate use experienced a clinically meaningful reduction in NRS score at Month 36 (58.3% [7/12] and 64.6% [42/65], respectively; **Figure 4**)

Table 2. Overall Safety Outcomes

n (%)	SEL 10 mg		
	Prior OCA/Fibrate Use (N=60)	Prior Fibrate Use[b] (N=19)	No Prior OCA/Fibrate Use (N=277)
Any AE	59 (98.3)	18 (94.7)	268 (96.8)
Serious AE	16 (26.7)	6 (31.6)	63 (22.7)
Treatment-related serious AE	0	0	0
AE with action taken as permanent withdrawal of study drug	8 (13.3)	3 (15.8)	32 (11.6)
AE leading to death[a]	1 (1.7)	0	2 (0.7)

ASSURE data cutoff: January 31, 2026. All AEs listed were treatment-emergent. All patients who received seladelpar 10 mg initially in ASSURE were included. [a]The three AEs leading to death included autoimmune hemolytic anemia, metastatic lung cancer, and an intracranial hemorrhage associated with a head injury. All events were assessed by the investigators as not related to seladelpar. [b]Patients with prior fibrate use could have also had prior OCA use.
AE, adverse event; OCA, obeticholic acid; SEL, seladelpar.

- No treatment-related serious adverse events were reported, and no new safety signals were observed, regardless of prior OCA/fibrate use up to Month 60 of treatment (**Table 2**); no muscle or renal safety signals were observed