Seladelpar Is Associated With Stable Renal Function Over 5 Years of Treatment: Interim Results From the ASSURE Study

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Conclusions

- In the ASSURE study, renal function remained stable with seladelpar exposure up to Month 54
- Renal-related adverse events were infrequent, and there were no events attributed to seladelpar
- These data suggest treatment with seladelpar 10 mg has a favorable renal safety profile
- Small creatinine elevations did occur in a minority of patients, though most were transient and not associated with clinical signs or symptoms, and occurred in the context of comorbidities known to affect renal function

Plain Language Summary

- Primary biliary cholangitis (PBC) is a long-term liver disease that can lead to liver scarring (cirrhosis) and liver failure
- Seladelpar is an approved drug that is used to treat people with PBC; previous studies have shown it is a safe and effective treatment for people with PBC
- In this study, we show that kidney function remained stable when seladelpar was used long-term at the approved dose, suggesting no increased risk to the kidneys or kidney-related side effects with seladelpar

Introduction

- Primary biliary cholangitis (PBC) is a chronic, autoimmune, cholestatic liver disease that disproportionately affects women and is associated with progressive liver injury and significant symptom burden[1]
- Approximately 10% of people with PBC also present with chronic kidney disease at baseline, which can increase the risk of mortality[2]
- 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[3-5]
- PPAR agonism has been associated with increases in creatinine[6,7] and other renal-related adverse events (AEs)[8,9]
- In the Phase 3 placebo-controlled RESPONSE trial (NCT04620733), mean serum creatinine values were similar overall in the seladelpar and placebo groups, and there were no renal-related AEs[10]

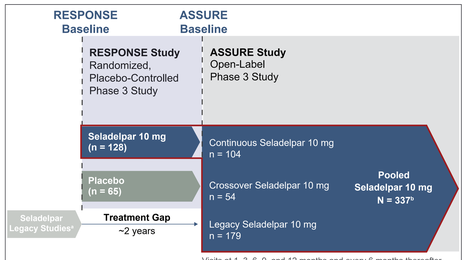
Objective

- To evaluate long-term changes in creatinine, estimated glomerular filtration rate (eGFR), and other renal safety parameters in patients treated with seladelpar for up to 54 months in the ongoing open-label Phase 3 ASSURE study (NCT03301506)

Methods

- Patients from RESPONSE and legacy seladelpar studies enrolled in ASSURE and received open-label seladelpar 10 mg once daily (**Figure 1**)
  - Patients with eGFR ≤45 mL/min/1.73 m^2 were excluded
- This analysis is based on a pooled population of all patients enrolled in ASSURE; the data cutoff for this interim analysis was January 31, 2026
- Baseline was defined as the time of seladelpar initiation in RESPONSE or ASSURE
- Mean values and percent change from baseline in creatinine and eGFR were examined up to Month 54, as were shifts in values from normal to abnormal
- Safety was assessed through renal-related AEs through a predefined search strategy using Medical Dictionary for Regulatory Activities version 28.1 and Common Terminology Criteria for Adverse Events version 5.0

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 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

- Overall, this analysis included 337 patients (**Table 1**)
- Baseline mean (SD) age was 58 (9.7) years, and most of the patients enrolled were female (318/337; 94%)

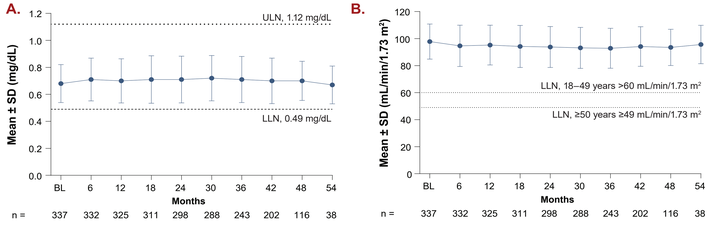
Table 1. Baseline Demographic and Clinical Characteristics

	Overall Seladelpar 10 mg (N = 337)
Age, years, mean (SD)	58 (9.7)
Female, n (%)	318 (94)
Patients with cirrhosis at baseline, n (%)	52 (15)
Child-Pugh class A, n (% of patients with cirrhosis)	48 (92)
Patients with hypertension at baseline, n (%)	99 (29)
ALP, U/L, mean (SD)	287 (128.2)
Total bilirubin, mg/dL, mean (SD)	0.75 (0.339)
Creatinine, mg/dL, mean (SD)	0.68 (0.141)
> ULN, n (%)	1 (0.3)
eGFR, mL/min/1.73 m^2, mean (SD)	97.8 (12.97)
<45 mL/min/1.73 m^2, n (%)	0
45 to <60 mL/min/1.73 m^2, n (%)	2 (0.6)
60 to <90 mL/min/1.73 m^2, n (%)	87 (26)
≥90 mL/min/1.73 m^2, n (%)	248 (74)

Data cutoff: January 31, 2026.
ALP, alkaline phosphatase; eGFR, estimated glomerular filtration rate; ULN, upper limit of normal.

- At seladelpar initiation, mean creatinine and mean eGFR values were normal (**Table 1**) and remained normal through Month 54 (**Figure 2**)

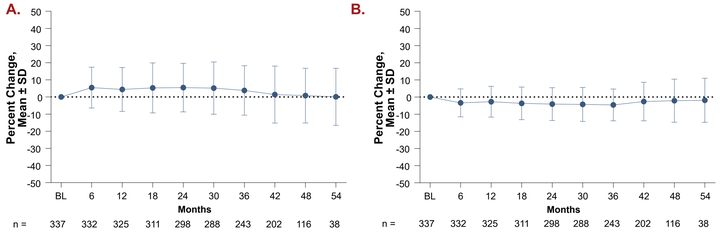
Figure 2. Mean (A) Creatinine Levels and (B) eGFR Values Over Time With Seladelpar in Patients With PBC in the ASSURE Study



Data cutoff: January 31, 2026.
BL, baseline; eGFR, estimated glomerular filtration rate; LLN, lower limit of normal; PBC, primary biliary cholangitis; ULN, upper limit of normal.

- Mean (SD) percent changes from baseline through Month 54 for creatinine and eGFR were 0.1% (16.69) and −1.9% (12.87; **Figure 3**)

Figure 3. Mean (A) Creatinine and (B) eGFR Percent Changes From Baseline Through Month 54



Data cutoff: January 31, 2026.
BL, baseline; eGFR, estimated glomerular filtration rate.

- Through Month 54, 17/337 (5%) patients experienced a shift in creatinine level from normal to elevated (**Table 2**)
  - These shifts all remained less than 2.0 × the upper limit of normal, were generally transient and short-lived, and most frequently occurred in patients with underlying comorbidities, most commonly hypertension
- Of these 17 patients, 13/17 (76%) experienced resolution of the creatinine elevation while on continued seladelpar treatment
  - In 4/17 (24%) patients with a shift to elevated creatinine, the laboratory change persisted, or the status was unknown as of the data cutoff

Table 2. Case Details of Patients With a Shift From Normal to Elevated Creatinine Values

	Time Point of Elevation	Baseline Creatinine (mg/dL)	Creatinine at Time of Elevation (mg/dL)	Resolved While on Treatment?	Time Point of Resolution	Clinical Details
Patient 1	Month 1	1.08	1.33	Yes	Month 9	Baseline creatinine was just below ULN. HTN treated with bisoprolol and perindopril; type 2 DM treated with semaglutide, insulin, and dulaglutide; MASLD; CKD Grade 3A; AV block; incomplete RBBB. Elevation followed gastroenteritis with resulting hypotension.
Patient 2	Month 13	0.81	1.20	Yes	Month 15	Past medical history of obesity and HTN treated with nebivolol and losartan.
Patient 3	Month 42	0.80	1.53	Yes	Month 48	HTN treated with lisinopril. Elevation occurred the day after a root canal.
Patient 4	Month 9	0.83	1.18	Yes	Month 15	HTN treated with carvedilol; recurrent UTI.
Patient 5	Month 6	0.85	1.14	Yes	Month 9	HTN treated with losartan and amlodipine.
Patient 6	Month 18	0.81	1.21	Yes	Month 24	HTN treated with metoprolol, amlodipine, hydrochlorothiazide, and olmesartan. Elevation occurred shortly after post-ERCP pancreatitis.
Patient 7	Month 3	0.91	1.22	Yes	Month 6	HTN treated with nifedipine.
Patient 8	Month 18	0.85	1.14	Yes	Month 24	Type 1 DM; HTN treated with carvedilol, losartan, and isosorbide mononitrate; history of myocardial infarction.
Patient 9	Month 12	0.92	1.16	Yes	Month 18	HTN treated with amlodipine, hydralazine, and metoprolol; type 2 DM; coronary artery disease with stent; lupus.
Patient 10	Month 12	0.79	1.22	Yes	Month 24	HTN treated with furosemide, lisinopril, metoprolol, and spironolactone; coronary artery disease; myocardial infarction; gout treated with allopurinol. Elevation occurred at the time of an AE of worsening HTN.
Patient 11	Month 3	0.83	1.24	Yes	Month 3	HTN treated with metoprolol and amlodipine; type 2 DM.
Patient 12	Month 3	0.97	1.23	Yes	Month 6	HTN treated with ramipril.
Patient 13	Month 12	0.99	1.25	Yes	Month 13	HTN treated with metoprolol; type 2 DM.
Patient 14	Month 18	0.79	1.79	No	Not resolved	HTN treated with ramipril, doxazosin, hydralazine, and lercandipine. An AE of renal artery stenosis preceded the elevation and led to withdrawal of the study drug.
Patient 15	Month 9	0.89	1.30	No	Unknown[a]	Past medical history of Sjögren's; transient creatinine increase occurred in the setting of an AE of lymphoma, which led to treatment discontinuation.
Patient 16	Month 48	0.90	1.16	No	Unknown[a]	Resolution unknown (AE occurred immediately before the data cutoff). Past medical history of obesity; elevation did not occur in the setting of any AEs.
Patient 17	Month 24	0.84	1.16	No	Not resolved	Past medical history of scleroderma. No clear event preceded the creatinine increase.

Data cutoff: January 31, 2026. Only first events of creatinine elevations were described. Visits occurred every 3 months for the first year and every 6 months after that; therefore, a resolution at 6 months after an elevation often reflects the time point of the next visit, as special safety monitoring was not required for these creatinine elevations.
[a]No further data was available after the initial elevation.
AE, adverse event; AV, atrioventricular; CKD, chronic kidney disease; DM, diabetes mellitus; ERCP, endoscopic retrograde cholangiopancreatography; HTN, hypertension; MASLD, metabolic dysfunction-associated steatotic liver disease; RBBB, right bundle branch block; ULN, upper limit of normal; UTI, urinary tract infection.

- AEs were reported in 323/337 (96%) patients receiving seladelpar (**Table 3**)
- Renal-related AEs were infrequent and occurred in 2 patients (1%) cumulatively through Month 54
  - One patient experienced an event of acute kidney injury secondary to a urinary tract infection and sepsis, which resolved but led to treatment discontinuation
  - The other patient experienced a creatinine increase and proteinuria, which resolved, and the patient remained on seladelpar treatment
  - Both events were assessed by the investigators as unrelated to seladelpar

Table 3. Overall Safety

Patient Incidence, n (%)	Overall Seladelpar 10 mg (N = 337)
Any AE	323 (96)
Grade ≥3 AEs (per CTCAE)	82 (24)
SAEs	77 (23)
Treatment-related SAEs	0
AEs leading to treatment discontinuation	40 (12)
AEs leading to death	3 (1)[a]
Renal-related AEs[b]	2 (1)

Data cutoff: January 31, 2026. All AEs listed were treatment emergent unless otherwise stated.
[a]The 3 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]AEs were coded according to MedDRA version 27.1; renal-related AEs were determined based on predefined search strategy. The renal artery stenosis case from Patient 14 in Table 2 is not included in the renal-related AEs, as this is categorized under vascular disorders per MedDRA version 27.1.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious AE.

Limitations

- This study was an interim analysis of an ongoing study with no control group
- This study is currently ongoing, so the number of evaluable patients at later time points is limited

References: 1. European Association for the Study of the Liver. *J Hepatol*. 2017;67(1):145-72. 2. Sousa JM, et al. *J Gastrointestin Liver Dis*. Accepted manuscript 2026. doi: 10.15403/jgld-5526. 3. Livdelzi. US prescribing information. Gilead Sciences, Inc.; 2024. 4. Livdelzi. UK summary of product characteristics. Gilead Sciences, Inc.; 2024. 5. Livdelzi. EMA prescribing information. Gilead Sciences, Inc.; 2025. 6. Antara (fenofibrate). US prescribing information. Lupin Pharma; 2012. 7. Corpechot C, et al. *N Engl J Med*. 2018;378(23):2171-81. 8. Kowdley KV, et al. *N Engl J Med*. 2024;390(9):795-805. 9. IQIRVO (elafibranor). US prescribing information. Ipsen Biopharmaceuticals, Inc.; 2024. 10. Hirschfield GM, et al. *N Engl J Med*. 2024;390(9):793-94.

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