Change in Pruritus in Patients With Primary Biliary Cholangitis and Moderate to Severe Pruritus: A Pooled Analysis From the RESPONSE and ENHANCE Studies

THU-294

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Conclusions

- Consistent with previous studies, this pooled analysis demonstrated that seladelpar treatment for up to 6 months reduced pruritus to a greater extent vs placebo in patients with primary biliary cholangitis (PBC) who had moderate to severe pruritus at baseline
  - Separation from placebo was evident at month 1 of treatment and was sustained through month 6 across 3 different measures of pruritus
  - Improvements in sleep disturbance were seen in patients receiving seladelpar through month 6 when compared with patients receiving placebo
- Safety and tolerability were similar between the seladelpar and placebo groups among patients with moderate to severe pruritus at baseline

Plain Language Summary

- Primary biliary cholangitis (PBC) is a chronic liver disease that gets worse over time and often causes itching, which can lessen the quality of life in patients with PBC
- Seladelpar is a medication used to treat patients with PBC and has been shown to improve itching
- In this analysis, the results from 2 studies were combined to further test whether seladelpar can improve itching for patients with PBC
- The results showed that seladelpar reduced itch intensity in patients who had moderate to severe itching before starting treatment
- Seladelpar was well tolerated in these patients

References: **1.** European Association for the Study of the Liver. *J Hepatol*. 2017;67:145-72 **2.** Bowlus C, et al. *J Hepatol*. 2022;77(2):353-64. **3.** Carey E, et al. *Lancet*. 2015;385(10003):1565-75. **4.** Livdelzi. US prescribing information. Gilead Sciences, Inc.; 2024. **5.** Livdelzi. UK Summary of Product Characteristics. Gilead Sciences, Inc.; 2024. **6.** Seladelpar Gilead. EMA prescribing information. Gilead Sciences, Inc.; 2025. **7.** Hirschfield G, et al. *N Engl J Med*. 2024;390(9):783-94. **8.** Hirschfield G, et al. *Hepatol*. 2023;78(2):397-415. **9.** von Maltzahn R, et al. *J Patient Rep Outcomes*. 2024;8(1):60. **10** Jacoby A, et al. *Gut*. 2005;54(11):1622-9. **11.** Mayo M, et al. *Dig Dis Sci*. 2023;68(3):995-1005. **12.** Eilman S, et al. *Br J Dermatol*. 2010;162(3):587-93.

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Disclosures: Conflict of interest disclosures may be viewed using the QR code at the top right.

Introduction

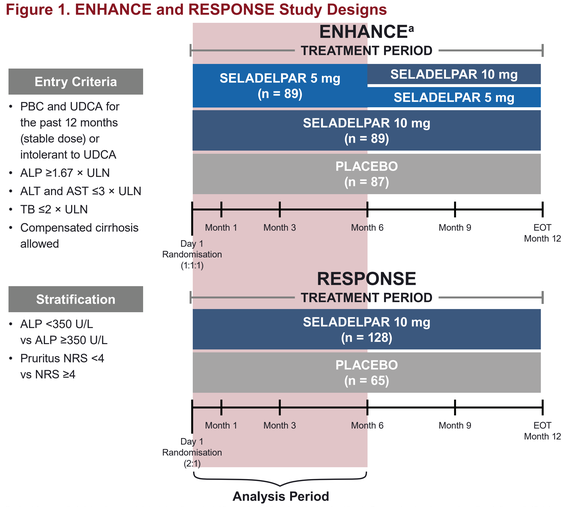
- PBC is a chronic, progressive, autoimmune, cholestatic liver disease[1]
- Pruritus may occur in up to 70% of patients with PBC during the course of disease and can greatly reduce quality of life[2,3]
- Seladelpar is a first-in-class delpar (selective peroxisome proliferator–activated receptor delta [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 a monotherapy in patients unable to tolerate UDCA[4-6]
- In two Phase 3, placebo-controlled trials—ENHANCE (NCT03602560) and RESPONSE (NCT04620733)—seladelpar significantly reduced pruritus among patients who had moderate to severe pruritus at baseline, defined as numerical rating scale (NRS) score ≥4[7,8]

Objective

- To explore pruritus outcomes from a pooled dataset of patients with PBC and NRS ≥4 at baseline in ENHANCE and RESPONSE

Methods

Figure 1. ENHANCE and RESPONSE Study Designs



Pruritus data were collected via e-diary on a daily basis from the run-in visit through the first 6 months of treatment and then for 7 consecutive days during each month up to the month 12 visit.
Study drug administered orally once daily as an add-on to UDCA or as monotherapy in patients intolerant to UDCA.
[a]Primary endpoint was amended to be month 3 before unblinding due to early termination.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EOT, end of treatment; NRS, numerical rating scale; PBC, primary biliary cholangitis; TB, total bilirubin; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

- In ENHANCE and RESPONSE, patients with PBC who had an inadequate response or intolerance to UDCA were randomised to receive seladelpar or placebo for 12 months (**Figure 1**)
  - In both studies, the change in pruritus NRS from baseline up to month 6 of treatment in patients with moderate to severe pruritus at baseline was a prespecified key secondary endpoint
  - ENHANCE was terminated early with key endpoints amended to month 3 prior to unblinding because of unexpected histological findings in a concurrent phase 2 study of seladelpar in patients with nonalcoholic steatohepatitis, which were deemed unrelated to seladelpar by an independent committee of pathologists and hepatologists[8]
- In this pooled analysis, change in NRS scores, change in PBC-40 itch domain scores, and change in 5-D itch scale scores up to month 6 were assessed in patients with moderate to severe pruritus at baseline (defined by an NRS score ≥4)
  - Data through month 6 were assessed due to only a few ENHANCE patients reaching time points beyond month 6
- Scores on the pruritus NRS ranged from 0 to 10, with higher scores indicating worse itch[9]
- Scores on the PBC-40 itch domain ranged from 0 to 15, with higher scores indicating poorer quality of life[10, 11]
- Scoring on the 5-D itch scale included 5 domains: duration, degree, direction, distribution, and disability; these domains were added to obtain the total score[12]
- Sleep disturbance data were based on the sleep disturbance questions within the itch domain of the PBC-40 and the 5-D itch disability domain

Results

- A total of 126 patients with moderate to severe pruritus at baseline (NRS ≥4) were pooled from the ENHANCE and RESPONSE studies, representing 50 patients who were randomised to placebo (ENHANCE: 27; RESPONSE: 23) and 76 who were randomised to seladelpar 10 mg (ENHANCE: 27; RESPONSE: 49); baseline characteristics are shown in **Table 1**

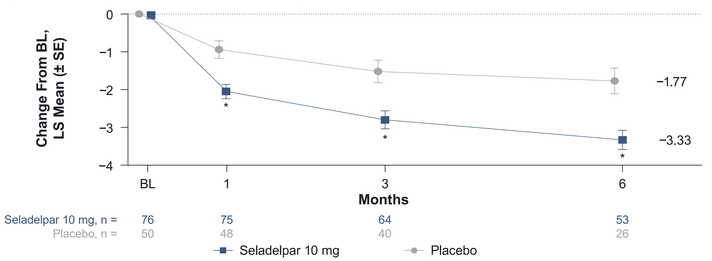
Table 1. Baseline Demographics and Clinical Characteristics

	Seladelpar 10 mg (n = 76)	Placebo (n = 50)
Age, years, mean (SD)	53.4 (10.6)	53.8 (9.5)
Female, n (%)	73 (96)	48 (96)
Age at PBC diagnosis, years, mean (SD)	47.3 (10.5)	46.7 (9.7)
On UDCA, yes, n (%)	69 (91)	48 (96)
History of fatigue, yes, n (%)	44 (58)	33 (66)
Antipruritic use[a], yes, n (%)	19 (25)	12 (24)
NRS, mean (SD)	6.2 (1.4)	6.3 (1.4)
NRS ≥7, n (%)	25 (33)	18 (36)
PBC-40 itch domain, mean (SD)	8.8 (2.8)	9.3 (2.9)
5-D itch total score, mean (SD)	16.1 (3.5)	15.9 (3.6)

[a]Antipruritic medications at baseline were determined via a search engine including colestyramine, rifampicin, naltrexone, naloxone, nalmefene, sertraline, gabapentin, nalfurafine, colesevelam, colestipol, sertraline hydrochloride, naltrexone hydrochloride, and naloxone hydrochloride.
NRS, numerical rating scale; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid.

- NRS, PBC-40 itch domain, and 5-D itch scale scores were similar between the seladelpar and placebo groups at baseline

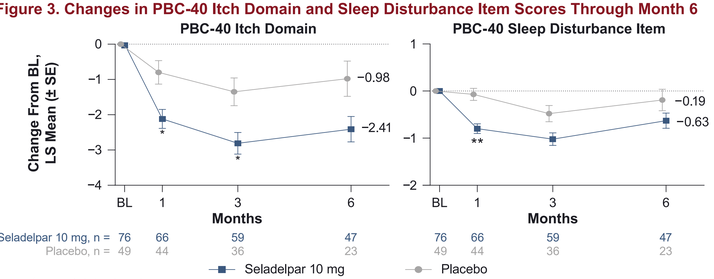
Figure 2. Changes in Pruritus NRS Through Month 6



n = number of evaluable patients at each time point.
Pruritus NRS scores range from 0 to 10, with higher scores indicating worse itch.
*P <.01 vs placebo.
BL, baseline; LS, least-squares; NRS, numerical rating scale.

- At months 1, 3, and 6, there were greater decreases in pruritus NRS among the seladelpar 10 mg group compared with the placebo group (**Figure 2**)
- At month 6, a mean decrease of −3.33 was seen in the seladelpar 10 mg group compared with −1.77 in the placebo group (*P* = .0004)

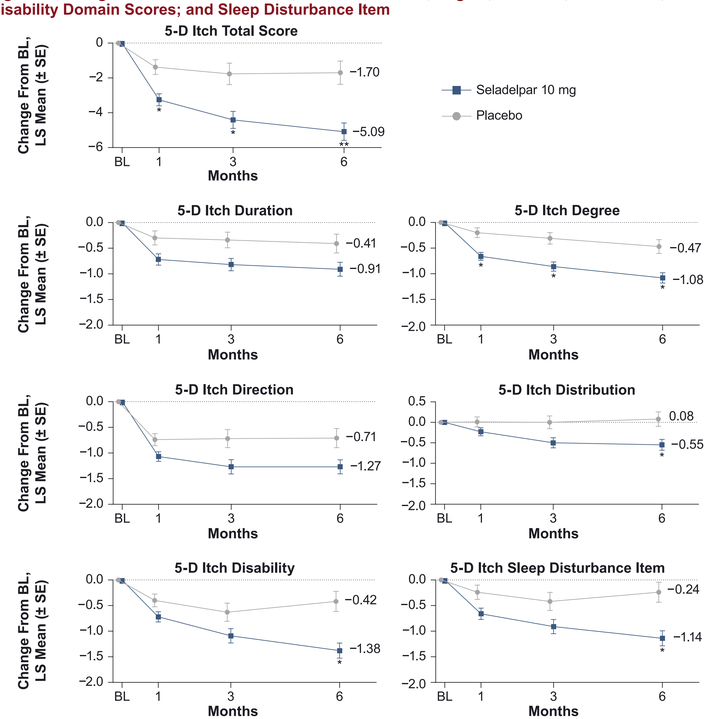
Figure 3. Changes in PBC-40 Itch Domain and Sleep Disturbance Item Scores Through Month 6



n = number of evaluable patients at each time point.
PBC-40 itch domain scores range from 0 to 15, with higher scores indicating poorer quality of life. In the PBC-40 itch domain, sleep is a single item that grades how often itching disturbs sleep on a scale from 0 to 5, with higher scores indicating greater sleep disturbance.
*P <.01 vs placebo. **P < 0001 vs placebo.
BL, baseline; LS, least-squares.

- At months 1, 3, and 6, patients who received seladelpar experienced greater improvements in PBC-40 itch domain and sleep disturbance item scores compared with those who received placebo (**Figure 3**)
- At month 6, mean change from baseline in PBC-40 itch domain and sleep disturbance item scores for seladelpar 10 mg vs placebo were:
  - PBC-40 itch domain scores: −2.41 vs −0.98, *P* = .023
  - PBC-40 sleep disturbance item scores: −0.63 vs −0.19, *P* = .114
- At months 1, 3, and 6, patients who received seladelpar experienced greater improvements in the 5-D itch scale total and domain scores as early as month 1 that were sustained through month 6 (**Figure 4**)
- At month 6, mean change from baseline 5-D itch scale scores for seladelpar 10 mg vs placebo were:
  - 5-D itch total scores: −5.09 vs −1.70, *P* <.0001
  - 5-D sleep disturbance item scores: −1.14 vs −0.24, *P* = .0004

Figure 4. Changes in 5-D Itch Total Score; 5-D Itch Duration, Degree, Direction, Distribution, and Disability Domain Scores; and Sleep Disturbance Item



n = number of evaluable patients at each time point.
Each of the 5-D itch scale domains are scored from 1 to 5, and the total score ranges from 5 to 25, with higher scores indicating increased itch severity.
In the 5-D itch scale, sleep is scored 1 to 5, where 1 indicates sleep is not affected and 5 indicates delays in falling asleep and frequent awakenings from sleep.
*P <.01 vs placebo. **P < 0001 vs placebo.
BL, baseline; LS, least-squares.

Table 2. Safety Overview

Patient Incidence n, (%)	Seladelpar 10 mg (n = 76)	Placebo (n = 50)
Any AE	57 (75)	40 (80)
Grade ≥3 AEs (per CTCAE)	6 (8)	6 (12)
SAEs[a]	4 (5)	2 (4)
AEs leading to treatment discontinuation	3 (4)	3 (6)
AEs leading to death	0	0
Pruritus AEs[b]	6 (8)	7 (14)

All AEs were treatment emergent and occurred through month 6 unless otherwise stated.
[a]All SAEs were not treatment related.
[b]Pruritus AEs were identified by a predefined search strategy of preferred terms containing "prur"; seladelpar: pruritus (5), vulvovaginal pruritus (1); placebo: pruritus (7).
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; SAE, serious adverse event.

- Overall, safety and tolerability among patients with moderate to severe pruritus at baseline were similar between the seladelpar and placebo groups (**Table 2**)