Reduction in Itch-Associated Disability and Pruritus Distribution in Patients With Primary Biliary Cholangitis Treated With Seladelpar in the RESPONSE Trial

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Conclusions

- In the Phase 3, placebo-controlled RESPONSE trial, seladelpar improved itch vs placebo per the 5-D Itch scale in patients with primary biliary cholangitis (PBC) and moderate to severe pruritus (numeric rating scale [NRS] score of ≥4) at baseline and in the overall population (regardless of baseline NRS score)
- These new data add additional patient-relevant findings to previously published data that seladelpar improves pruritus and sleep as assessed by the 5-D Itch scale
- Following seladelpar treatment, reductions in patients' itch-related disabilities (eg, leisure/social, housework/errands, and work/school) were seen in both populations
- In both populations, distribution of itch was reduced through 12 months following seladelpar treatment
- Patients treated with seladelpar spent fewer hours per day itching compared with placebo, which was an effect observed in both populations
- These data suggest that seladelpar as a second-line therapy may fulfill an unmet need in PBC given the high prevalence and impact of pruritus on activities of daily living

Plain Language Summary

- Primary biliary cholangitis (PBC) is a long-term liver disease that gets worse over time
- Most people with PBC experience itching at some point in their lives, which can impact daily life
- Seladelpar is a drug used to treat people with PBC and is known to reduce itching
- This study looked further into the impact of seladelpar on different aspects of itching in people with PBC
- The study showed that seladelpar helped to:
  - Improve how often itching stopped people from doing things with friends, family, or neighbors; at home or while running errands; or at work or school
  - Reduce the number of body parts that felt itchy
  - Reduce the amount of time people spent itching

References: **1.** European Association for the Study of the Liver. *J Hepatol*. 2017;67(1):145-72. **2.** Onofrio FQ, et al. *Hepatol Gastroenterol*. 2019;15(3):145-54. **3.** Trivella J, et al. *Hepatol Commun*. 2023;7(6):e0179. **4.** Mayo MJ, et al. *Dig Dis Sci*. 2023;68(3):995-1005. **5.** Dull MM, et al. *Clin Liver Dis*. 2022;26(4):727-45. **6.** Livdelzi. US prescribing information. Gilead Sciences, Inc.; 2024. **7.** Livdelzi. UK summary of product characteristics. Gilead Sciences, Inc.; 2024. **8.** Livdelzi. EMA prescribing information. Gilead Sciences, Inc.; 2025. **9.** Hirschfield GM, et al. *N Engl J Med*. 2024;390(9):783-94. **10.** Elman S, et al. *Br J Dermatol*. 2010;162(3):587-93. **11.** Kremer AE, et al. *Liver Int*. 2022;42(1):112-23.

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

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]
- Pruritus is a common symptom of PBC, affecting up to 80% of patients[2,3]
- PBC-associated pruritus may cause substantial disability, including disruptions in sleep and impacts on everyday life[4]
- Pruritus can affect any body part of a patient with PBC but is often reported on the head, lower legs, back, palms, and soles[4,5]
- 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[6-8]
- In the Phase 3 RESPONSE trial (NCT04620733), seladelpar significantly decreased pruritus in patients with PBC with moderate to severe pruritus (numeric rating scale [NRS] score of ≥4) at baseline vs placebo[9]
  - A greater reduction in itch and an improvement in sleep were also observed with seladelpar vs placebo as measured by the 5-D Itch and PBC-40 scales in RESPONSE[9]

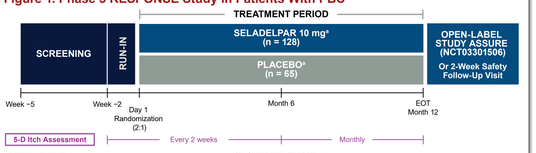
Objective

- The 5-D Itch scale has multiple domains, and for this analysis, data on the disability, distribution, and duration domains were examined closely because they provide a different patient perspective that is not captured with other instruments included in the trial that assessed pruritus
- Here, we further evaluated domains and specific items not previously published, including components of the disability domain (leisure/social, housework/errands, and work/school), distribution, and duration of itch from the 5-D Itch scale in the RESPONSE study

Methods

- In the RESPONSE study, patients with PBC who had an inadequate response or intolerance to UDCA were randomized 2:1 to receive daily oral seladelpar 10 mg or placebo for 12 months (**Figure 1**)
  - Key entry criteria: Alkaline phosphatase ≥1.67 × the upper limit of normal (ULN), alanine aminotransferase and aspartate aminotransferase ≤3 × ULN, and total bilirubin ≤2 × ULN

Figure 1. Phase 3 RESPONSE Study in Patients With PBC



Primary Endpoint:
Composite response at month 12
(ALP <1.67 × ULN, ≥15% decrease in ALP, total bilirubin ≤ULN)

Key Secondary Endpoint:
- ALP normalization at month 12[c]
- Change from baseline in pruritus NRS at 6 months in patients with baseline NRS ≥4[c]

RESPONSE study: NCT04620733. Seladelpar was administered orally once daily.
[a]Study drug given as an add-on to UDCA in patients on UDCA for at least 12 months, or as monotherapy in patients intolerant to UDCA. [b]ALP normalization was defined as ALP ≤1 × ULN. [c]Pruritus NRS data collected via e-diary on a daily basis from the run-in visit through the first 6 months of treatment, then monthly for 7 consecutive days each month until EOT.
ALP, alkaline phosphatase; EOT, end of treatment; NRS, numeric rating scale; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

- **Table 1** explains what the 5-D Itch questionnaire covers and how it is scored for analysis
  - Within the 5-D Itch disability domain, trends in the leisure/social, housework/errands, and work/school items were assessed in patients with moderate to severe pruritus (NRS ≥4) at baseline and in the overall population (regardless of baseline NRS score)
  - Changes in the 5-D Itch distribution domain across different body regions and the 5-D Itch duration domain were also analyzed in patients with NRS ≥4 at baseline and in the overall population

Table 1. 5-D Itch Scale Overview[10,11]

5-D Itch Domain	Description[a]	Answer Choices[b]
Duration	Hours per day	<6; 6–12; 12–18; 18–23; all day
Degree	Severity	Not present; Mild; Moderate; Severe; Unbearable
Direction	Improvement or worsening	Completely resolved; Much better but still present; Little bit better but still present; Unchanged; Getting worse
Disability	4 items addressing impact of itch on: (1) sleep[c] (2) leisure/social (3) housework/errands (4) work/school	Sleep • Never affects sleep • Occasionally delays falling asleep • Frequently delays falling asleep • Delays falling asleep and occasionally wakes me up at night • Delays falling asleep and frequently wakes me up at night Leisure/social; housework/errands, work/school • Never affects this activity • Rarely affects this activity • Occasionally affects this activity • Frequently affects this activity • Always affects this activity
Distribution[d]	16 potential affected body regions (abdomen, back, buttocks, chest, contact with clothing, face, forearms, groin, head/scalp, lower legs, palms, soles, thighs, tops of feet/toes, tops of hands/fingers, upper arms)	Absent or present

Shading indicates data shown on the present poster.
[a]The recall period is over the past 2 weeks for all domains. [b]Answers correspond to a score of 1 to 5, with higher scores indicating greater impairment. [c]The 5-D Itch disability domain sleep item data have been previously published; itch-related sleep disturbance improved with seladelpar.[11] [d]For the distribution domain, the score equals the total number of affected body parts sorted into 5 bins: 1 = sum of 0–2 body parts, 2 = sum of 3–5, 3 = sum of 6–10, 4 = sum of 11–13, 5 = sum of 14–16.

Results

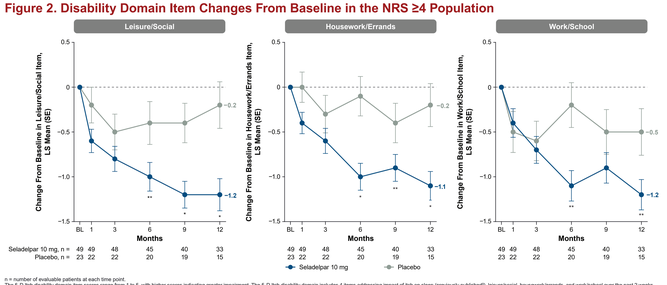
Table 2. Demographics and Baseline Clinical Characteristics of the NRS ≥4 and Overall Populations in the RESPONSE Trial

	NRS ≥4 Population		Overall Population	
	Seladelpar 10 mg (n = 49)	Placebo (n = 23)	Seladelpar 10 mg (n = 128)	Placebo (n = 65)
Age, years, mean (SD)	53 (10.7)	55 (10.3)	57 (10.0)	57 (9.2)
Female, n (%)	48 (98)	22 (96)	123 (96)	60 (92)
NRS score, mean (SD)[a]	6.1 (1.4)	6.6 (1.4)	3.0 (2.8)	3.0 (3.0)
Any pruritus medication at baseline, n (%)[b]	11 (22)	5 (22)	18 (14)	11 (17)
5-D Itch disability domain score, mean (SD)[c]	3.5 (1.1)	3.5 (0.8)	2.3 (1.4)	2.2 (1.2)
Leisure/social item	3 (1.2)	3 (1.0)	2 (1.3)	2 (1.2)
Housework/errands item	3 (1.1)	3 (1.0)	2 (1.2)	2 (1.1)
Work/school item	2 (1.3)	2 (1.4)	1 (1.2)	1 (1.2)
5-D Itch distribution domain score, mean (SD)[c,d]	3.1 (1.2)	3.1 (1.1)	2.2 (1.3)	2.1 (1.2)
5-D Itch duration domain score, mean (SD)[c]	2.4 (1.4)	2.4 (1.4)	1.6 (1.1)	1.6 (1.1)

[a]Patients rate their worst itch in the past 24 hours on a scale of 0 (no itch) to 10 (worst itch imaginable). [b]Pruritus medications included cholestyramine, colestipol, rifampicin, gabapentin, and sertraline. [c]The 5-D Itch disability, distribution, and duration domains are scored on a scale of 1 to 5, with higher scores indicating greater impairment. [d]The 5-D Itch distribution domain items assess whether patients are experiencing itch (absent or present) at various body regions; the score equals the total number of affected body parts sorted into 5 bins: 1 = sum of 0–2 body parts, 2 = sum of 3–5, 3 = sum of 6–10, 4 = sum of 11–13, 5 = sum of 14–16.
NRS, numeric rating scale.

- Of the 193 patients in RESPONSE, 128 received seladelpar and 65 received placebo
  - A total of 49 patients (38%) receiving seladelpar and 23 patients (35%) receiving placebo had NRS ≥4 at baseline
- Scores for individual questions within the 5-D Itch disability and distribution domains were similar between seladelpar and placebo groups in both the NRS ≥4 and overall populations at baseline (**Table 2**)
- Patients in the NRS ≥4 population had higher scores across domains than patients in the overall population

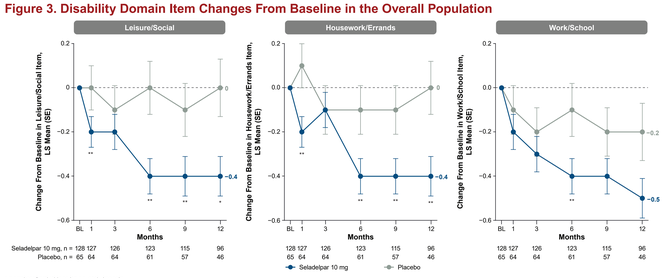
Figure 2. Disability Domain Item Changes From Baseline in the NRS ≥4 Population



n = number of evaluable patients at each time point.
The 5-D Itch disability domain item scores range from 1 to 5, with higher scores indicating greater impairment. The 5-D Itch disability domain includes 4 items addressing impact of itch on sleep (previously published[9]), leisure/social, housework/errands, and work/school over the past 2 weeks.
*P <.005. **P <.05.
BL, baseline; LS, least-squares; NRS, numeric rating scale.

- At 12 months, patients with NRS ≥4 at baseline receiving seladelpar had greater reductions vs those receiving placebo in the leisure/social item (mean change from baseline, −1.2 vs −0.2, *P* <.005), housework/errands item (−1.1 vs −0.2, *P* <.005), and work/school item (−1.2 vs −0.5, *P* <.05), suggesting improvement in the impact of itch on daily activities (**Figure 2**)

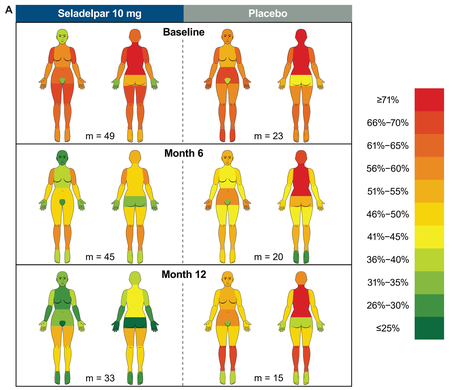
Figure 3. Disability Domain Item Changes From Baseline in the Overall Population



n = number of evaluable patients at each time point.
The 5-D Itch disability domain item scores range from 1 to 5, with higher scores indicating greater impairment. The 5-D Itch disability domain includes 4 items addressing impact of itch on sleep (previously published[9]), leisure/social, housework/errands, and work/school over the past 2 weeks.
*P <.005. **P <.05.
BL, baseline; LS, least-squares.

- Greater improvements in the leisure/social item (mean change from baseline, −0.4 vs 0, *P* <.005), the housework/errands item (−0.4 vs 0, *P* <.05), and the work/school item (−0.5 vs −0.2, *P* = .07) were also seen with seladelpar vs placebo in the overall population at 12 months (**Figure 3**)

Figure 4. Body Regions[a] With Pruritus Over Time Based on the 5-D Itch Distribution Domain in the NRS ≥4 Population



B

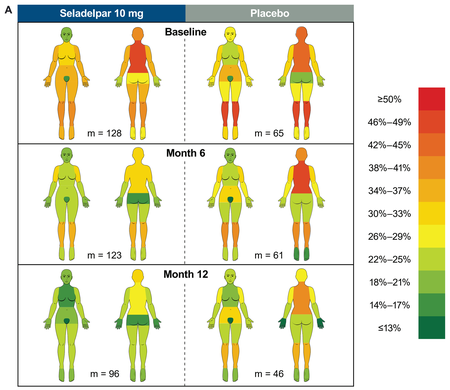
Average Number of Itchy Body Regions[b]

	NRS ≥4 Population		
	Seladelpar 10 mg (n = 49)	Placebo (n = 23)	Difference
Baseline	8.94	9.30	—
Month 1	7.61	8.91	−1.30
Month 3	6.81	8.64	−1.83
Month 6	6.49	8.20	−1.71
Month 9	5.85	7.79	−1.94
Month 12	5.52	7.87	−2.35

[a]Percentages represent the number of patients who reported itching in that body region at that analysis visit divided by the number of patients who had a value in that body region at that analysis visit (m). [b]Averages were calculated by the total number of itchy body regions at the time point divided by the number of patients who had a value at that analysis visit.
NRS, numeric rating scale.

- Among patients with NRS ≥4 at baseline, fewer seladelpar-treated patients reported itching across different body regions, including on the head, back, and other regions, vs placebo-treated patients at 12 months (**Figure 4A**; scan QR code to view color-blind accessible version of this figure)
  - Among patients with NRS ≥4 at baseline, seladelpar-treated patients had a 38% decrease in the average number of itchy body regions by month 12, whereas placebo-treated patients had a 15% decrease (**Figure 4B**)

Figure 5. Body Regions[a] With Pruritus Over Time Based on the 5-D Itch Distribution Domain in the Overall Population



B

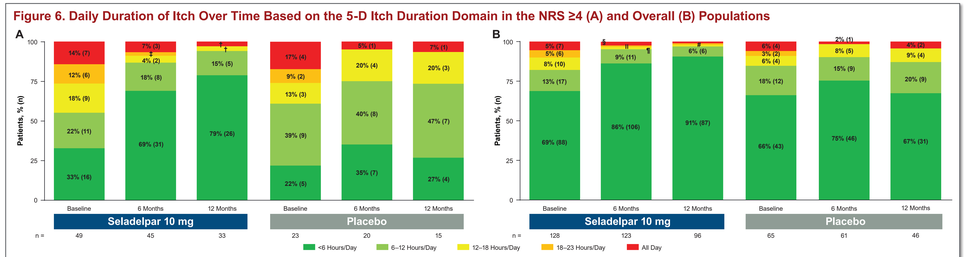
Average Number of Itchy Body Regions[b]

	Overall Population		
	Seladelpar 10 mg (n = 128)	Placebo (n = 65)	Difference
Baseline	5.11	4.78	—
Month 1	4.46	4.73	−0.28
Month 3	4.33	4.58	−0.24
Month 6	3.82	4.41	−0.59
Month 9	3.51	4.26	−0.75
Month 12	3.19	3.85	−0.66

[a]Percentages represent the number of patients who reported itching in that body region at that analysis visit divided by the number of patients who had a value in that body region at that analysis visit (m). [b]Averages were calculated by the total number of itchy body regions at the time point divided by the number of patients who had a value at that analysis visit.

- Among the overall population, fewer seladelpar-treated patients reported itching across different body regions, including on the abdomen, back, lower legs, and other regions, vs placebo-treated patients at 12 months (**Figure 5A**; scan QR code to view color-blind accessible version of this figure)
  - In the overall population, seladelpar-treated patients had a 38% decrease in the average number of itchy body regions by month 12, whereas placebo-treated patients had a 19% decrease (**Figure 5B**)

Figure 6. Daily Duration of Itch Over Time Based on the 5-D Itch Duration Domain in the NRS ≥4 (A) and Overall (B) Populations



n = number of evaluable patients at each time point. Values on the figure report % (n).
*0% (1), 13% (1), 12% (3), 14% (1), 12% (2), 11% (1) for red, orange, and yellow.
NRS, numeric rating scale.

- In the NRS ≥4 population, seladelpar treatment progressively decreased the duration of itch over time; daily duration of itch remained generally stable with placebo (**Figure 6A**; scan QR code to view color-blind accessible version of this figure)
- In the overall population, daily duration of itch decreased with seladelpar treatment and remained generally stable with placebo (**Figure 6B**; scan QR code to view color-blind accessible version of this figure)