Clinically Meaningful Fatigue Improvement With Seladelpar in Patients With Primary Biliary Cholangitis: Data From the Open-Label ASSURE Study

5040

Alan Bonder[1], Andreas E Kremer[2], Marlyn J Mayo[3], K Gautham Reddy[4], David EJ Jones[5], Kyung min Kwon[6,*], Peyvand Amini[6], Caroline Burk[6], Jie Liu[6], Daria B Crittenden[6], Gideon M Hirschfield[7]

[1]Beth Israel Deaconess Medical Center, Boston, MA, USA; [2]Department of Gastroenterology and Hepatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland; [3]Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, Dallas, TX, USA; [4]University of Chicago Medicine, Chicago, IL, USA; [5]Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK; [6]Gilead Sciences, Inc., Foster City, CA, USA; [7]The Autoimmune and Rare Liver Disease Programme, Toronto General Hospital, Toronto, ON, Canada

*Affiliation when this research was conducted.

Copies of this poster obtained through QR (Quick Response) code are for personal use only and may not be reproduced without written permission of the authors.

Conclusions

- In ASSURE, sustained fatigue improvement was observed in symptomatic patients with primary biliary cholangitis (PBC) up to 4 years after starting open-label seladelpar
  - After 4 years, clinically meaningful improvements in fatigue were observed in more than one-third of symptomatic patients, including those with moderate-to-severe fatigue, pruritus, or both
  - Patients with both moderate-to-severe fatigue and pruritus at baseline achieved the highest rates of improvement in fatigue
- Correlations across fatigue, pruritus, and sleep disturbance highlight the interrelated nature of these symptoms and support the multifactorial nature of fatigue in PBC, including contributions from pruritus-related burden
- The improvements in pruritus and sleep disturbance observed with long-term seladelpar use in this study are likely contributors to reducing fatigue burden; however, additional factors driving fatigue in patients with PBC remain incompletely understood
- Additional research is needed to characterize mechanisms of fatigue and the effect of treatment to advance care for patients with PBC

Plain Language Summary

- Primary biliary cholangitis (PBC) is a long-term liver disease, and some of its most common symptoms are fatigue and itching
  - Seladelpar is a medicine used to treat PBC; previous studies have shown that seladelpar can improve liver function and reduce itching, but less is known about its effects on fatigue
- This study showed that people with PBC who had fatigue, itching, or both at the start of the study reported less fatigue after receiving seladelpar, with improvements observed up to 4 years after starting treatment
- One reason for this may be that seladelpar reduces itching and improves sleep, but additional studies are needed to understand the main reasons why seladelpar may improve fatigue in patients with PBC

References: **1.** Lindor KD, et al. *Hepatology*. 2019;69:394-419. **2.** LIVDELZI® (seladelpar) capsules, for oral use [package insert]. Gilead Sciences, Inc.; 2026. **3.** Hirschfield GM, et al. *N Engl J Med*. 2024;390:783-94. **4.** Kowdley KV, et al. *N Engl J Med*. 2024;390:795-805. **5.** Levy C, et al. *Aliment Pharmacol Ther*. 2026;64:23-35.

Acknowledgments: We express our gratitude to all the patients, investigators, and site staff who participated in the study. This study was funded by Gilead Sciences, Inc. Medical writing and editorial support were provided by Catherine Bautista, PhD, of Lumanity Communications Inc., and were funded by Gilead Sciences, Inc.

Correspondence: Alan Bonder, abonder@bidmc.harvard.edu

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 is associated with progressive liver injury and significant symptom burden[1]
  - Pruritus and fatigue are common symptoms of PBC, impairing quality of life[1]
  - There are no treatments approved for fatigue in PBC, which is multifactorial in nature
- 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[2]
  - In the pivotal placebo-controlled, Phase 3 RESPONSE trial (NCT04620733), seladelpar significantly improved biochemical markers of cholestasis and reduced pruritus versus placebo in patients with PBC over a 1-year treatment period[3]
- Pivotal Phase 3 studies for the approved second-line treatments seladelpar and elafibranor (RESPONSE and ELATIVE, respectively) were not specifically designed to assess fatigue[3,4]
  - In RESPONSE, fatigue measures were improved with seladelpar versus placebo in patients with severe pruritus at baseline; itch-related sleep disturbance also improved with seladelpar[5]
- The Phase 3 ASSURE trial (NCT03301506) is an ongoing, open-label study of the long-term use of seladelpar in patients with PBC (**Figure 1**)

Objective

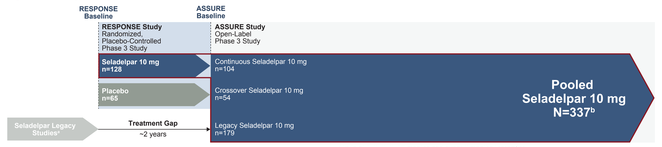
- To explore the effect of long-term seladelpar use on fatigue in patients with PBC enrolled in the ongoing ASSURE trial, with data up to 48 months

Methods

Study Design

- 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
- 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

Figure 1. Study Design

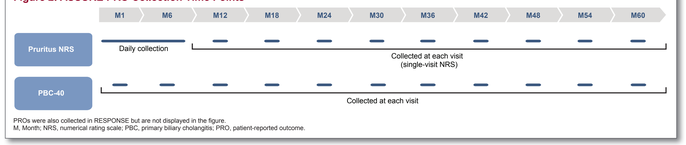


Data cutoff: January 31, 2026.
[a]Phase 2 dose-ranging study (NCT02955602), Phase 3 long-term safety study (NCT03301506), Phase 3 ENHANCE study (NCT03602560), Phase 1b hepatic impairment study (NCT04950764). The Phase 2 and 3 parent studies required inadequate response or intolerance to first-line UDCA. [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.

Study Analyses

- Analyses were conducted in the overall population and the following 3 groups defined by PBC-40 fatigue domain and pruritus numerical rating scale (NRS) scores at baseline:
  - Moderate-to-severe fatigue (PBC-40 fatigue domain score ≥29)
  - Moderate-to-severe pruritus (pruritus NRS score ≥4)
  - Moderate-to-severe fatigue (PBC-40 fatigue domain score ≥29) AND moderate-to-severe pruritus (pruritus NRS score ≥4)
- Analyses included change from baseline in PBC-40 fatigue domain score and the proportion of patients achieving clinically meaningful improvement in PBC-40 fatigue domain score, defined as an improvement of ≥5 points, among evaluable patients up to Month (M) 48 (**Figure 2**)
- The following associations at baseline and for change from baseline at M48 were assessed via Spearman correlation in the overall population:
  - PBC-40 fatigue domain score versus sleep disturbance score (PBC-40 item "itching disturbed my sleep")
  - PBC-40 fatigue domain score versus pruritus NRS score
  - PBC-40 sleep disturbance score versus pruritus NRS score

Figure 2. ASSURE PRO Collection Time Points



PROs were also collected in RESPONSE but are not displayed in the figure.
M, Month; NRS, numerical rating scale; PBC, primary biliary cholangitis; PRO, patient-reported outcome.

Results

Patients

- Among the 337 patients who enrolled and received seladelpar 10 mg, 147 (44%) had moderate-to-severe fatigue, 108 (32%) had moderate-to-severe pruritus, and 67 (20%) had moderate-to-severe fatigue and pruritus at baseline (**Table 1**)
  - PBC-40 fatigue domain and pruritus NRS scores at baseline reflected higher symptom burden in these groups than in the overall population

Table 1. Demographic and Baseline Characteristics

	Overall Population (N=337)	Patients With Moderate-to-Severe Fatigue (N=147)	Patients With Moderate-to-Severe Pruritus (N=108)	Patients With Moderate-to-Severe Fatigue and Pruritus (N=67)
Age, y, mean (SD)	58 (9.7)	57 (9.4)	55 (10.5)	54 (9.8)
Sex, female, n (%)	318 (94)	141 (96)	100 (93)	63 (94)
Race,[a] n (%)				
American Indian or Alaska Native	11 (3)	7 (5)	9 (8)	7 (10)
Asian	24 (7)	9 (6)	5 (5)	3 (4)
Black or African American	7 (2)	3 (2)	3 (3)	2 (3)
White	291 (86)	126 (86)	88 (81)	53 (79)
Ethnicity, Hispanic or Latino,[b] n (%)	72 (21)	31 (21)	31 (29)	20 (30)
Body mass index, kg/m², mean (SD)	27.3 (5.8)	28.0 (6.4)	27.9 (6.7)	28.9 (7.2)
PBC-40 fatigue domain score, mean (SD)	26.8 (10.7)	36.9 (5.7)	31.2 (9.8)	37.2 (6.2)
Pruritus NRS score, mean (SD)	2.8 (2.84)	3.7 (2.95)	6.3 (1.58)	6.6 (1.52)
ALP, U/L, mean (SD)	287 (128.2)	302 (132.3)	315 (125.4)	306 (113.7)
ALT, U/L, mean (SD)	43 (23.0)	46 (25.9)	48 (22.5)	47 (22.0)
AST, U/L, mean (SD)	38 (16.3)	41 (18.4)	42 (16.4)	43 (17.0)
GGT, U/L, mean (SD)	235 (211.5)	252 (207.1)	267 (228.5)	250 (191.6)
TB, mg/dL, mean (SD)	0.75 (0.339)	0.77 (0.331)	0.87 (0.392)	0.82 (0.332)
Cirrhosis, n (%)	52 (15)	25 (17)	24 (22)	14 (21)

Data cutoff: January 31, 2026.
[a]For race, 2 patients in the overall population declined to provide a response, and 2 patients had missing responses. [b]For ethnicity, 3 patients in the overall population declined to provide a response, and 2 patients had missing responses.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; NRS, numerical rating scale; PBC, primary biliary cholangitis; TB, total bilirubin.

- As of January 31, 2026, 109 (32%) patients who initiated seladelpar 10 mg were treated for ≥4 years (**Table 2**)

Table 2. Seladelpar Treatment Duration at Data Cutoff

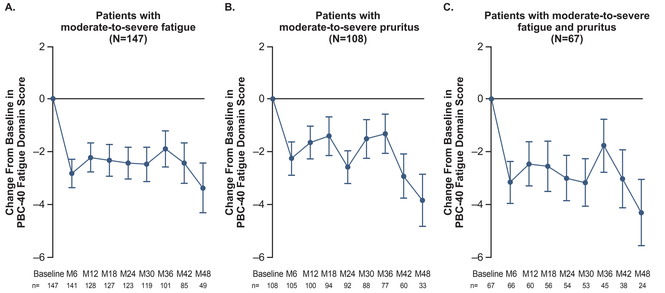
	Overall Population (N=337)
Patients who completed treatment through time point, n (%)	
Year 1	325 (96)
Year 2	298 (88)
Year 3	243 (72)
Year 4	116 (34)

Data cutoff: January 31, 2026.

Change From Baseline in PBC-40 Fatigue Domain Score

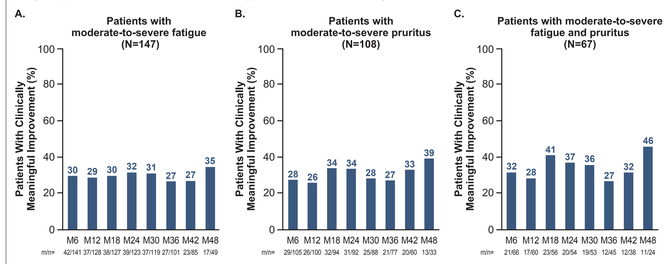
- The moderate-to-severe fatigue group experienced a sustained improvement in PBC-40 fatigue domain score, with similar findings in the moderate-to-severe pruritus group and the moderate-to-severe fatigue and pruritus group (**Figure 3**)
- Clinically meaningful improvement in PBC-40 fatigue domain score at M48 was achieved in 35% to 46% of patients across groups, with the highest rates observed in patients with both moderate-to-severe fatigue and pruritus at baseline (**Figure 4**)

Figure 3. Mean (SE) Change From Baseline in PBC-40 Fatigue Domain Score in Patients With (A) Moderate-to-Severe Fatigue, (B) Moderate-to-Severe Pruritus, and (C) Moderate-to-Severe Fatigue and Pruritus at Baseline



Data cutoff: January 31, 2026.
M, Month; PBC, primary biliary cholangitis.

Figure 4. Proportion Achieving a ≥5-Point Improvement in PBC-40 Fatigue Domain Score in Patients With (A) Moderate-to-Severe Fatigue, (B) Moderate-to-Severe Pruritus, and (C) Moderate-to-Severe Fatigue and Pruritus at Baseline



Data cutoff: January 31, 2026. m/n represents the number of patients achieving a ≥5-point improvement in PBC-40 fatigue domain score divided by number of evaluable patients at that visit.
M, Month; PBC, primary biliary cholangitis.

Correlations Between Fatigue, Sleep Disturbance, and Pruritus

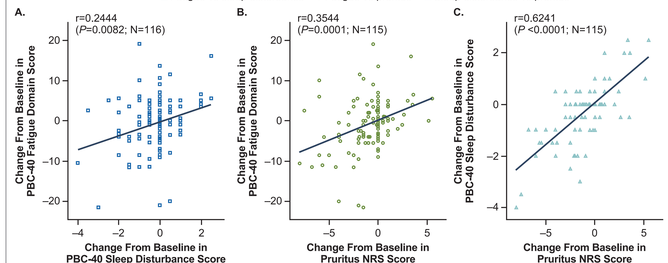
- At baseline, correlations were moderate for fatigue versus sleep disturbance, moderate for fatigue versus pruritus, and strong for sleep disturbance versus pruritus (all P <0.0001; **Table 3**)
- At M48, correlations in change from baseline were weak for fatigue versus sleep disturbance, moderate for fatigue versus pruritus, and strong for sleep disturbance versus pruritus (all P <0.01; **Table 3**; **Figure 5**)

Table 3. Correlations Between PBC-40 Fatigue Domain, PBC-40 Sleep Disturbance, and Pruritus NRS Scores at Baseline and M48 in the Overall Population

Correlation	n	r	*P* Value
PBC-40 fatigue domain score and PBC-40 sleep disturbance score			
Baseline	335	0.4186	<0.0001
Change from baseline at M48	116	0.2444	0.0082
PBC-40 fatigue domain score and pruritus NRS score			
Baseline	328	0.3826	<0.0001
Change from baseline at M48	115	0.3544	0.0001
PBC-40 sleep disturbance score and pruritus NRS score			
Baseline	328	0.8153	<0.0001
Change from baseline at M48	115	0.6241	<0.0001

Data cutoff: January 31, 2026.
M, Month; NRS, numerical rating scale; PBC, primary biliary cholangitis; *r*, Spearman's correlation coefficient.

Figure 5. Correlations Between (A) PBC-40 Fatigue Domain Score and PBC-40 Sleep Disturbance Score, (B) PBC-40 Fatigue Domain Score and Pruritus NRS Score, and (C) PBC-40 Sleep Disturbance Score and Pruritus NRS Score at M48 in the Overall Population



Data cutoff: January 31, 2026.
M, Month; NRS, numerical rating scale; PBC, primary biliary cholangitis; *r*, Spearman's correlation coefficient.