Improvements in Patient-Reported General Health and Well-Being in Patients With Primary Biliary Cholangitis Treated With Seladelpar in the RESPONSE Trial

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Conclusions

- Patients with primary biliary cholangitis (PBC) reported worse general health and well-being after PBC diagnosis than before diagnosis
- Seladelpar therapy was associated with greater improvement than placebo in general health and well-being at 12 months across all baseline levels of pruritus
- These findings provide early insights into the potential overall benefits of seladelpar treatment from the patient perspective

Plain Language Summary

- Primary biliary cholangitis (PBC) is a lifelong liver disease that is often associated with symptoms such as itching, fatigue, and dry mouth and eyes
- Seladelpar is a new treatment shown to help patients with PBC who cannot take or do not improve with the usual first treatment for the disease
- The effects of seladelpar on general health and well-being have not yet been studied
- We looked at patient-reported data from a recent clinical trial to help patients and their doctors understand how this new treatment may affect general health and well-being
- We found that patients receiving seladelpar saw greater gains in general health and well-being than those receiving a placebo
- This suggests that seladelpar may improve general health and well-being in patients with PBC who cannot receive or do not improve with the first-line treatment

References: **1**. Primary biliary cholangitis. Accessed August 7, 2025. https://www.mayoclinic.org/diseases-conditions/primary-biliary-cholangitis/symptoms-causes/syc-20376874. **2.** Mayo MJ et al. *Dig Dis Sci*. Mar 2023;68(3):995-1005. **3.** Livdelzi® (seladelpar) capsules, for oral use. Initial U.S. Approval: 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217899s000lbl.pdf. **4.** Hirschfield GM et al. *N Engl J Med*. 2024;390(9):783-794. **5.** Kremer A et al. Abstract number 843 THU-277. European Association for the Study of the Liver; 07–10 May 2025; Amsterdam, the Netherlands.

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Introduction

- Primary biliary cholangitis (PBC) is a chronic, progressive, autoimmune, cholestatic liver disease that is associated with symptoms of pruritus and fatigue and disproportionately affects female patients[1,2]
- Seladelpar is a first-in-class delpar (selective peroxisome proliferator–activated receptor delta [PPARδ] agonist) indicated for treating PBC[3]
- It is used either combined with standard-of-care ursodeoxycholic acid (UDCA) in patients with inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA[3]
- In the phase 3 RESPONSE trial (NCT04620733), seladelpar significantly improved biochemical markers of cholestasis vs placebo in adults with PBC and significantly reduced pruritus in those with moderate to severe pruritus at baseline[4]
- We analyzed patient-reported outcomes from the RESPONSE trial to understand the impact of seladelpar on general health and well-being in adults with PBC

Methods

- The RESPONSE trial was a phase 3 study of seladelpar in adults with PBC who had an inadequate response or intolerance to UDCA[4]
- Patients were randomized 2:1 to receive seladelpar (10 mg daily) or placebo for 12 months
- Pruritus was assessed using the 11-point Pruritus Numerical Rating Scale (Pruritus NRS; 0, no itch; 10, worst itch imaginable), whereby scores ≥4 indicated moderate to severe pruritus and scores <4 indicated no to mild pruritus[5]
- Outcomes were analyzed post hoc using 3 general health and well-being questions from the Primary Biliary Cholangitis Quality of Life Measure Questionnaire (PBC-40), a disease-specific tool (**Table 1**)
  - The PBC-40 was completed at run-in, day 1, month 1, and every 3 months until month 12[5]
  - Each question was scored 1 to 5, with lower scores denoting better general health and well-being
  - Responses were scored individually and compared by treatment group

Table 1. PBC-40 General Health and Well-Being Questions

	Question	1	2	3	4	5
A	In general, would you say your health is:	Excellent	Very good	Good	Fair	Poor
B	And how would you have rated it before you had PBC?	Excellent	Very good	Good	Fair	Poor
C	Compared to one year ago, how would you rate your health in general now?	Much better	Some what better	About the same	Some what worse	Much worse

PBC, primary biliary cholangitis; PBC-40, Primary Biliary Cholangitis 40-Item Questionnaire

Results

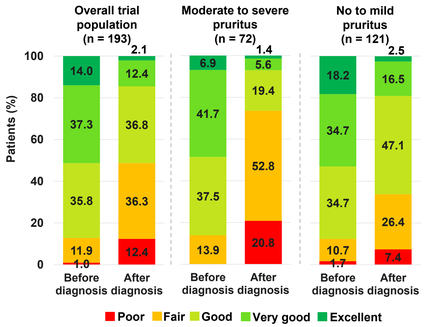
Patient Sample

- The overall trial population included 193 patients
- Of them, 72 had moderate to severe pruritus and 121 had no to mild pruritus at baseline; baseline demographic and clinical characteristics have been reported[4]
- In the 3 cohorts of interest (overall trial population, moderate to severe pruritus, no to mild pruritus), there were no significant demographic or clinical differences (eg, age, race, sex, time since PBC diagnosis) between patients receiving seladelpar vs placebo

General Health Before and After PBC Diagnosis

- In the overall population and both subgroups:
  - Percentages of patients with poor/fair general health were higher after PBC diagnosis than before diagnosis (assessed at study baseline) (**Figure 1**)
  - Percentages of patients with excellent/very good general health were significantly lower after diagnosis than before diagnosis ($P < 0.001$) (**Figure 1**)

Figure 1. General Health Ratings Before PBC Diagnosis (Question B) and After Diagnosis (Question A)

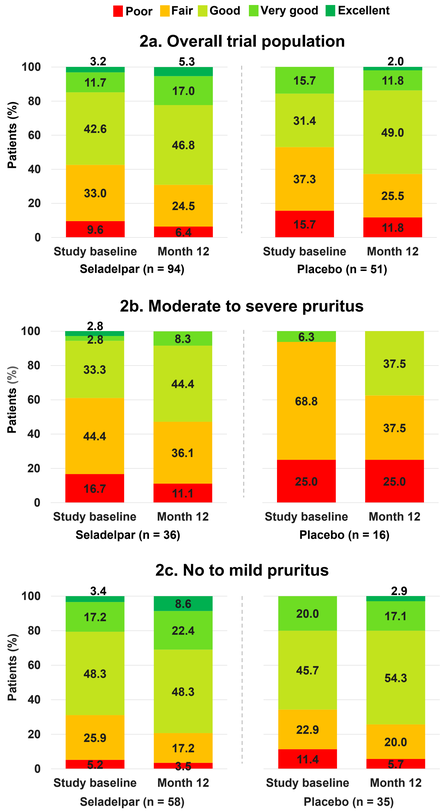


Data show responses at baseline. PBC, primary biliary cholangitis

Change in General Health in Patients Receiving Seladelpar or Placebo

- In the overall trial population, excellent/very good health rose from 14.9% at baseline to 22.3% at month 12 among patients receiving seladelpar but fell from 15.7% to 13.8% among patients receiving placebo (**Figure 2a**).
- In patients with moderate to severe pruritus, excellent/very good health rose from 5.6% to 8.3% for seladelpar but fell from 6.3% to 0% for placebo (**Figure 2b**).
- In patients with no to mild pruritus, excellent/very good health rose from 20.6% to 31.0% at month 12 for seladelpar but were maintained at 20.0% for placebo (**Figure 2c**).

Figure 2. General Health Ratings at Baseline and Month 12, Seladelpar vs Placebo (Question A)

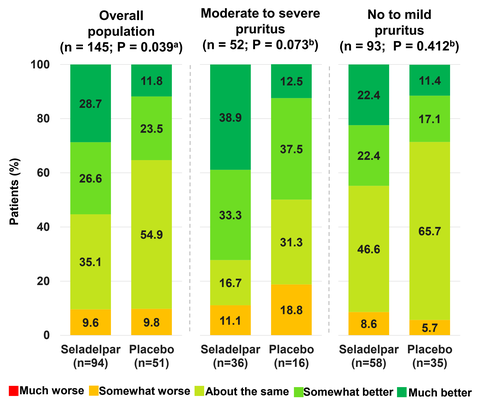


Data show responses to question A at study baseline and responses to question A at month 12. Patients with missing responses were excluded.

General Health Compared to 1 Year Ago in Patients Receiving Seladelpar vs Placebo

- After 12 months, general health improved at greater rates in patients taking seladelpar than those taking placebo, with higher percentages of patients in the overall trial population and both pruritus subgroups reporting "much better" health (**Figure 3**)
  - In the overall trial population, this difference was significant

Figure 3. General Health Compared to 1 Year Ago (Question C), Seladelpar vs Placebo



Data show responses to question C at month 12. No patients responded "Much worse." Patients with missing responses were excluded. [a]Chi-square test was used to compare responses by treatment group. [b]Fisher's exact test was used to compare responses by treatment group.

Limitations

- All outcomes were analyzed post hoc, potentially introducing reporting bias or multiple comparison bias
- Patient-reported outcomes may be subject to recall bias (especially for health before PBC diagnosis) and varying perspectives of good vs bad health
- Relatively small sample sizes (particularly among patients with moderate to severe pruritus) limit generalizability of the results
- Non-responses at month 12 by nearly a quarter of patients limit generalizability
- The 12-month study duration limits assessment of long-term outcomes