A Cost Calculator for Estimating Direct Medical Cost Avoidance from Second-Line Seladelpar Use in Patients with Primary Biliary Cholangitis

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#EE168

Conclusions

- In this US analysis, alkaline phosphatase (ALP) normalization and pruritus resolution/near-resolution were associated with short-term (1-year) cost avoidance of direct medical costs for those with primary biliary cholangitis (PBC) receiving second-line therapy, providing evidence that although PBC is a slow-moving disease, cost avoidance may occur early, with biomarker normalization and pruritus reduction
  - Cost avoidance is highest among patients who normalize from highly elevated baseline ALP levels
  - However, there may be similar cost avoidance opportunity if a larger proportion of inadequate responders (ALP between 1–1.67×ULN) at baseline achieve normalization
- Given the availability of second-line PBC treatments with favorable risk/benefit profiles, numbers of eligible patients for second-line PBC therapy may increase in the US over time. Therefore, cost avoidance may become more relevant and increase in magnitude in the future as an economic benefit of therapy
- Overall, further evaluation of longer-term outcomes is required to fully characterize economic value in the second-line setting for PBC

Plain Language Summary

- PBC is a long-term liver disease that worsens over time
- ALP is a substance that doctors can measure to assess liver function, and pruritus (itching) is a symptom of PBC that can affect patients' quality of life. Therefore, treatments for PBC, such as seladelpar, aim to reduce ALP levels and relieve symptoms such as pruritus
- The results of this analysis predicted that short-term (1-year) medical costs may be avoided in the US healthcare setting if ALP levels decrease or pruritus improves in patients with PBC. However, there were some limitations, and future research is needed to assess economic value in the longer-term

Background

- PBC is a chronic, autoimmune, cholestatic liver disease that disproportionately affects women and is associated with progressive liver injury and significant symptom burden[1]
- The aim of treatment is to prevent disease progression and slow liver damage, primarily through ALP reduction/normalization and stabilization of liver stiffness, as well as to relieve symptoms such as pruritus to improve patients' quality of life[1–5]
- PBC is associated with economic burden, with US studies demonstrating that higher ALP levels and presence of pruritus are associated with higher healthcare resource utilization (HCRU) and/or costs[6,7]
- The treatment landscape for second-line therapy of PBC following inadequate response to ursodeoxycholic acid (UDCA) is evolving, with treatments such as seladelpar and elafibranor now becoming more widely available[8,9]
- This analysis aimed to estimate short-term healthcare costs avoided with achievement of ALP normalization or reduced pruritus with second-line seladelpar treatment for PBC

Abbreviations: **ALP:** alkaline phosphatase; **HCRU:** healthcare resource utilization; **PBC:** primary biliary cholangitis; UDCA: ursodeoxycholic acid; **ULN:** upper limit of normal.

References: **1.** European Association for the Study of the Liver. *J Hepatol.* 2017;67(1):145–172. **2.** Murillo Perez CF et al. *Am J Gastroenterol.* 2020;115(7):1066–1074. **3.** Corpechot C et al. *J Hepatol.* 2022;77(6):1545–1553. **4.** Wong YJ et al. *J Hepatol.* 2026;84(2):275–283. **5.** Yosipovitch G et al. *Br J Dermatol.* 2019;181(4):761–769. **6.** Gish R et al. Poster #3096. Presented at The Liver Meeting (AASLD): November 2025; Washington, DC, USA. **7.** Gish RG et al. *J Med Econ.* 2025;28(1):2173–2185. **8.** Hirschfield GM et al. *N Engl J Med.* 2024;390(9):783–794. 9. Study NCT04526665. ClinicalTrials.gov. Accessed March 2026. **10.** Kremer AE et al. Oral Presentation #167. Presented at The Liver Meeting (AASLD): November 2024; San Diego, CA, USA. **11.** Gilead Sciences Data on File. **12.** Study NCT06060665. ClinicalTrials.gov. Accessed March 2026.

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Methods

- A decision tree cost calculator was developed from a healthcare payer perspective to quantify short-term cost avoidance. Outputs were per-patient direct all-cause medical costs avoided with seladelpar vs no treatment. Cost of therapy was not included
- The calculator had a 1-year time horizon, in alignment with available data sources (RESPONSE and US claims analyses)
- Two analyses were conducted: analysis 1 (ALP normalization) and analysis 2 (pruritus reduction). Each considered second-line-eligible PBC patients. Additionally, in analysis 2, all patients were assumed to have a pruritus diagnosis
- ALP normalization and pruritus resolution/near-resolution rates were derived from the pivotal RESPONSE trial (NCT04620733). In the base case (patients with ALP >1×ULN), the RESPONSE average ALP normalization rate (25.0%) or pruritus resolution/near-resolution rate (26.5%) was applied[10]
- ALP level distribution and costs associated with ALP levels and pruritus were derived from US claims analyses comparing patients with normal ALP (ALP ≤1× the upper limit of normal [ULN]) vs patients with ALP above normal (ALP >1×ULN) and those with a pruritus diagnosis (and who received treatment within 90 days of diagnosis, if a stricter definition of pruritus was used) vs controls[6,7,11]
  - In a claims analysis focusing on ALP levels, increased economic burden associated with higher baseline ALP related primarily to inpatient and emergency room utilization. In analyses relating to pruritus, presence of pruritus was associated with higher HCRU and costs across emergency room, prescription, inpatient, and outpatient settings
- Scenario and threshold analyses were conducted
  - Analysis 1
    - Scenario analyses considered a population of inadequate responders (ALP between 1–1.67×ULN) at baseline in alignment with the population of the ongoing IDEAL trial (NCT06060665).[12] An ALP normalization rate range of 25.0–75.0% was used[8]
    - A threshold analysis was conducted to assess the ALP normalization rate required for only inadequate responders (ALP between 1–1.67×ULN) at baseline to reach equipoise in terms of per-patient cost savings with the base case analysis
  - Analysis 2
    - A scenario analysis for Analysis 2 considered a stricter definition of pruritus (as reported above), using the same resolution rate as the base case
- A model schematic is presented in **Figure 1**, and a summary of key model inputs in **Table 1**

Figure 1. Model schematic

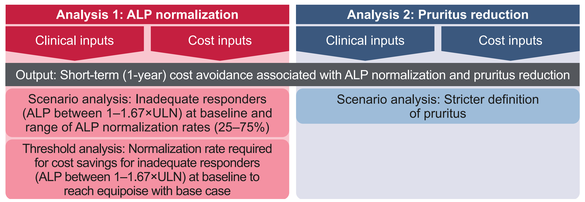


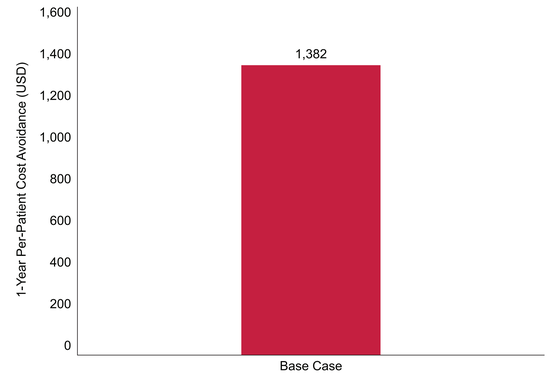
Table 1. Key model inputs

Input	Value	Source
Analysis 1: ALP normalization		
ALP normalization rate	25.0%	RESPONSE[8]
Normal ALP, total annual healthcare costs	$15,721	US claims analyses[11]
ALP >1 to ≤1.67×ULN, incremental annual cost	$2,128	
ALP >1.67 to ≤3×ULN, incremental annual cost	$10,289	
ALP >3×ULN, incremental annual cost	$12,229	
Analysis 2: Pruritus reduction		
Pruritus resolution/near-resolution rate	26.5%	RESPONSE[9]
Control, total annual healthcare costs	$25,695	US claims analyses[12]
Pruritus, total annual healthcare costs	$39,949	

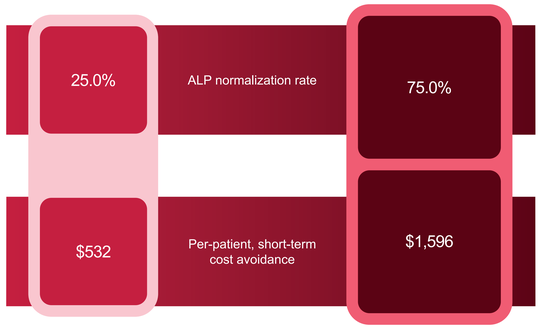
Results

Figure 2. 1-year cost avoidance: ALP normalization (analysis 1)

A. Base case: Patients with ALP >1×ULN and 25.0% ALP normalization rate



B. Scenario analysis: Inadequate responders (ALP between 1–1.67×ULN) at baseline and range of ALP normalization rates



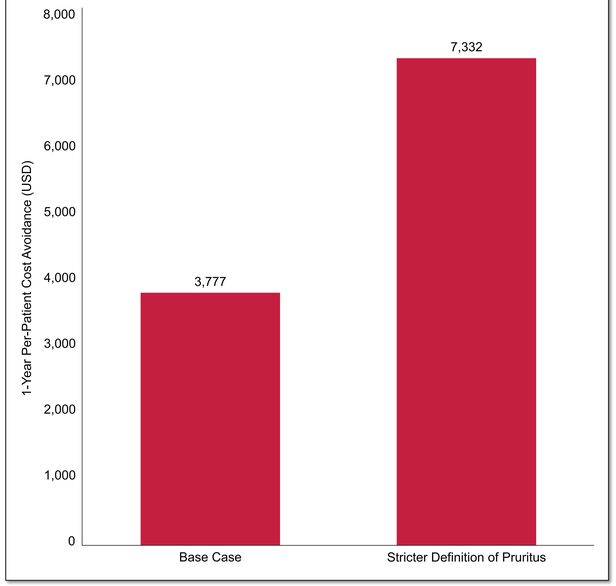
C. Threshold analysis

ALP normalization rate of:	Per-patient, short-term cost avoidance of:
65.0%	**$1,382**

for only inadequate responders (ALP between 1–1.67×ULN) at baseline to reach equipoise in per-patient cost avoidance with the base case analysis

- In Analysis 1, using an average ALP normalization rate of 25.0%, $1,382 was avoided in per-patient 1-year costs (**Figure 2A**)
  - In scenario analyses of inadequate responders (ALP between 1–1.67×ULN), a normalization rate range of 25.0%–75.0% for these patients led to 1-year cost avoidance of $532–$1,596 per patient (**Figure 2B**)
  - The threshold analysis revealed that, in order for patients with lower ALP at baseline (inadequate responders [ALP between 1–1.67×ULN]) to offer the same 1-year cost avoidance as costlier higher-at-baseline ALP populations (e.g., ALP >1.67×ULN), ALP normalization after one year of treatment would need to increase from 25.0% to 65.0% (**Figure 2C**)

Figure 3. 1-year cost avoidance: pruritus reduction (analysis 2)



- In Analysis 2, using a pruritus resolution/near-resolution rate of 26.5% and a broad definition of pruritus patients, $3,777 were avoided in per-patient 1-year costs (**Figure 3**)
  - In the scenario analysis of patients using a stricter definition of pruritus, short-term cost avoidance was $7,332 per patient annually (**Figure 3**)

Limitations

- Although long-term cost avoidance is not captured in this analysis as the model relies on annual average costs from a heterogeneous, slowly-progressive PBC population and only includes high-cost liver events in the first year after treatment, it is important to note that evidence from the Global PBC cohort demonstrated that improvements in biomarkers during the first and second years are strong predictors of death- and liver transplant–free survival. Further data generation is needed to enable future models to follow patients over the course of 5–10 years to fully capture the cost avoidance from long-term liver events
- In addition, cost avoidance in the analyses may be underestimated for the following reasons:
  - All cost estimates from the US claims analyses were based on imputed (rather than ultimately paid) values from Komodo Health
  - It was assumed in ALP normalization analyses that there was no migration between non-normalized ALP severity levels over the course of the model time horizon
- In the ALP normalization scenario analysis, the upper-end share of normalizers was informed by assumption only
- Near-resolution of pruritus (including scores of 0 or 1) corresponded to all-cause healthcare costs for the control cohort (those without a pruritus diagnosis or pruritus-related treatment during the study window) in the relevant US claims analysis
- Clinical inputs were based on data for seladelpar, and this was not a comparative analysis of all second-line treatment options. Data from the US claims analyses did not exclude patients who responded to UDCA and thus may not reflect patients treated with seladelpar in real-world settings