Real-World Clinical and Economic Burden of Primary Biliary Cholangitis in the United States

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Background

- Primary biliary cholangitis (PBC) is a rare chronic cholestatic liver disease[1]
  - Patients with untreated PBC are at risk of disease progression to cirrhosis and end-stage liver disease, often without obvious symptoms[1]
- First-line (1L) treatment for PBC is ursodeoxycholic acid (UDCA); obeticholic acid (OCA) is used as second-line (2L) treatment after UDCA or as 1L treatment for patients who do not tolerate UDCA[2]
- Fibrates have been used off-label for treatment of PBC in patients with incomplete response to UDCA[2]
- Lack of treatment or delayed treatment are associated with worse prognosis and contribute to increased morbidity, mortality, and medical resource use[1,3]

Objective

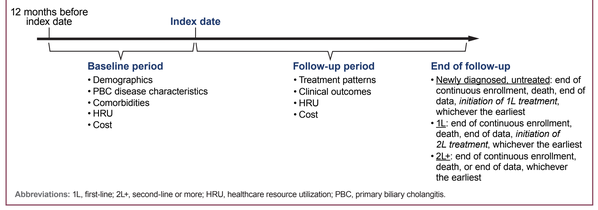
- **This study assessed the real-world clinical and economic burden of PBC in the United States (US) by line of treatment**

Methods

Study Design and Cohorts

- This retrospective study used IQVIA PharMetrics® Plus data (2016–2022) for 3 non-mutually exclusive cohorts of adults with diagnosed PBC on or after January 1, 2017 (age ≥18 years at initial diagnosis):
  - Newly diagnosed cohort: Patients with newly diagnosed PBC
  - Untreated cohort: Patients in the newly diagnosed cohort who did not receive any PBC treatment
  - 1L cohort: Patients who initiated 1L treatment (UDCA)
  - 2L+ cohort: Patients who initiated 2L+ treatments (OCA/fibrates ± UDCA)
- Index date: PBC diagnosis or 1L/2L+ treatment initiation (Figure 1)
- Baseline: 12 months pre-index date

Figure 1. Study Design



Abbreviations: 1L, first-line; 2L+, second-line or more; HRU, healthcare resource utilization; PBC, primary biliary cholangitis.

Assessments

- Parameters summarized per cohort:
  - Baseline demographic characteristics
  - Treatment sequence
  - Time-to-treatment initiation/discontinuation
  - Per-patient per-year (PPPY) healthcare costs post-index
  - Time from index date to earliest clinical outcome (including liver transplant, cirrhosis, hospitalization for hepatic decompensation, hepatocellular carcinoma, clinically significant portal hypertension, and death)

Data Analysis

- Key patient characteristics and comorbidities during the baseline period were analyzed descriptively
- All-cause PPPY healthcare resource utilization (HRU) and PPPY healthcare costs during the baseline and follow-up periods were summarized and compared for each cohort
  - Generalized estimating equations (GEE) models with a negative binomial distribution and log-link function were used to compare baseline and follow-up period HRU values and estimate incidence rate ratios (IRRs)
  - GEE models with a Tweedie distribution and a log link function were used to compare baseline and follow-up period healthcare costs and estimate the mean cost difference; all costs were reported in 2023 US dollars
- Time to treatment initiation and time to treatment discontinuation were described for each cohort using Kaplan-Meier (KM) analysis

TAKE-HOME MESSAGE

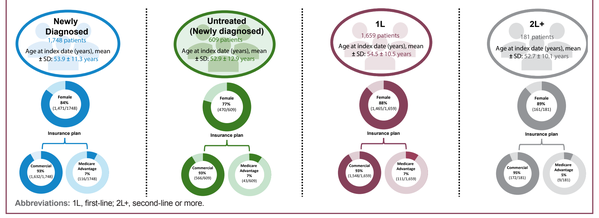
- **These findings indicate an unmet need for additional treatments that help improve clinical outcomes and reduce HRU among all patients with PBC, especially in the untreated and 2L+ settings**

Results

Baseline Demographics and Disease Characteristics

- 1,748, 1,659, and 181 patients were included in the newly diagnosed, 1L, and 2L+ cohorts, respectively (Figure 2)
  - Mean age at index across cohorts: 53.9–54.5 years
  - In the newly diagnosed cohort, 609 patients did not initiate any PBC treatment during follow-up (untreated cohort)

Figure 2. Patient Demographics

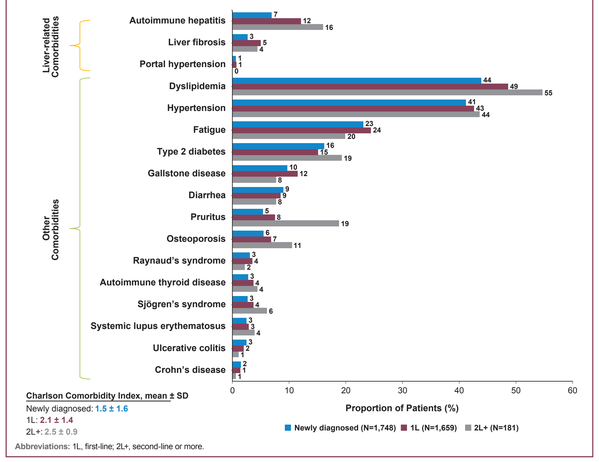


Abbreviations: 1L, first-line; 2L+, second-line or more.

Common Comorbidities

- The most common comorbidities were dyslipidemia (43.9%–54.7%), hypertension (41.2%–43.6%), and fatigue (19.9%–24.4%) (Figure 3)
  - Baseline comorbidity burden and pruritus rate were higher in the 2L+ cohort than in the newly diagnosed and 1L cohort

Figure 3. Comorbidities at Baseline



Abbreviations: 1L, first-line; 2L+, second-line or more.

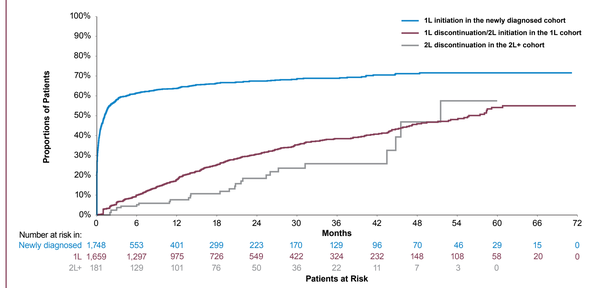
Time to Treatment Initiation and Time to Treatment Discontinuation

Table 1. Time to Treatment Initiation and Time to Treatment Discontinuation

	Newly diagnosed (N=1,748)	1L (N=1,659)	2L+ (N=181)
Median follow-up, months	19.6	21.0	15.2
Median time from PBC diagnosis to 1L initiation, months	1.2*	–	–
Discontinued 1L treatment, n (%)	–	484 (29.2)	–
Median time to 1L treatment discontinuation, months (95% CI)	–	55.6 (48.6–[upper range limit not reached])	–
Initiated 2L+ treatment, n (%)	97 (5.5)†	144 (8.7)	–
Discontinued 2L+ treatment, n (%)	–	–	28 (15.5)
Median time to 2L treatment discontinuation, months (95% CI)	–	–	51.0 (44.4–[upper range limit not reached])

Abbreviations: 1L, first-line; 2L+, second-line or more; PBC, primary biliary cholangitis.
*34.8% of patients did not initiate treatment by 4 years postdiagnosis (N=609, untreated cohort). Most patients used UDCA (N=1,123, 64.2%) for 1L treatment.
†55 patients used OCA + UDCA in 2L+.

Figure 4. Time to Treatment Initiation and Time to Treatment Discontinuation



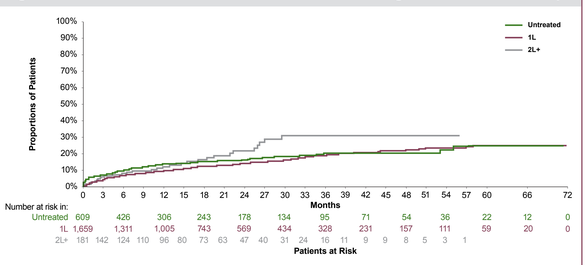
Abbreviations: 1L, first line; 2L, second-line; 2L+, second-line or more.

Clinical Outcomes

- 19% (n=115), 14% (n=239), and 19% (n=35) of patients in the newly diagnosed*, 1L, and 2L+ cohorts developed ≥1 negative clinical outcome
  - Among those who had ≥1 negative clinical outcome during follow-up, cirrhosis was the most common and earliest clinical outcome during follow-up (newly diagnosed, 69/115; 1L, 212/239; 2L+, 31/35) (Figure 5)

** Newly diagnosed patients who did not initiate PBC treatment*

Figure 5. Time to Liver Cirrhosis in Each Cohort Through 4 Years of Follow-Up



Abbreviations: 1L, first line; 2L+, second-line or more.

Healthcare Costs

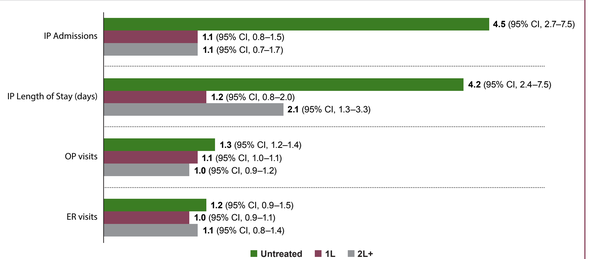
- Total healthcare costs, including costs of inpatient, outpatient, emergency room, other medical services, PBC-related medications, and fatigue/pruritus-related medications, increased from pre-index to post-index periods in all 3 cohorts (Table 1)
- At follow-up, HRU compared to baseline was greater across all cohorts (Figure 6)
- Inpatient admissions, outpatient visits, and PBC-related treatment were the biggest drivers of post-index healthcare costs in the untreated, 1L, and 2L+ cohorts, respectively

Table 2. Mean Healthcare Costs

PPPY Cost	Untreated (N=609)	1L (N=1,659	2L+ (N=181)
Pre-index total	$15,687	$14,470	$14,288
Post-index total	$54,226	$18,460	$71,356
Inpatient	$37,974	$5,854	$6,898
Outpatient	$14,298	$9,377	$9,613
Emergency room	$1,855	$887	$1,052
PBC treatment	–	$2,251	$53,698

Costs are inflated to 2023 USD.
Abbreviations: 1L, first-line; 2L+, second-line or more; PBC, primary biliary cholangitis; PPPY, per person per year.

Figure 6. HRU IRRs



Abbreviations: 1L, first-line; 2L+, second-line or more; CI, confidence interval; ER, emergency room; HRU, healthcare resource use; IP, inpatient; IRR, incidence rate ratio; OP, outpatient.

Limitations

- This study is subject to general limitations of analyses using administrative claims data, including potential for incorrectly documented diagnosis codes and inability to capture medical services or pharmacy dispensing obtained outside of a patient's plan
- Most of the beneficiaries in the PharMetrics data are covered by commercial plans, so the results from this study may not be generalizable to patients with PBC covered by other healthcare plans, such as Medicare and Medicaid
- Lab testing results are not available in PharMetrics data. As such, some important prognosis factors for this disease that are routinely measured to assess treatment response, such as the levels of alkaline phosphatase and total bilirubin, cannot be evaluated in the current study

CONCLUSIONS

- This claims data analysis suggests that many patients with PBC remain untreated years after diagnosis despite approved treatments
- Comorbidity burden increases as lines of therapy increase, likely due to disease progression
- Patients left untreated after diagnosis had high IP costs, which accords with existing studies reporting poor outcomes associated with untreated/undertreated patients with PBC[1]

References

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2. Levy C, et al. *Hepatol Commun.* 2018;2(5):484-491.
3. Peery AF, et al. *Gastroenterology.* 2019;156(1):254-272 e211.

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