European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied
Website: https://farmclin.es/

Original Research Article

Real-World Results of the Use of Obeticholic Acid in the Treatment of Primary Biliary Cholangitis

Article History:

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How to cite this article:
Sara H.R., et, al. Real-World Results of the Use of Obeticholic Acid in the Treatment of Primary Biliary Cholangitis. *Eur J Clin Pharm.* 2022;4(1);22-24

Received: 26-05-2022
Revised: 02-06-2022
Accepted: 17-06-2022
Published: 08-07-2022

Abstract: Primary biliary cholangitis (PBC) is a progressive cholestatic liver disease often inadequately controlled by ursodeoxycholic acid (UDCA) monotherapy. Obeticholic acid (OCA) has emerged as a second-line agent, but data on its real-world effectiveness and safety are still evolving. This research critically reviews real-world clinical outcomes of OCA in PBC, including response rates, biochemical markers, survival, adverse effects, and patient quality of life. Comparative analyses with clinical trial data and adverse outcome predictors are discussed. The article includes contemporary multi-cohort data and graphical representations of treatment outcomes.

Keywords: Primary biliary cholangitis (PBC), Obeticholic acid (OCA), Ursodeoxycholic acid (UDCA), Real-world effectiveness, Treatment outcomes.

INTRODUCTION

PBC is a chronic autoimmune liver disease characterized by destruction of intrahepatic bile ducts, leading progressively to fibrosis and potential cirrhosis or liver failure. While UDCA remains the standard first-line therapy, suboptimal biochemical response is observed in up to 40% of patients. Obeticholic acid, a potent farnesoid X receptor (FXR) agonist, was approved as a second-line agent in PBC patients with inadequate UDCA response[1][2]. In real-world clinical practice, understanding actual patient outcomes, tolerability, and predictors of success or failure is critical for optimizing therapy.

MECHANISM OF ACTION AND CLINICAL RATIONALE

OCA decreases bile acid synthesis, hepatic inflammation, and fibrosis through FXR activation, complementing the effect of UDCA[3][2]. This mechanistic synergy underpins its recommendation for use in UDCA-inadequate responders or intolerant patients, aiming to slow biochemical progression and improve survival indicators.

STUDY OVERVIEW AND REAL-WORLD COHORTS

Recent years have seen an increasing number of observational cohort studies and registry data publications, which offer valuable insights beyond controlled clinical trials[4][5][6][7][8]. These cohorts commonly include:

- Adult PBC patients with a defined incomplete UDCA response (Paris II or POISE criteria)
- Prevalence of cirrhosis at initiation: ~22%

- Baseline mean age: ~54–56 years
- Female predominance (>90%)
- Median OCA follow-up: 9–18 months in most cohorts

REAL-WORLD EFFICACY

Biochemical Outcomes

- *Alkaline phosphatase (ALP)*: Real-world studies consistently show significant reductions in ALP after 12 months of OCA, confirming its role as a surrogate for improved outcomes. Mean ALP reductions typically range from 50–81U/L over a year, sustained through three years in extension cohorts[5][6][8].
- *ALT, AST, GGT, Bilirubin*: Notably, ALT and GGT as well as both total and direct bilirubin decrease in most patients, particularly those with elevated baseline bilirubin, indicating hepatic function improvement[1][5][7].
- *Paris II and POISE criteria responses*: Rates of biochemical response (i.e., normalization or significant reduction of ALP) range from 29–43% at 12 months in true real-life conditions[9][6][8], slightly lower than controlled trials but clinically meaningful.

Table 1: Biochemical Responses to OCA in Real-World Studies

Endpoint	12-Month Response (%)	Long-Term Response (%)	Notable References
ALP reduction	40–43	44–52 (24–48 mo.)	[9][5][6][8]
POISE criteria	29–35		[6][8]
Bilirubin decline	Significant in subset	Maintained up to 3 yr	[1][5]

Hospitalization, Survival, and Disease Progression

A comprehensive real-world study with over 400 OCA-treated patients found a 63% reduction in risk of hepatic decompensation, liver transplant, or death compared to matched controls over 9–17 months of follow-up[4]. This translates to meaningful improvement in event-free survival and represents one of the strongest confirmations of OCA's benefit outside clinical trials.

- *Hazard ratio for event-free survival*: 0.37 (95% CI: 0.14–0.75; $p<0.001$)[4]
- Consequence: Fewer hospitalizations and improved transplant-free outcomes.

Comparison to Clinical Trials

These real-world response rates parallel but are slightly lower than pivotal trial data (e.g., POISE), reflecting more advanced disease and broader comorbidity in the observational setting[1][5].

Tolerability and Safety in Real Practice

- *Pruritus* remains the primary adverse effect (35–77% of patients), causing discontinuation in 8–11%[1][3][5][6]. Intensity is generally mild–moderate and decreases with ongoing therapy; severe cases are managed by dose adjustment or concurrent medications.
- *Other adverse events*: Fatigue, headache, musculoskeletal pain, and elevated LDL. Serious liver-related events (ascites, jaundice, worsening cholangitis) are rare, but caution is advised in those with advanced cirrhosis[3][6][10].
- *Adherence and persistence*: Real-world studies show OCA is generally well tolerated over 1–3 years, but a subset of patients require dose changes or drug discontinuation due to side effects[5][6].

Predictors of Response and Failure

Evidence points to several potential predictors:

- Better biochemical responses in patients with less advanced liver stiffness (lower FIB-4/APRI) at baseline[6].
- More pronounced bilirubin reductions and histological stabilization in those with higher baseline cholestasis markers[1].
- Concomitant use of fibrates in a minority, though data on additive effects remain sparse.

Quality of Life and Patient-Reported Outcomes

Most patients report improved disease-awareness and reduced worry about disease progression; symptoms related to pruritus and fatigue are important to monitor and mitigate in clinical follow-up[5][7].

Clinical Recommendations and Guidelines Implications

- OCA should be considered in all PBC patients with suboptimal UDCA response, barring contraindications such as advanced liver failure[1][2][10].
- Biochemical monitoring (ALP, bilirubin, transaminases, pruritus assessment) is critical for follow-up and dose adjustments.
- Early initiation, before advanced fibrosis or cirrhosis, optimizes response rates and safety[6][8][10].

DISCUSSION

Real-world data confirms the sustained and clinically meaningful biochemical improvement of OCA in PBC, with lower but still substantial response rates relative to clinical trials. Safety profiles remain predictable, with pruritus the most prominent adverse effect. Event-free survival appears improved in treated cohorts, and ongoing monitoring of advanced disease and rare side effects remains vital. Future directions include optimizing combination therapies and individualized dose titration protocols.

CONCLUSION

OCA is a valuable real-world addition to the PBC treatment arsenal, offering improved biochemical control, lower rates of disease progression, and acceptable tolerability in UDCA-inadequate responders. Ongoing studies will clarify long-term clinical benefits, individual predictors of response, and the optimal deployment of OCA in clinical hepatology.

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