Long-Term Obeticholic Acid Treatment is Associated With Improvements in Collagen Morphometry in Patients With Primary Biliary Cholangitis

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INTRODUCTION

Primary biliary cholangitis (PBC) is a rare autoimmune liver disease of the intrahepatic bile ducts, leading to progressive fibrosis and eventual cirrhosis.

In patients with PBC, cirrhosis-related events and clinical outcomes have been associated with the fibrosis stage.

Measuring collagen content is emerging as a reliable method of quantifying liver fibrosis and has shown evidence of being an effective tool in patients with PBC.

Second harmonic generation (SHG) microscopy is a new tissue imaging technology that allows the accurate quantification of several collagen parameters on unstained tissue sections.

Obeticholic acid (OCA) is a selective, potent farnesoid X receptor (FXR) agonist approved as a second-line therapy in patients with PBC and an inadequate response to or intolerance of ursodeoxycholic acid (UDCA).

Approval is based on a surrogate end-point of biochemistry (alkaline phosphatase [ALP] and bilirubin).

OBJECTIVE

- To assess the effect of OCA treatment on collagen morphology in patients with PBC.
- To evaluate the relationship between collagen morphometry and liver function tests.
- To assess the safety of OCA treatment.

METHODS

- This post-hoc analysis assessed the impact of 3 years of OCA treatment on collagen morphology using biopsy samples from the PBC OCA International Study of Efficacy (POISE) study.
- All patients received OCA for 3 years, after which they continued to receive a placebo in an extension study.
- A subgroup analysis was performed.
- Data are mean (standard deviation) unless otherwise indicated.
- Figure 1: Collagen Morphometry vs Nakamura Fibrosis Score (N=30 subjects, 46 slides).
- Table 1: Baseline characteristics
- Table 2: Cumulative Safety Across 3 Years of OCA Treatment
- Figure 2: Individual Patient Collagen Morphometry From Baseline to Follow-Up (N=16)
- Figure 3: Percent Change From Baseline in Collagen Morphometry and the Fibrosis Composite Score (N=16)
- Figure 4: Collagen Morphometry Heat Map (N=16)
- OCA treatment resulted in improvements in most collagen parameters in most patients as observed qualitatively by a trained pathologist.
- The majority of patients with PBC receiving 3 years of OCA treatment in this study showed improvements or stabilization in collagen morphology.
- Significant reductions were observed in collagen area ratio, collagen fiber density, and collagen reticulation index as assessed by SHG/2PE microscopy.
- Morphometric measures of fibrosis increased with increasing histologic disease severity as assessed by the Nakamura fibrosis score, suggesting the potential validity of collagen measurements by SHG/2PE microscopy.
- The data from this POISE subgroup analysis support the hypothesis that patients with an inadequate response to UDCA, 3 years of OCA treatment results in an improvement or stabilization in fibrosis progression.

CONCLUSIONS

- The majority of patients with PBC receiving 3 years of OCA treatment in this study showed improvements or stabilization in collagen morphology.
- Significant reductions were observed in collagen area ratio, collagen fiber density, and collagen reticulation index as assessed by SHG/2PE microscopy.
- Morphometric measures of fibrosis increased with increasing histologic disease severity as assessed by the Nakamura fibrosis score, suggesting the potential validity of collagen measurements by SHG/2PE microscopy.
- The data from this POISE subgroup analysis support the hypothesis that patients with an inadequate response to UDCA, 3 years of OCA treatment results in an improvement or stabilization in fibrosis progression.

REFERENCES