

**Figure 2.** Mean (SD) change from BL in ALP levels through month 72 by biochemical subgroup. ALP, alkaline phosphatase; BL, baseline; OCA, obeticholic acid; SD, standard deviation; ULN, upper limit of normal. <sup>a</sup> $P < .05$  vs BL. Adapted from Bowlus CL et al. AASLD abstract 1250. *Hepatology*. 2020;72(suppl 1).<sup>4</sup>

among patients with bilirubin less than or equal to the ULN at baseline. After 72 months of treatment, patients who had ALP of greater than 3 times the ULN at baseline experienced a mean change in ALP of  $-266.3$  U/L (Figure 2). Patients who had ALP of 3 times the ULN or less at baseline experienced a mean change of  $-63.9$  U/L. For ALT, the mean change after 72 months of OCA treatment was  $-48.9$  U/L among patients who had ALP above 3 times the ULN at baseline, and  $-20.9$  U/L among patients who had ALP of 3 times the ULN or less at baseline. For AST, the respective mean changes were  $-27.3$  U/L and  $-9.3$  U/L.

Among the 142 patients whose ALP was 3 times the ULN or less at baseline, 8 (6%) reached a Model for End-Stage Liver Disease (MELD) score (an indicator of liver disease severity) of 15 or more after having a baseline MELD score of less than 12. By comparison, 5 of the 51 patients (10%) in the group with ALP above 3 times the ULN at baseline experienced this change in MELD score. Pruritus was the most common adverse event in all of the subgroups over 72 months of OCA treatment.

The researchers concluded that long-term OCA was effective and well tolerated, with lasting improvements

in meaningful markers of liver injury and cholestasis, regardless of baseline ALP and total bilirubin.

## References

1. Younossi ZM, Bernstein D, Shiffman ML, et al. Diagnosis and management of primary biliary cholangitis. *Am J Gastroenterol*. 2019;114(1):48-63.
2. Hirschfield GM, Dyson JK, Alexander GJM, et al. The British Society of Gastroenterology/UK-PBC primary biliary cholangitis treatment and management guidelines. *Gut*. 2018;67(9):1568-1594.
3. Nevens F, Andreone P, Mazzella G, et al; POISE Study Group. A placebo-controlled trial of obeticholic acid in primary biliary cholangitis. *N Engl J Med*. 2016;375(7):631-643.
4. Bowlus CL, Trauner M, Liberman A, et al. Long-term efficacy and safety of obeticholic acid in patients with PBC from the POISE trial grouped biochemically by risk of disease progression [AASLD abstract 1250]. *Hepatology*. 2020;72(suppl 1).

## Long-Term Efficacy and Safety of Obeticholic Acid in Primary Biliary Cholangitis: Responder Analysis of More Than 5 Years of Treatment in the POISE Trial

The 12-month double-blind phase of the POISE trial had a primary endpoint of ALP of less than 1.67 times the ULN, a reduction of at least 15% in ALP from baseline, and total bilirubin of less than or

equal to the ULN.<sup>1</sup> After this initial phase, PBC patients were able to enroll in a 5-year, open-label extension.

An analysis presented in a poster at the AASLD 2020 Liver Meeting Digital Experience assessed the safety

and efficacy of OCA treatment over 5 years by comparing responders and incomplete responders.<sup>2</sup> The former were defined as patients who achieved the POISE primary endpoint after 1 year of OCA treatment and the latter

were defined as patients who did not.

The researchers found that 95 responders (48%) and 101 incomplete responders (52%) had ALP of less than 1.67 times the ULN, 179 responders (91%) and 18 incomplete responders (9%) had total bilirubin of less than or equal to the ULN, and 131 responders (67%) and 65 incomplete responders (33%) experienced a decrease in ALP of at least 15%.

The researchers analyzed changes from baseline in ALP, ALT, AST, GGT, and bilirubin (total and direct) for responders and incomplete responders. Figure 3 shows the mean change from baseline in ALP for responders

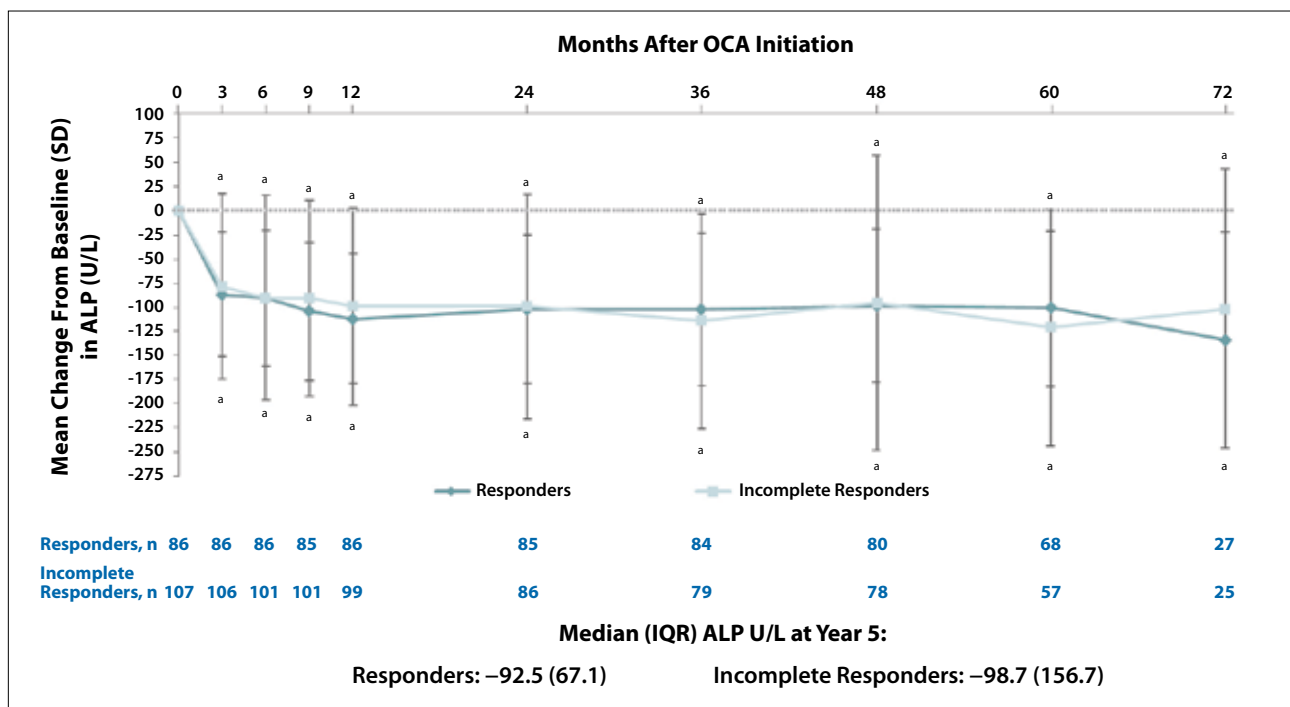
and incomplete responders. The mean change from baseline at year 5 for responders and incomplete responders was  $-19$  U/L and  $-28$  U/L, respectively, for ALT;  $-9$  U/L and  $-16$  U/L, respectively, for AST; and 155 U/L and 165 U/L, respectively, for GGT. In addition, responders and incomplete responders experienced similar mean changes from baseline in direct bilirubin over the 72 months of the extension study. Pruritus was the most common adverse event among both responders and incomplete responders, but caused few patients to discontinue treatment.

The researchers concluded that OCA improved important biochemi-

cal markers of PBC, regardless of meeting the POISE primary endpoint, following 1 year of treatment with OCA. Changes in biochemical markers over time were frequently similar between groups, suggesting that the POISE primary endpoint does not completely capture the benefit of OCA.

## References

1. Nevens F, Andreone P, Mazzella G, et al; POISE Study Group. A placebo-controlled trial of obeticholic acid in primary biliary cholangitis. *N Engl J Med*. 2016;375(7):631-643.
2. Hansen BE, Jones D, Carbone M, et al. Long-term efficacy and safety of obeticholic acid in primary biliary cholangitis: responder analysis of more than 5 years of treatment in the POISE trial [AASLD abstract 1251]. *Hepatology*. 2020;72(suppl 1).



**Figure 3.** Mean (SD) change from baseline in ALP levels through month 72 by responder subgroup. <sup>a</sup> $P < .05$  vs baseline. ALP, alkaline phosphatase; IQR, interquartile range; OCA, obeticholic acid; SD, standard deviation. Adapted from Hansen BE et al. AASLD abstract 1251. *Hepatology*. 2020;72(suppl 1).<sup>2</sup>

## ENHANCE: Safety and Efficacy of Seladelpar in Patients With Primary Biliary Cholangitis—A Phase 3, International, Randomized, Placebo-Controlled Study

Seladelpar is currently under investigation as a second-line treatment for PBC.<sup>1</sup> It is a potent and selective peroxisome prolif-

erator-activated receptor (PPAR)-delta agonist, targeting a receptor found in hepatocytes, cholangiocytes, Kupffer cells, macrophages, and stellate cells—

cell types that play a key role in liver disease. PPAR-delta agonism with seladelpar is both anti-inflammatory and antifibrotic. This approach also