ABSTRACT SUMMARY Durability of Biochemical Improvements Through Six Years of Open-Label Treatment With Obeticholic Acid in Patients With Primary Biliary Cholangitis Who Did Not Achieve the POISE Criteria

This analysis (EASL abstract FRI146) looked at whether the 107 patients with PBC who did not reach the primary endpoint criteria in the POISE study could achieve a durable and meaningful response to OCA with extended treatment. With continued OCA, patients experienced a durable and significant reduction in ALP. Total bilirubin remained within the normal range, as did direct bilirubin. Other disease markers were also reduced, including ALT, AST, and GGT. Adverse events followed the same patterns seen in the POISE study, with pruritus and fatigue being the most common issues over the full 6-year study period. Long-term studies are needed to confirm whether these outcomes lead to a reduction in hepatic complications, the need for liver transplantation, and mortality rates.

with bezafibrate. It is important to note that 98% of patients treated with bezafibrate received this drug in combination with UDCA.

The researchers also looked at mortality data. According to their analysis, 37% of patients who had never been treated died of any cause and 28% died from liver-related issues. Among patients treated with UDCA, the death rates were 12% and 7%, respectively, and among patients treated with bezafibrate-containing therapy, the death rates were 3% and 2%, respectively. Figure 8 shows the survival curve according to treatment exposure.

Limitations of this study include the exclusion of significant numbers of patients from the analyses, unclear risk profiles of the patients who received bezafibrate compared with patients treated with UDCA, and the younger age and lower bilirubin of patients treated with bezafibrate compared with patients treated with UDCA (which may affect survival).

Tanaka and colleagues concluded that bezafibrate combination therapy is associated with a statistically significant reduction in both mortality and the need for liver transplantation in patients who had an incomplete response to first-line treatment with UDCA.

References

1. Honda A, Ikegami T, Nakamuta M, et al. Anticholestatic effects of bezafibrate in patients with primary biliary cirrhosis treated with ursodeoxycholic acid. *Hepatology.* 2013;57(5):1931-1941.
2. Corpechot C, Chazouillè O, Rousseau A, et al. A placebo-controlled trial of bezafibrate in primary biliary cholangitis. *N Engl J Med.* 2018;378(23):2171-2181.
3. Tanaka A, Hirohara J, Nakano T, et al. Bezafibrate add-on therapy improves liver transplantation-free survival in patients with primary biliary cholangitis: a Japanese nationwide cohort study [EASL abstract GS01]. *J Hepatol.* 2020;73(suppl 1).

GLIMMER Trial—A Randomized, Double-Blind, Placebo-Controlled Study of Linerixibat, an Inhibitor of the Ileal Bile Acid Transporter, in the Treatment of Cholestatic Pruritus in Primary Biliary Cholangitis

Cholestatic pruritus is a common issue for individuals diagnosed with PBC, and it detracts from quality of life.[1] Linerixibat, a minimally absorbed oral small molecule of the human ileal bile acid transporter, may treat cholestatic pruritus in this disease setting.[2,3]

An international group of researchers conducted a study to examine the dose response and tolerability of linerixibat for cholestatic pruritus in patients with PBC, and findings were presented in a poster at the AASLD 2020 Liver Meeting Digital Experience.[4] The researchers randomized 147 patients to treatment with a range of linerixibat doses—40 mg twice daily,

ABSTRACT SUMMARY The Pervasive Impact of Pruritus on Quality of Life in Patients With Primary Biliary Cholangitis: Real-World Experience in TARGET-PBC

This study assessed how pruritus affects quality of life for patients with PBC (AASLD abstract 1276). Using data from TARGET-PBC, a longitudinal, observational study that is ongoing at 38 sites across the United States, researchers evaluated the PBC-40, 5D Itch, and PROMIS Fatigue questionnaires. Itch that reached 7 points or higher on the itch domain (Mells et al. *Hepatology*. 2013;58[1]:273-283) was defined as clinically significant. Among the 211 patients who completed the PBC-40, 63% reported mild itch and 37% reported clinically significant itch. Patients with clinically significant itch reported more cognitive and social issues compared with patients who had only mild itch. These scores were an estimated 80% higher for the former group. Fatigue and emotional issues were also different between the 2 groups, but less so.

90 mg twice daily, 180 mg once daily, 20 mg once daily, and 90 mg once daily—or placebo. Linerixibat dose level assignments were determined according to ALP and total bilirubin levels. Treatment was single-blinded for 4 weeks, double-blinded for 12 weeks, and then single-blinded for a final 4 weeks, followed by a 4-week follow-up period.

The primary endpoint of the trial was the mean change from baseline in the mean score for worst daily itch, 16 weeks after study entry. The researchers also evaluated itch efficacy, quality of life (measured using the PBC-40 questionnaire), and pharmacodynamic biomarkers, as well as the safety and tolerability of linerixibat.

Most of the patients were female and over 50 years of age. Most patients were white, but approximately one-quarter were Japanese, East Asian, or South East Asian. Every morning and evening during the study, patients recorded their worst itch severity in an eDiary, using a numeric rating scale of 0 to 10; the worse of these scores was recorded as the worst daily itch.

All patients experienced a reduction in their worst daily itch score from baseline. For the placebo group (36 patients), that change was –1.73. The other groups had more dramatic reductions: –2.19 in the 20-mg once-daily group (16 patients), –2.60 in the 90-mg once-daily group (23 patients), –2.60 in the 180-mg once-daily group (27 patients), –2.86 in the 40-mg twice-daily group (23 patients), and –2.25 in the 90-mg twice-daily group (22 patients). The change in worst itch score between the start and end of the study was statistically significantly different between the placebo group and patients receiving linerixibat doses of 180 mg once daily, 40 mg twice daily, and 90 mg twice daily.

In terms of quality of life, only the group receiving 40 mg twice daily of linerixibat reported a statistically significant social and emotional improvement after 12 weeks. Regarding safety, 19% of patients in the placebo arm and 31% to 78% of patients in the treatment arms reported drug-related adverse events. The most common adverse event was diarrhea, experienced by up to 64% of patients, with 10% of patients withdrawing due to diarrhea or abdominal pain.

ABSTRACT SUMMARY Predicted Risk of End-Stage Liver Disease Utilising the UK-PBC Risk Score With Continued Standard of Care and Subsequent Addition of Obeticholic Acid for 60 Months in Patients With Primary Biliary Cholangitis

This analysis (EASL abstract THU114) evaluated the change in predicted risk of end-stage liver disease with the UK-PBC model in patients in the POISE study who had received placebo during the double-blind phase and then transitioned to OCA during the open-label extension for up to 60 months. Seventy-three patients were randomized to placebo; 70 completed the double-blind phase and 66 enrolled in the open-label extension. The UK-PBC risk score predicted a trend for increased risk of end-stage liver disease in PBC patients treated with placebo for 12 months in addition to standard of care. The addition of OCA reduced the predicted risk of end-stage liver disease for up to 60 months of treatment. This approach also led to sustained improvements in serum biochemistry.

ABSTRACT SUMMARY Final Data of the Phase 2a INTREPID Study With EDP-305, a Non–Bile Acid Farnesoid X Receptor Agonist

In the INTREPID study (AASLD abstract 1242), 68 patients with PBC were randomized to 12-week treatment with EDP-305, which has been shown to suppress liver injury and fibrosis in animal models, vs placebo. All patients were female and white, and the average age was 57 years. The intent-to-treat analysis found that among the 31 patients treated with EDP-305 1 mg, 45% experienced a response in ALP levels. For the 28 patients who received EDP-305 2 mg, that rate was 46%. By comparison, patients receiving placebo (9) had an ALP response rate of 11%. The absolute change in ALP among the EDP-305 arms was statistically significantly different from that seen with placebo. However, the study did not meet its primary endpoint of a 20% reduction in ALP.

References

1. Hegade VS, Mells GF, Fisher H, et al; UK-PBC Consortium. Pruritus is common and undertreated in patients with primary biliary cholangitis in the United Kingdom. *Clin Gastroenterol Hepatol*. 2019;17(7):1379-1387.e3.

2. Ino H, Endo A, Wakamatsu A, Ogura H, Numachi Y, Kendrick S. Safety, tolerability, pharmacokinetic and pharmacodynamic evaluations following single oral doses of GSK2330672 in healthy Japanese volunteers. *Clin Pharmacol Drug Dev*. 2019;8(1):70-77.

3. Hegade VS, Kendrick SFW, Dobbins RL, et al. Effect of ileal bile acid transporter inhibitor GSK2330672 on pruritus in primary biliary cholangitis: a double-blind, randomised, placebo-controlled, crossover, phase 2a study. *Lancet*. 2017;389(10074):1114-1123.

4. Levy C, Kendrick S, Bowlus C, et al. GLIMMER trial: a randomized double-blind placebo-controlled study of linerixibat, an inhibitor of the ileal bile acid transporter, in the treatment of cholestatic pruritus in primary biliary cholangitis [AASLD abstract LP38]. *Hepatology*. 2020;72(suppl 1).