P22 OBETICHOLIC ACID IMPROVES TRANSAMINASES IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS: RESULTS FROM THE 18-MONTH INTERIM ANALYSIS OF THE REGENERATE STUDY

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10.1136/gutjnl-2020-BASL.33

In the REGENERATE interim analysis, obeticholic acid (OCA) improved liver histology in patients with non-alcoholic steatohepatitis (NASH). Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels may be associated with fibrosis progression in NASH. We evaluated OCA-mediated improvement in these transaminases, and their utility in monitoring treatment of NASH patients with fibrosis.

REGENERATE NASH patients with stage 2 or 3 fibrosis (N=931) were randomized 1:1:1 to placebo, OCA 10 mg, or OCA 25 mg. Changes in ALT and AST (upper limit of normal [ULN], 55 U/L and 34 U/L, respectively) were analysed.

Baseline characteristics were well balanced across groups (mean ± SD): age (55±11 years), ALT (79±53 U/L), AST (58 ±36 U/L); ALT >ULN, 60% (>3×ULN, 8%); AST >ULN, 73% (>3×ULN, 9%). OCA treatment improved transaminase levels at Month 1 through Month 18. In patients with baseline ALT and AST >ULN, ALT normalized in 36% (placebo), 49% (OCA 10 mg), and 66% (OCA 25 mg), and AST normalized in 28%, 42%, and 49% in the respective groups by Month 18. In patients with normal baseline transaminases, elevations to >ULN were greater for placebo than OCA 10 mg or OCA 25 mg. OCA-mediated improvements in transaminases were greater in patients who achieved the REGENERATE primary endpoints (figure 1).

OCA treatment rapidly improved and sustained ALT and AST, suggesting transaminase may be useful in monitoring treatment response. OCA-treated patients who did not achieve REGENERATE primary endpoints also had marked improvement in transaminases, suggesting longer-term treatment may result in additional histologic improvement.

P23 PREDICTED RISK OF END-STAGE LIVER DISEASE UTILIZING THE UK-PBC RISK SCORE WITH CONTINUED STANDARD OF CARE AND SUBSEQUENT ADDITION OF OCA FOR 60 MONTHS IN PATIENTS WITH PBC

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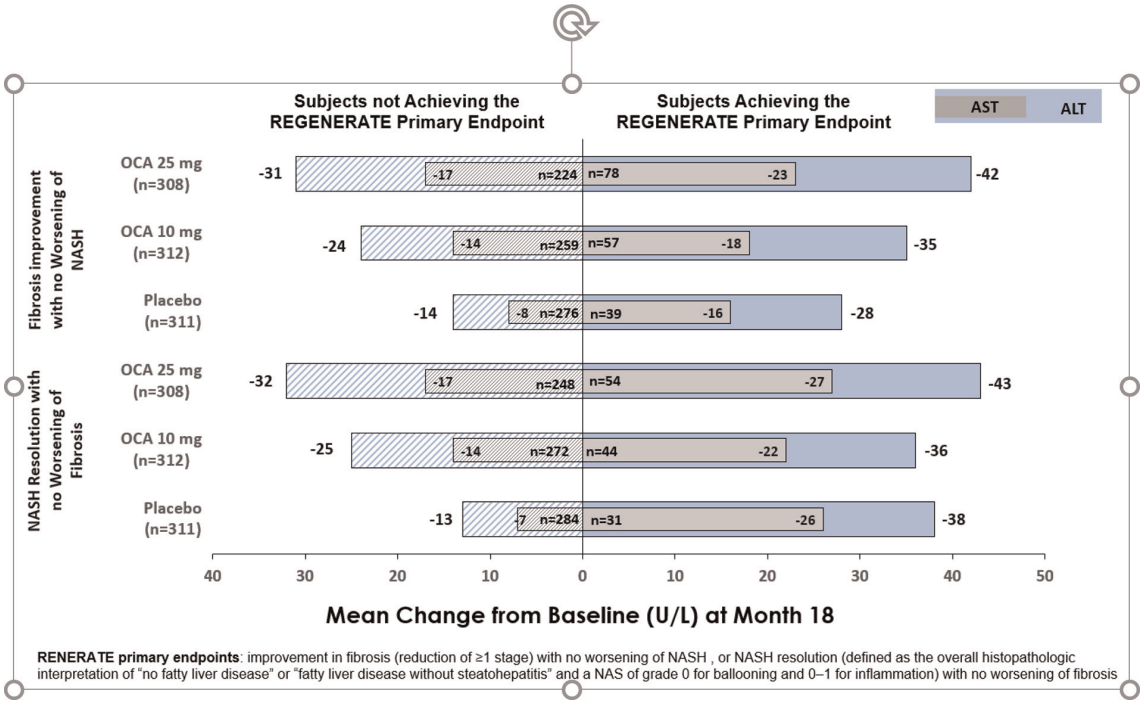
10.1136/gutjnl-2020-BASL.34

The UK-PBC Study group validated a long-term prognostic model of primary biliary cholangitis (PBC) that identified independent predictors of end-stage liver disease (ESLD). POISE was a randomized, double-blind (DB), placebo-controlled 12-month Phase 3 trial investigating obeticholic acid (OCA) treatment of PBC; a 5-year open-label extension (OLE) followed. We assessed the change in predicted risk of ESLD with the UK-PBC model in placebo patients (DB phase) who transitioned to OCA (OLE).

POISE inclusion criteria: PBC diagnosis, alkaline phosphatase ≥1.67x upper limit of normal (ULN) and/or total bilirubin >ULN to <2x ULN, stable ursodeoxycholic acid (UDCA) dose or intolerant to UDCA. 73 patients were randomized to placebo; 66 enrolled in the OLE. Baseline, DB month 12, and OLE data through 60 months of OCA treatment were included in the UK-PBC algorithm to assess predicted risk of ESLD at 5, 10, and 15 years.



Abstract P22 Figure 1 Changes in ALT and AST by responder status in REGENERATE primary endpoints