The median age at baseline in the placebo group was 55 years; 93% were female, and 93% received daily UDCA (median dose, 15 mg/kg). After 1 year of standard-of-care (SOC), placebo patients demonstrated a slight increase in predicted risk of ESLD (table 1). After 1 year of OCA, predicted risk of ESLD at 5, 10, and 15 years was reduced to below baseline levels; these were sustained through the 60-month OLE.

In POISE, the UK-PBC risk score predicted an increased risk of ESLD in PBC patients treated with SOC and placebo for 12 months. OCA treatment led to sustained reductions in predicted risk of ESLD through 60 months.

The global pooled prevalence of NAFLD is 25% (Youssoufi 2016). Genetic factors have been shown to play a significant role in determining the risk for the development and progression of NAFLD in Caucasian/East Asian populations where robustly replicated associations have been found, many at genome-wide significance, with variants in PNPLA3, MBOAT7, TM6SF2, GCKR and HSD17B13, showed much lower significance than expected (p value range 1.93 × 10⁻⁸ to 5.83 × 10⁻⁶) including SNPs in chromosome 20 open reading frame 78 (C20orf78), Transmembrane Protein 63C (TMEM63C), Bromodomain Adjacent To Zinc Finger Domain 1A (BAZ1A), Fibroblast Growth Factor 21 (FGF21), and Insulin Receptor Substrate 1 (IRS1). Variants in previously associated loci viz PNPLA3, MBOAT7, TM6SF2, GCKR and HSD17B13, showed much lower significance than expected (p value range 1.20 × 10⁻³ to 0.730).

These findings suggest that there may be divergence in the genetic risk profile for developing NAFLD in the South Asian population compared with European/East Asian populations. This is concordant with the observed divergence in NAFLD phenotype, but needs to be validated in further, larger cohorts.

ND, JC, GM share first authorship. MM, KS, GA share senior authorship.

No associations were identified with NAFLD at genome-wide significance (p < 5 × 10⁻⁸). However, a number of genetic variants implicated in liver-related and metabolic pathology showed suggestive evidence of association (p value range 1.93 × 10⁻⁸ to 5.83 × 10⁻⁶) including SNPs in chromosome 20 open reading frame 78 (C20orf78), Transmembrane Protein 63C (TMEM63C), Bromodomain Adjacent To Zinc Finger Domain 1A (BAZ1A), Fibroblast Growth Factor 21 (FGF21), and Insulin Receptor Substrate 1 (IRS1). Variants in previously associated loci viz PNPLA3, MBOAT7, TM6SF2, GCKR and HSD17B13, showed much lower significance than expected (p value range 1.20 × 10⁻³ to 0.730).

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