Background and Aims: One in three people who undergo liver transplantation (LT) for primary biliary cholangitis (PBC) develop disease recurrence. Ursodeoxycholic acid (UDCA) given prophylactically post-LT has been shown to reduce the risk of recurrent PBC (rPBC); and when administered as first-line treatment, slows liver disease progression. The aim of this international, multicentre study was to assess the efficacy and safety of currently available second-line treatments (SLTs) in the context of rPBC.

Method: We collected demographic, clinical and laboratory data from patients (pts) with PBC who underwent liver transplantation from 1999 to 2023, across six centres in Europe and North America. Eligible pts had biopsy proven disease recurrence, in the absence of biochemical dysfunction attributable to post-LT biliary strictures, hepatic arterial complications or allograft rejection, and who were treated with SLTs (obeticholic acid [OCA] or fibric acid derivatives [FA derivatives]). Biochemical trends, alongside discontinuation rates and tolerability data was accrued over a 12-month period from the point of starting second-line therapy.

Results: Over the course of the study, 21 individuals with rPBC were treated with SLT (10 OCA, 11 FA derivatives). In all, 15 study pts were women, with a median age of PBC diagnosis and at time of LT of 41y (IQR 35-49) and 46y (IQR 39-51), respectively. All pts were offered UDCA post-LT; however, nine were deemed UDCA-intolerant and discontinued therapy prior to starting SLT. The median time from transplantation to rPBC was 1035 days (IQR 684-1531 days; earliest diagnosis being made 183 days post-LT). The median transient elastography score at time of PBC recurrence was 8.80 (IQR 6.30-12.2) kPa. In total, 16, 14 and 14 pts completed 3, 6 and 12 months of follow up on SLT. Five pts discontinued OCA due to concerns over liver disease progression (n=3), drug intolerance (n=1) or pruritus (n=1). Four pts discontinued FA derivatives due to renal dysfunction (n=2) or concerns over liver disease progression (n=2). Three pts were referred for re-transplantation and 5 patients died (4 liver-related deaths). At 3, 6 and 12 months of OCA treatment, median percentage reduction in serum ALT from baseline were 8.3% (4.6%-11.5%; p=0.08), 42.4% (31.6%-51.3%; p=0.02), 30.3% (21.4%-45.4%; p=0.40) whereas median reduction in serum ALP were 17.8% (11.5%-24.6%; p=0.38), 30% (19%-39.4%; p=0.22) and 3.9% (1.4%-6.7%; p=0.40) at 12 months. In turn, median ALT reduction in the FA derivative group at 3, 6 and 12 months were 8%(4.1%-11.7%; p= 0.1), 16.2% (7.6%-25.6%; p=-0.19) and 8.1% (3.9%-17.4%; p=0.65) and for ALP were 25% (11.4-37.3%; p=0.03), 34.84% (25.6%-49.1%; p=0.01) and 34.8% (27.6%-45.4%; p=0.05), respectively.

Conclusions: This is the first, real world study assessing SLT in rPBC. Both OCA and FA derivatives appear safe after LT in rPBC and resulted in reduction in biochemical parameters with similar discontinuation rates.