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### Improvement in GGT predicts event-free survival in primary sclerosing cholangitis regardless of ursodeoxycholic acid treatment: data from the Pediatric PSC Consortium

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**Background:** Ursodeoxycholic acid (UDCA) is commonly used to treat primary sclerosing cholangitis (PSC) in children. Randomized-controlled trials in adults with PSC demonstrate that UDCA does not improve survival with native liver. We evaluated the effect of UDCA on clinical and biochemical outcomes in children with PSC using a large, multicenter cohort. **Methods:** The pediatric PSC consortium is a research collaboration between 36 international centers. We recorded liver biochemistries at diagnosis and 1 year, and UDCA treatment status. Survival analysis from PSC diagnosis to several clinical events was performed: 1) portal hypertensive complications (ascites, encephalopathy, varices), 2) biliary complications (dominant stricture requiring dilation, stenting or drainage), 3) liver transplantation (LT), 4) cholangiocarcinoma (CCA) or 5) liver-related death. A biochemical response (BR) was defined as GGT >50 U/L at diagnosis that was <50 at 1

year. The probability of event-free survival at 5 years was calculated among four groups: UDCA treated (T) and untreated (U) patients, with or without BR. Results: The cohort consisted of 309 patients, 40% female, mean age at diagnosis 11.4 years, with 2026 person-years of follow-up (mean 6.6 years). Inflammatory bowel disease (IBD) occurred in 84%, autoimmune hepatitis (AIH) in 39%, and large duct involvement in 74% studied patients. UDCA was used in 81% patients at a mean dose of 17 mg/kg/day. T and U patients had similar mean liver biochemistries at diagnosis [GGT 314 vs. 300 U/L; ALT 239 vs. 175 U/L (p=NS)], lower values at 1 year [GGT 99 vs. 175 (p=0.002); ALT 63 vs. 96 (p=0.008)], and greater reduction in values over the first year [GGT decreased by 215 vs. 125 (p=0.039) and ALT decreased by 175 vs. 79 (p=0.037)]. BR occurred in 45% overall. Patients with and without BR had similar baseline liver biochemistries, AST to platelet ratio index, age and prevalence of IBD, AIH and large duct involvement (all p=NS). Despite biochemical improvement, T and U patients had similar rates of adverse events: portal hypertensive complications 19 vs. 18%, biliary complications 6 vs. 8%, LT 11 vs. 12%, CCA 1 vs. 0%, and death 1 vs. 0% (all p=NS). The 5-year event-free survival was 91% in patients with BR (90% in T vs. 100% in U, p=0.45) and 67% in patients without BR (66% in T vs. 69% in U, p=0.96), p<0.001. **Conclusions:** UDCA treatment was associated with improvement in GGT and ALT, but not reduction in rates of adverse clinical outcomes. Patients with GGT <50 at one year did markedly better than those with GGT >50, regardless of UDCA treatment. These data support GGT as a surrogate marker of clinical outcomes in pediatric PSC.

**Disclosures:**

Katryn Furuya - Advisory Committees or Review Panels: Alexion; Speaking and Teaching: Alexion

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### FXR Agonist GW4064 Prevents Parenteral Nutrition Associated Cholestasis (PNAC) in Mice

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**Background:** Parenteral nutrition (PN) associated cholestasis (PNAC) complicates the care of patients with intestinal failure. In mice and humans, phytosterol (PS)-containing PN synergizes with intestinal injury to suppress FXR signaling and promote PNAC. Here we hypothesized that pharmacological activation of FXR would prevent PNAC. **Methods and Results:** Combining intestinal injury (oral dextran sulfate sodium (DSS)) with continuous infusion of PS-containing PN (DSS/PN mice) x 14 days resulted in PNAC (increased serum bilirubin, bile