Ileal bile acid transporter inhibition corrects protein-losing enteropathy post-liver transplant in progressive familial intra-hepatic cholestasis type 1 and allows safe reversion of internal biliary diversion.

Background: Protein-losing enteropathy (PLE) complicates liver transplantation (LT) in progressive familial intra-hepatic cholestasis type 1 (PFIC1) patients [1], supposedly due to inability of the native bowel to process the restored normal bile flow. Subsequent diarrhea, malnutrition, failure to thrive and abdominal pain drastically impair quality of life (QOL). Surgical biliary derivation (BD) reverts PLE, but can cause severe diarrhea, fat and vitamin malabsorption inducing essential fatty acid deficiency. We report the efficacy of ileal bile acid transporter inhibitors (IBATi) as a safer alternative to BD.

Materials and methods: Two PFIC1 patients suffered from severe post-LT PLE. Patient 1 had chronic diarrhea, hypoproteinemia and failure to gain weight. Patient 2 had undergone for the same reasons an internal colonic BD which corrected PLE [1], complicated by severe watery diarrhea, fat malabsorption, essential fatty acid deficiency, requiring Q2W parenteral lipids and vitamins administration. Odevixibat (Ipsen, Paris, France) was prescribed to both patients with the scope of healing PLE in patient 1 and to prevent its recurrence after reverting colonic to jejunal bile flow in patient 2. Diarrhea, abdominal pain and QOL were scored according to Patient Reported Outcome 3 (PRO3) scale [2].

Results: In patient 1, odevixibat resolved diarrhea and abdominal pain, allowed weight gain and normalized serum proteins (Table 1). In patient 2, jejunal bile flow was restored under odevixibat with no recurrence of PLE, weight gain, decrease of watery diarrhea and abdominal pain and stable biochemical values (Table 1). QOL significantly improved in both patients following IBATi introduction.

Conclusion: IBATi cured PLE and prevented recurrence of PLE after restoring jejunal bile flow in our patients, supporting to maintain PFIC1 patients under IBATi after LT as a safer alternative to BD and providing evidence that IBATi may allow to revert poorly tolerated BD.

(1) *Nicastro & al, Pediatr Transplant 2012*
(2) *Khanna & al, Aliment Pharmacol Ther 2015*

	Patient 1	**Patient 2**
Age at LT	2 years	3 years
Timing of PLE development	2 months post-LT	1 month post-LT
Surgical BD attempt	No	Yes (2 years post-LT)
Age at IBATi start	13 years	19 years
FU under IBATi	15 months	3 months
IBATi dosage	40 µg/kg/d	120 µg/kg/d
Follow up under IBATi:		
Average stool number per day	8 → 1	7 → 4
Abdominal pain score	2 (moderate) → 0 (none)	3 (severe) → 1 (mild)
General well-being score	3 (very poor) → 0 (generally well)	3 (very poor) → 0 (generally well)
Weight (Z-score)	-2.8 → -0.89	-1.63 → -1.32
Albumin (g/L) (>35)	27 → 45	41 → 41
Gammaglobulins (g/L) (>7)	5.1 → 8.84	14 → 15.39
ALT (UI/L) (< 40)	289 → 343	38 → 24
AST (UI/L) (<40)	187 → 181	41 → 31
GGT (UI/L) (<60)	117 → 442	41 → 53

Table 1. Patient's characteristics. BD: biliary diversion; IBATi: ileal bile acid transporter inhibitors; LT: liver transplantation; PLE: protein-losing enteropathy.