Abstract PTU-007 Figure 1

Conclusion In conclusion, the MMP28 gene knockout effect and the change of gut microbiome upon changing living environments influence the metabolic profile through modulations in the insulin and FXR signalling pathways.

PTU-008 DIABETES MELLITUS IN PATIENTS WITH AUTOIMMUNE HEPATITIS (AIH): AT DIAGNOSIS AND FOLLOWING PREDNISOLONE TREATMENT

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Introduction Patients receiving corticosteroids are at increased risk of new-onset diabetes mellitus (NODM), related to steroid dose and duration and which may persist despite steroid withdrawal. Treatment of Autoimmune Hepatitis (AIH) remains corticosteroid-based, yet there are few data on NODM in patients with AIH. We sought to assess the incidence, time course and risk factors for NODM in patients with AIH, treated with prednisolone.

Methods Retrospective single-centre audit of patients with AIH (1999 IAHG criteria), presenting 1987–2016. We collected data on age, gender, BMI, ethnicity, diagnosis and treatment of diabetes, corticosteroid dose/duration and presence of cirrhosis at AIH diagnosis. NODM was defined according to World Health Organization criteria or commencement of drug treatment for diabetes mellitus.

Results Of 309 informative patients (80% women, 92% White British, age (mean) 55 years and BMI 28 at AIH diagnosis), 30 (10%) already had diabetes mellitus at diagnosis of AIH (Type 2 in 27, Type 1 in 3); these were older than those without diabetes (mean±SD 62±15 vs 53±19 years; $p=0.013$) and had higher BMI (30 ± 7 vs 27 ± 6 ; $p=0.07$). Of the remaining 279 patients, 254 were treated with prednisolone, of which 49 (19%) subsequently developed NODM (Type 2 in 47, Type 1 in 2). Rate of NODM development was $7\pm2\%$, $10\pm2\%$, $13\pm2\%$, $16\pm2\%$ and $21\pm3\%$ after 3, 12, 36, 60 and 120 months respectively. In 25 non-diabetic patients who did not receive prednisolone (1 received budesonide, 24 untreated), rate of NODM was lower (1 patient, 14 years after AIH diagnosis; $p=0.08$).

Patients who developed NODM following prednisolone were older (mean±SD 55±14 vs 53±18 years; $p=0.006$), more overweight (BMI 30 ± 7 vs 27 ± 5 ; $p=0.019$) at AIH diagnosis and were more likely to be Asian or African-Caribbean (9/49 vs 12/205 patients) ethnicity than those that did not do so. Independent risk factors for developing NODM on Cox multivariate analysis were: higher BMI at AIH diagnosis ($p=0.001$); Asian or African-Caribbean ethnicity ($p=0.003$); older age at commencing prednisolone treatment ($p=0.008$) and initial dose of prednisolone ≥ 40 mg/day ($p=0.038$). For NODM developing within 12 months, cirrhosis was also a risk factor ($p=0.013$), along with Asian or African-Caribbean ethnicity and initial prednisolone dose ≥ 40 mg/day.

Of 42 patients followed up, NODM resolved in only 1 of 20 following prednisolone discontinuation and in 3 patients in whom prednisolone dose was reduced.

Conclusions NODM is common in patients with prednisolone-treated AIH; risk factors include older age, obesity, Asian or African-Caribbean ethnicity and high initial prednisolone dose. NODM usually persists following prednisolone reduction or withdrawal. In patients with AIH and risk factors for NODM, high-dose prednisolone should be used with caution.

PTU-009 LONG-TERM EFFECTS OF OBETICHOIC ACID IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS ON INFLAMMATORY MARKERS

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Introduction Obeticholic Acid (OCA) is a potent and selective farnesoid X receptor agonist approved for the treatment of primary biliary cholangitis (PBC). PBC is a chronic liver

Abstract PTU-009 Table 1 Median change from Baseline in Key immune, apoptotic and inflammatory markers

Median (Q1,Q3)	Baseline	Δ From Baseline to 36 Months OCA (N=161)	Δ From Baseline to 48 Months OCA (N=120)
CRP mg/L	3 (2,7)	-0.7*** (-2,0.3)	-0.6** (-2,0.5)
TNF- α pg/ml	11 (9,14)	-3*** (-4,-1)	-2*** (-3,-0.4)
TGF- β ng/mL	25 (19,35)	2 (-7,11)	0 (-5,7)
Ck-18 U/L	124 (83,201)	-28*** (-78,15)	-3 (-52,40)
IL-12 pg/mL	138 (94,198)	9 (-21,28)	21** (-6,43)
IgA g/L	2 (2,3)	-0.2*** (-0.5,-0.1)	-0.3*** (-1,-0.1)
IgG g/L	13 (11,15)	-1*** (-2,-0.03)	-1*** (-2,0.2)
IgM g/L	4 (2,6)	-1*** (-2,-0.4)	-1*** (-2,-0.4)

*p<0.05; **p<0.01; ***p<0.0001. p-values for the comparisons to baseline were obtained using a Wilcoxon signed rank test. Normal ranges: CRP 0-3 mg/L, TNF- α 8.1 pg/ml, TGF- β 18.3-63.4 ng/ml, Ck-18 80 U/L, IL-12 34-246 pg/mL, IgA 0.7-4 g/L, IgG 7-16 g/L, IgM 0.4-2.3 g/L

disease characterized by the immune mediated destruction of bile ducts resulting in cholestasis, cirrhosis and liver failure. The POISE study was a randomized, placebo-controlled phase 3 study investigating daily OCA 5–10 mg in PBC patients with an ongoing open label extension (OLE). The purpose of this analysis was to assess the long-term effects of OCA on key markers of liver damage and inflammation.

Methods Patients enrolled in the double-blind phase had an inadequate response to UDCA or were intolerant of UDCA. Patients were randomized to placebo, OCA 5–10 mg, or OCA 10 mg. Upon completion of the 12-month double-blind phase, 198 patients enrolled in the OLE and received OCA. For this analysis, patients were pooled and assessed from the time of first dose of OCA. Data are shown through 48 months of OCA exposure, for patients randomized to placebo in the double-blind phase, only 36 months of data are included.

Results At baseline (N=198), patients were 92% female, mean age was 55 years, PBC disease duration was 9 years, and 93% received UDCA (mean dose: 16 mg/kg/day). As observed in the table, there were sustained and significant reductions in immunoglobulins (Ig) A, G and M throughout 48 months of OCA treatment. In addition, significant reductions were observed in tumor necrosis factor (TNF)- α , c-reactive protein (CRP), and cleaved cytokeratin (CK)-18 throughout the duration of the OLE. No clinically meaningful changes were observed with transforming growth factor (TGF)- β and interleukin (IL)-12, both remained within the normal range.

Conclusions These results demonstrate that OCA has a durable anti-inflammatory effect in patients with PBC as observed by reductions on key markers of apoptosis (TNF- α and CK-18) and inflammation (CRP). Furthermore, a sustained reduction is observed in IgM, which is classically elevated in PBC patients. The clinical significance of OCA mediated reductions in IgA and IgG continues to remain unknown.

PTU-010 ROLE FOR GPR15 RATHER THAN BETA 7 INTEGRINS IN THE PATHOGENESIS OF AUTOIMMUNE LIVER DISEASE

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Introduction G protein-coupled receptor 15 (GPR15) is a chemoattractant receptor that directs homing of lymphocytes to the colon. Furthermore, it has been shown to be a mediator of effector T cell homing during intestinal inflammation. Evidence exists showing infiltration of gut derived $\alpha 4\beta 7$ + and CCR9+ T cells in the hepatic infiltrate of patients with autoimmune liver disease (AILD), in particular primary sclerosing cholangitis (PSC), with expression of their complementary ligands also being identified on the hepatic endothelium. However, the role of GPR15 in hepatic gut T cell homing remains to be defined.

Methods Explanted liver tissue was collected from patients undergoing orthotopic liver transplantation for chronic liver disease (Alcoholic liver disease [ALD] n=3, Non-alcoholic fatty liver disease [NAFLD] n=3, PSC n=4) with healthy control tissue sourced from patients undergoing hepatocellular carcinoma (HCC) resection (n=4). Liver infiltrating lymphocytes (LIL) were isolated using a mechanical homogenisation and centrifugation/filtration technique.

Abstract PTU-010 Figure 1