PWE-080 CHANGE IN BILIRUBIN WITH OBEThICOLIC ACID IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH HIGH BASELINE BILIRUBIN

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Introduction In patients with primary biliary cholangitis (PBC), bilirubin (BILI) is a recognised marker of disease progression and a strong predictor of survival. Recently, the Global PBC Study Group reported risk with elevated BILI extends into the normal range with a cutoff of 0.67 x ULN identifying patients at risk. Obeticholic acid (OCA) is indicated for treatment of PBC in patients with inadequate response or intolerability to ursodeoxycholic acid. This retrospective analysis aimed to evaluate the effect of OCA on BILI in this patient subpopulation.

Methods OCA has been evaluated in patients with PBC in one 12 month (mo) Phase 3 double-blind (DB) placebo (PBO)-controlled trial (POISE) and two 3-mo Phase 2 PBO-controlled trials (201 and 202). Patients were eligible to continue treatment in open-label extensions (OLE) with all patients controlled trial (POISE) and two 3-mo Phase 2 PBO-controlled trials (201 and 202). Patients were eligible to continue treatment in open-label extensions (OLE) with all patients receiving OCA. Patients from the Phase 2 and 3 trials with baseline (BL) total BILI (TBILI) >0.67 x ULN were evaluated for change in TBILI over 12 mo in the following manner: 1) DB comparison of OCA vs PBO at 12 mo in POISE and 2) DB + OLE OCA use totaling 1 year of treatment (POISE randomised to PBO, evaluated at 12 mo OLE; Phase 2 randomised to OCA for 3 mo, evaluated at 9 mo OLE; and Phase 2 randomised to PBO, evaluated at 12 mo OLE).

Results The analysis included patients with TBILI >0.67 x ULN at their OCA BL: POISE, n=51; 201, n=7; and 202, n=7. In patients with BL TBILI >0.67 x ULN, TBILI increased after 12 mo of PBO treatment, and decreased after 12 mo of OCA (table 1). In the DB phase of POISE, of the 7 PBO and 9 OCA patients with abnormal TBILI at BL, 14% of PBO and 78% of OCA patients attained normal TBILI levels after 12 mo. Further, of 10 PBO and 20 OCA patients with normal TBILI at BL, 60% of PBO and 13% of OCA patients worsened to abnormal TBILI after 12 mo.

Conclusions Patients treated with OCA had a trend toward reduction of TBILI compared with those treated with PBO. These data suggest that OCA may reduce progression of patients with more advanced liver disease.

PWE-081 EARLY CHANGE IN ORGAN FAILURE SCORES PREDICTS SURVIVAL IN ACUTE ON CHRONIC LIVER FAILURE

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Introduction Identification of patients with acute-on-chronic liver failure (ACLF) who will benefit from ongoing support on intensive care unit (ICU) remains a challenge. There is no agreed marker of futility or time-point. There has been recent consensus regarding the definition of ACLF grades, and chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score has been adopted. We aimed to determine if evolution in CLIF-SOFA or other markers of disease severity can predict mortality and survival in ACLF patients admitted to ICU.

Methods Prospectively recorded data was collected on 48 ACLF patients admitted to ICU at Guy’s and St Thomas’ hospital, a tertiary non-transplant centre, from May 2013 – May 2016. Scores were calculated at D0, D2, D5, D7.

Results The majority were male (n=34,700.8%), mean age 57.4±10.3 years and major aetiologies were ALD (n=34,700.8%) and viral hepatitis (n=11,290.2%). The major indication for ICU admission was infection (n=29,600.4%). Mean Child-Pugh (CP) score on admission to ICU was 12 ± 2 and the mean MELD 24 ± 9. Mortality at 7, 28 and 90 days was 16/48 (33.3%), 30/48 (62.5%), 36/48 (75%).

The best predictive model proved to be difference in CLIF-SOFA (delta C-SOFA) scores between D2 and D5 or D7. Mean delta C-SOFA D2-D5 was –2.25±1.9 and mean delta C-SOFA D2-D7 was –3.36±2 for survivors compared to 0.19 ± 1.73(p<0.001) and 0±2.58(p=0.001) for deceased at 90 days, with area under curve (AUC) of 0.839 and 0.835, respectively.

The mean survival time (days) for patients with improvement in delta C-SOFA between D2 and D5/D7 was 837 ± 144 and 814±149 vs patients with worsening or static scores 33.8±14.5 (p<0.001) and 37.6±18 (p<0.001). The negative predictive value at D5 and D7 was 95.5% and 94.1%, respectively.

Other prognostic scores at a single time point on D7 predicted survival at D28 and D90 with AUC of: CP (0.75/0.67),
MELD (0.73/0.79), UKELD (0.79/0.84), ACLF (0.75/0.78) and CLIF-SOFA (0.75/0.83).

**Conclusions** The evolution in CLIF-SOFA score between D2 and D5/7 is superior to evolution in other scores and scores assessed at single time points when predicting 90 day survival. The delta C-SOFA at D5 and D7 are comparable, thus delta C-SOFA D2-D5 may be used to guide therapeutic decisions.

**Results** Significant associations were found, in men, between the risk of developing khat-related CLD and CYP2D6: rs3892097 (p=0.029; odds ratio (OR)=2.61 [95% confidence interval (CI) 1.1–6.2]) and CYP2D6:rs1065852 (p=0.039; OR=2.42 [95% CI 1.1–5.6]). These two SNPs are in close linkage disequilibrium ($r^2=0.8$). The associations were not significant in women. No significant associations were identified between PNPLA3:rs738409, TM6SF2:rs58542926 and MBOAT7:rs641738 and either the overall or sex-specific risk of developing khat-related CLD.

**Conclusions** Carriage of rs3892097 and rs1065852 in CYP2D6 is associated with an increase in the risk of developing khat-related CLD. The male specificity of this association is unexplained; more extensive exploration of CYP2D6 variants in population at risk is warranted.

### Abstract PWE-081 Figure 1

a) CLIF-SOFA scores; b) CLIF-SOFA score evolution

### PWE-082 GENETIC VARIANTS IN CYP2D6 AND THE PROPENSITY TO CHRONIC LIVER DISEASE IN MEN CHEWING KHAT

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**Introduction** The chewing of the leaves of *Catha edulis* (khat) is widespread in Africa, Arabia and in the wider diaspora. Khat has been implicated in the development of chronic liver disease (CLD) but the determinants of susceptibility to its toxic effects are unknown. Genetic factors may play a role. Khat is metabolised in the liver *via* cytochrome P450 CYP2D6; genetic variants associated with low or null function, which may Result in khat accumulation, are possible candidates. In addition, variants in genes known to be associated with the development of other forms of CLD viz: PNPLA3: rs738409; TM6SF2:rs58542926 and MBOAT7:rs641738 could be implicated.

**Methods** The study was undertaken in Harar, Ethiopia where khat chewing is wide-spread and the proportion of patients with *unexplained* CLD exceeds 50%. The cases comprised of 120 khat-exposed hospital attendees (83% men) with CLD; the controls comprised of 195 khat-exposed attendees without CLD (68% men). Genotyping for single nuclear polymorphisms (SNPs) in CYP2D6 (rs1065852; rs3892097; rs28371706; rs28371725; rs59421388; rs67136512), PNPLA3:rs738409; TM6SF2:rs58542926 and MBOAT7: rs641738 was undertaken using KASPar on a RohCLightCycler480. All genetic association tests were performed in PLINK v1.07.

**Results** Significant associations were found, in men, between the risk of developing khat-related CLD and CYP2D6: rs3892097 (p=0.029; odds ratio (OR)=2.61 [95% confidence interval (CI) 1.1–6.2]) and CYP2D6:rs1065852 (p=0.039; OR=2.42 [95% CI 1.1–5.6]). These two SNPs are in close linkage disequilibrium ($r^2=0.8$). The associations were not significant in women. No significant associations were identified between PNPLA3:rs738409, TM6SF2:rs58542926 and MBOAT7:rs641738 and either the overall or sex-specific risk of developing khat-related CLD.

**Conclusions** Carriage of rs3892097 and rs1065852 in CYP2D6 is associated with an increase in the risk of developing khat-related CLD. The male specificity of this association is unexplained; more extensive exploration of CYP2D6 variants in population at risk is warranted.

### PWE-083 THE SPECIFICITY OF THE ELECTROENCEPHALOGRAM FOR DIAGNOSING HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CONFOUNDING COMORBIDITIES

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**Introduction** Hepatic encephalopathy is a common complication of chronic liver disease; it is characterised by impairment in neuropsychiatric/neuropsychological performance. However, other chronic conditions such as renal failure, chronic pulmonary disease and diabetes are also associated with the development of metabolic encephalopathies and show similar abnormalities. Difficulties can, therefore, arise in determining the aetiology of cognitive impairment in patients with cirrhosis if they have these additional co-morbidities. The aim of this study was to evaluate the specificity of the tests used to diagnose hepatic encephalopathy in patients with cirrhosis.

**Methods** The study population comprised of clinically stable patients with: (i) cirrhosis (n=52); (ii) end-stage renal failure (n=15); (iii) chronic renal failure (n=15); and, (iv) poorly controlled type II diabetes mellitus. All participants were assessed in one sitting, under standardised conditions, with a comprehensive test battery including: electroencephalography (EEG); Critical Flicker Fusion Frequency (CFF); the Psychometric Hepatic Encephalopathy Score (PHEs) test; and the computer-based Inhibitory Control Test (ICT), Stroop Test (EncephalApp) and Scan Package. Results were compared with appropriately age and sex-matched healthy volunteers (n=53) correcting for multiple testing.

**Results** Significant abnormalities were observed across all test systems in the four patient groups compared with healthy controls. However, EEG abnormalities were only observed in the patients with cirrhosis (table 1).

**Conclusions** The presence of co-morbidities may confound the assessment of cognitive function in patients with cirrhosis; the presence of EEG abnormalities would signal a major hepatic component.