

Abstract O23 Figure 1

hypertension. The difference in all-cause and liver-related mortality suggests that this survival benefit may not be entirely liver related.

## REFERENCES

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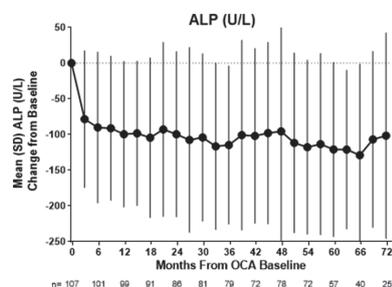
O24

## DURABILITY OF OBETICHOLIC ACID RESPONSE IN PBC PATIENTS WHO DID NOT ACHIEVE POISE TRIAL CRITERIA

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10.1136/gutjnl-2020-bsgcampus.24

**Introduction** In clinical studies and in clinical practice, response to primary biliary cholangitis (PBC) treatment has been assessed using dichotomous biochemical response criteria. Although achieving these criteria may be associated with improved clinical outcomes, the benefit in patients (pts) with an incomplete response to treatment may be underestimated.



This analysis assessed the extent and durability of obeticholic acid (OCA) response in pts with PBC not achieving the dichotomous primary endpoint in the phase 3 POISE study through 72 months of OCA treatment.

**Methods** Key inclusion criteria included PBC diagnosis, alkaline phosphatase (ALP)  $\geq 1.67 \times$  upper limit of normal (ULN) and/or total bilirubin  $>ULN$  to  $<2 \times ULN$ , and on a stable dose of—or intolerant of—ursodeoxycholic acid (UDCA). During the 12-month double-blind (DB) phase, 216 pts were randomised to daily placebo, OCA 5–10 mg, or OCA 10 mg. This analysis pooled DB placebo (OCA baseline [BL]) was open-label extension [OLE] day 0) and DB OCA pts to evaluate the efficacy and safety of up to 72 months of OCA treatment. Pts who achieved the POISE primary endpoint (ALP  $<1.67 \times ULN$ , with a  $\geq 15\%$  reduction from BL, and total bilirubin  $\leq ULN$ ) 12 months from OCA BL were excluded. Values shown are mean (SD) unless otherwise specified. P values were based on paired t-tests.

**Results** Of the 193 pts enrolled in the OLE, 107 (55%) did not achieve the POISE criteria after 12 months of OCA treatment. Pts were 93% female, 91% Caucasian, 56 (10) years old at BL, and 91% received UDCA (15 [4] mg/kg/day). At BL, ALP was 356 (138) U/L and total bilirubin was 13 (8)  $\mu\text{mol/L}$  ( $>ULN$  in 18 pts [17%]). Despite not achieving the POISE criteria after 12 months of OCA, a significant and durable reduction was observed in ALP ( $p < 0.01$  at all time points) through 72 months of treatment (figure 1). Total bilirubin levels remained stable and near BL values within the normal range throughout the duration of treatment. Throughout the 6-year study period, the most common adverse events were pruritus (92 pts [86%]) and fatigue (33 pts [31%]), consistent with previous reports from POISE and expected PBC symptoms.

**Conclusions** Despite not achieving the POISE primary endpoint, these pts showed significant and sustained biochemical improvements.

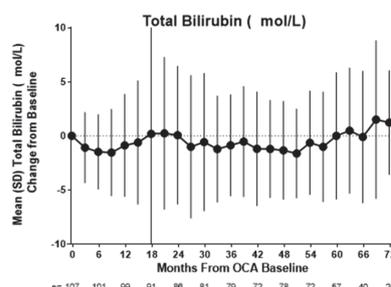
O25

## ALCOHOL RELATED LIVER DISEASE: DELAYED DIAGNOSIS AND MISSED OPPORTUNITIES FOR INTERVENTION

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10.1136/gutjnl-2020-bsgcampus.25

**Introduction** Death from alcohol related liver disease (ARLD) is preventable and increasing. Effective identification and brief



Abstract O24 Figure 1 Change from baseline in ALP and total bilirubin through 72 months of OCA treatment

advice (IBA), access to diagnostics and clear referral pathways to alcohol use disorder (AUD) services are key to reducing harm. This study characterises use of secondary care services by patients dying with ARLD, to identify missed opportunities for intervention.

**Methods** We identified Nottinghamshire residents dying with ARLD (ICD10-K70) from 2012 to 2017 in the linked HES-ONS Mortality dataset. Late diagnosis was defined as no ARLD code >6 months before death. Logistic regression was used to identify characteristics associated with late diagnosis. Numbers of admissions, A&E and outpatient attendances were identified. The consultant speciality, primary and non-primary diagnoses were ascertained and compared between diagnosis groups.

**Results** Of the 799 patients identified, half had a late diagnosis of ARLD. The hospital providing care and emergency presentation at first ARLD diagnosis were significantly associated with late diagnosis. Overall, people dying of ARLD had 5 admissions, 4 A&E attendances and 16 outpatient appointments in the 5 years prior to death. For those with a late diagnosis the numbers were 3,3 and 9, respectively. In-patient care was provided by general medicine in 87.8% of patients with a late diagnosis compared to only 39.1% in the late diagnosis group. Admission under gastroenterology and hepatology was also much lower in the late diagnosis than the early diagnosis group, 18.5% vs 66.5% and 2.5% vs 31.3%, respectively. For the late diagnosis group, trauma and orthopaedics (T&O) was a common speciality for in-patient and out-patient activity, but also a range of other specialties. Although the late diagnosis group did not have an inpatient diagnosis of ARLD >6 months prior to death, 14.3% of this group were admitted for mental and behavioural disorders due to use of alcohol in this time-period.

**Conclusions** This study shows those later dying of ARLD have multiple contacts with care. Those presenting late with a alcohol related liver diagnosis also have many opportunities for intervention primarily in T&O and general medicine. It provides a powerful methodology that can be used to evaluate and improve how alcohol issues are managed and where action can be targeted effectively.

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**OBETICHOIC ACID IMPROVES EXPERIMENTAL NONINVASIVE MARKERS OF NONALCOHOLIC STEATOHEPATITIS AND ADVANCED FIBROSIS: RESULTS FROM REGENERATE**

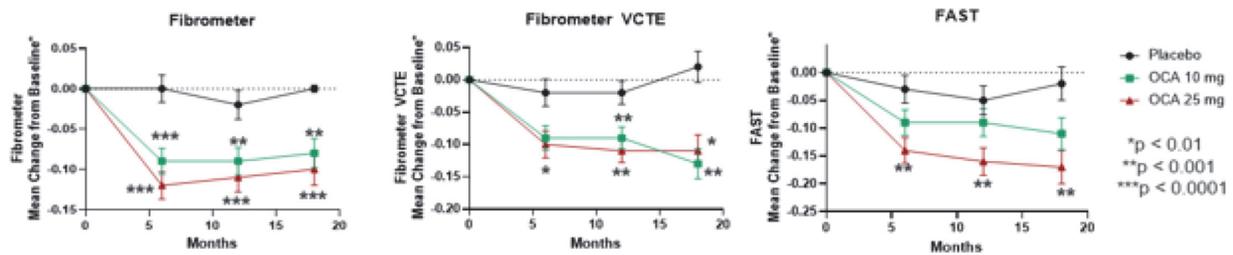
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10.1136/gutjnl-2020-bsgcampus.26

**Introduction** In the REGENERATE Month 18 interim analysis, obeticholic acid (OCA) treatment improved liver fibrosis in patients (pts) with nonalcoholic steatohepatitis (NASH). Non-invasive tools (NITs) were established to assess fibrosis stage (F) and NASH. FibroMeter (FM) uses age, gender, alpha 2 macroglobulin, international normalized ratio, platelets, urea, and gamma-glutamyltransferase to predict significant fibrosis ( $\geq F2$ ). FM VCTE excludes urea and includes liver stiffness (LS) by vibration-controlled transient elastography (VCTE). The FAST score, designed to identify NASH pts with NAFLD Activity Score  $\geq 4$  and fibrosis  $\geq F2$ , combines LS by VCTE with Controlled Attenuation Parameter score and aspartate aminotransferase.

**Methods** F2/3 pts (N=931) with NASH were randomised 1:1:1 to daily placebo, OCA 10 mg, or OCA 25 mg. In a subset of pts, changes in FM (N=604), FM VCTE (N=604), and FAST (N=391) were analyzed using a mixed-effect repeated measures model with treatment, baseline, visit, visit by treatment interaction, and stratification factors included. Least square mean and p-values are based on mixed-effect repeated measure model.

**Results** At baseline, there was no significant difference in scores across treatment groups (figure 1). F3 pts had higher scores than F2 pts, consistent with prior publications (not shown). OCA-treated pts showed improvements in FM, FM



Baseline Values	Placebo	OCA 10 mg	OCA 25 mg
Fibrometer	0.53 (0.023)	0.57 (0.020)	0.57 (0.021)
Fibrometer VCTE	0.59 (0.025)	0.64 (0.021)	0.60 (0.024)
FAST	0.60 (0.021)	0.60 (0.023)	0.6 (0.021)

Abstract O26 Figure 1 Least square mean change in FM, FM VCTE and FAST