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PATHOPHYSIOLOGICAL BASIS OF RESOLUTION OF ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) INDUCED BY THE NOVEL LIVER DIALYSIS DEVICE, DIALIVE (ALIVER CONSORTIUM)

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Background In ACLF, systemic inflammation (SI) due to pathogen and damage associated molecular patterns (PAMPs and DAMPs), albumin and endothelial dysfunction results in organ failure. DIALIVE, a liver dialysis device replaces dysfunctional albumin and removes PAMPs and DAMPs. In a randomised controlled trial, DIALIVE resolved ACLF faster and in a greater proportion of patients compared with standard of care (SOC). This substudy aimed evaluated the effect of DIALIVE on pathophysiological processes that are causally associated with ACLF.

Methods Study included patients with ACLF 1–3a, randomized to DIALIVE or SOC. End points were evaluated at Day 10. DIALIVE group received treatments in the first 3-days (range 1–6). Plasma samples were obtained on Days 0, 5 and 10. A post-hoc inferential Mixed Models for Repeated Measurements analysis was performed to evaluate the statistically significant

differences between groups at the Day 10. Changes in variables from baseline in the groups is shown in the figure 1 SAS system v.9.4 used.

Results 32 ACLF patients were randomised to DIALIVE (N=17; CLIF-OFs: 10.3 (1.6)) or SOC (n=15;CLIF-OFs: 9.9 (1.2)). 30-evaluable patients (n=15 each group) comprised this substudy. PAMPs: Endotoxin activity: The patient-level pre-defined reduction goals were 20%. Marked advantage seen for DIALIVE (80%) vs SOC (36.4%) at Day 5. LAL assay. Significant reduction in DIALIVE group (p=0.005). Albumin Function: DIALIVE increased human mercaptalbumin (p<0.001) and reduced human nonmercaptalbumins 1 and 2 (p=0.003 and p=0.203); improved binding capacity (p=0.073; EPR spectroscopy) and reduced ischemia modified albumin ratio (p=0.014) vs SOC. DAMPs: M30 and M65 components of cytokeratin 18 (p=0.079; p=0.192) and RIPK3 (marker of necroptosis) (p=0.624) were reduced in the DIALIVE group. SI: IL-8, IL-18 and TNFα were reduced in the DIALIVE compared with SOC group (p=0.021; p=0.021; p=0.08). Endothelial function: ADMA and Factor VIII were markedly reduced in the DIALIVE patients (p<0.001; p=0.070). TLR4 and Inflammasome ligands: Incubation of plasma with a 1L1b/IL18 Inflammasome cell line reduced signalling significantly (p=0.021); favourable reductions were also seen with TLR4 reporter cell line (p=0.403), in favour of DIALIVE vs SOC.

Conclusions DIALIVE impacts significantly on DAMPs, PAMPs, albumin and endothelial function, markers of SI and, reduces TLR4 and inflammasome ligands that collectively contribute to its ability to resolve ACLF.

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READMISSIONS POST LIVER TRANSPLANTATION: A 10 YEAR STUDY

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Introduction Short-term readmissions post liver transplantation (LT) are a marker of patient care and a high-cost burden. Studies from the U.S. suggest a 30–45% readmission rate at

Abstract P077 Figure 1 Impact of DIALIVE on the pathophysiological processes deranged in ACLF - change from baseline at Days 5 and 10 for DIALIVE (green) and SOC (red) group

30 days. European data are sparse. We aimed to define the readmission rate in Scotland and identify reasons and predictors for readmission.

Methods Patients undergoing primary transplant with cirrhosis between January 2009 and December 2018 were included (n=639). Data were collected on patient and disease demographics and blood results at transplant and discharge. Differences between those readmitted and not readmitted at 30 days were assessed using Chi-squared or Mann-Whitney U tests. Survival was assessed using Kaplan-Meier analysis. Cox proportional hazards were used to predict readmissions.

Results Patients were predominantly male (n=410; 64.2%) with a median age of 58.9 years (IQR 51.8–64.1) at transplant. The commonest aetiologies were alcohol-related liver disease (n=226; 35.4%), chronic viral hepatitis (n=111; 17.4%) and non-alcoholic fatty liver disease (n=104; 16.4%). 208 patients (32.6%) had a hepatocellular carcinoma. Patients had a median UKELD of 55 (52–59) and a median length of stay of 13 days (10–18). One year mortality was 4.1% (n=26).

Readmission rates were: 30 days, 19.4% (n=124); 90 days, 30.6% (n=194); 1 year, 46.9% (n=300). Demographics and blood results were similar between those readmitted at 30 days and those not, although significant differences were haemoglobin (g/dL) at transplant (readmitted vs not readmitted) (105 vs. 111; p=0.02), urea (mmol/L) at discharge (7.5 vs 6.3; p=0.009), and creatinine (mmol/L) at discharge (80 vs 73; p=0.007).

Readmission within 30 days post LT conferred a significantly higher 1-year mortality (10 (8.1%) vs. 16 (3.1%) (p=0.012) (OR=2.74; (95% CI 1.210–6.186)); and represented a significant survival disadvantage at 1 year in a Kaplan-Meier analysis (readmitted within 30 days: mean survival 348 days (95% CI 337–359) vs not readmitted within 30 days: mean survival 361 days (95% CI 358–363). Log rank p=0.01).

The main reasons for admissions were deranged LFTs (34%; n=42), AKI (22%; n=27), and infection (18%; n=22).

Significant differences on multivariate analysis were found for haemoglobin at transplant (HR=0.988 (95% CI 0.979–0.996); p=0.005) and creatinine at discharge (HR=1.006 (95% CI 1.003–1.010); p=0.001).

Discussion In Scotland, readmission rates following LT were lower than in previously published, American, data. Haemoglobin and creatinine were predictors of readmission.

Patients readmitted within 30 days of LT were more than twice as likely to die within 1 year.

The commonest reasons for readmission were deranged LFTs, AKI and infection.

P079

APPROACH TO PRIMARY BILIARY CHOLANGITIS MANAGEMENT IN A DISTRICT GENERAL HOSPITAL

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Introduction Primary biliary cholangitis (PBC) is a rare progressive immune-mediated liver disease that, if not adequately treated, may culminate in end-stage disease and need for transplantation. Both genetic and environmental influences are presumed relevant to disease initiation. PBC is most prevalent in women and those over the age of 50, but a spectrum of

disease is recognised in adult patients globally; male sex, younger age at onset (<45) and advanced disease at presentation are baseline predictors of poorer outcome. According to current guidelines, PBC is diagnosed in the presence of anti-mitochondrial antibodies (AMA) or specific antinuclear antibodies, and of a cholestatic biochemical profile, while biopsy is recommended only in selected cases. All patients receive ursodeoxycholic acid (UDCA) in first line; the only registered second-line therapy is obeticholic acid (OCA) for UDCA-inadequate responders

Method Retrospective review of clinical records of patients with antimitochondrial antibody positive status were reviewed by help of local immunology department. Patients involved were the ones who were AMA positive between 2015 to 2020. 26 patients were included in this review and results are summarised below

Results Out of 26 patients 11 were AMA positive only without any LFTs abnormality so no treatment was started, were planned to be followed up by yearly LFTs.

1 patient was AMA positive plus abnormal LFTs and histology consistent with PBC who presented with developed cirrhosis and variceal bleed requiring TIPPS so services were transferred to tertiary care so no record on our system.

14 patients out of 26 were AMA positive and cholestatic LFT abnormality. 6 patients out of 14 were on urso dose of 13 – 15mg/kg. 5 patient out of 14 had record of pruritis and fatigue documented. Only 3 patients out of 14 had DEXA scan done in last 5 years. Only 2 had developed cirrhosis who were not considered for transplant due to multiple comorbidities but were followed by as per guideline for HCC and varices.

None of these 26 patients had overlapping diagnosis of autoimmune hepatitis.

Conclusion Significant issues were identified in management of patients with PBC when it comes to correct dose of ursodeoxycholic acid and mentioning about symptoms of fatigue and pruritis. Initial management needs to be optimized before consideration of obeticholic acid for these patients

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SOCIOECONOMIC DEPRIVATION AND ITS EFFECT ON REFERRAL FOR AND OUTCOMES FOLLOWING LIVER TRANSPLANTATION

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Introduction In Scotland lower socio-economic status is associated with a greater risk of liver-related mortality. Limited data exist on whether socio-economic status influences referral for liver transplantation (OLT) or outcomes following listing and OLT.

Methods Adult patients with chronic liver disease referred for the first time for OLT between January 2009 and December 2018 were identified. Deprivation score related to postcode (Scottish Index of Multiple Deprivation [SIMD]) was recorded. Severity of liver disease, listing decision and post listing outcomes were documented. SIMD groups were paired into quintiles (1=most deprived, 5=least deprived). Liver related deaths in Scotland were used as an estimate of severe liver disease in the remaining population. We calculated the chance of referral for each group as follows: (number of referrals/((number of