reviewed. Data were collected included baseline demographics, social factors including index of multiple deprivation (IMD), aetiology of liver disease, period of abstinence and assessment outcome (table 1).

Results 125 patients with a history of ArLD were referred for transplant assessment over the 3-year period. The majority (78%) were male and most (39%) were 50–59 years. Patients living in the most deprived quintile comprised just 17% of the group. In 50% ArLD was the only aetiology listed, 27% of patients also had hepatocellular carcinoma (HCC) and 28% had a second, non-malignant, aetiology listed. Patients were divided into groups based on demographics, social factors, aetiology and period of abstinence and the outcome of the transplant assessment was recorded for each group. Table 1 illustrates the percentage of patients in each group listed for transplant. Psychological, social or substance misuse issues (including smoking) were cited as concern for listing in just 7 (5%) of cases.

Conclusion Our data demonstrates that in patients with a history of ArLD referred to this unit for transplant assessment, there is no listing bias based on socioeconomic background. However, whilst ArLD occurs more often in lower socioeconomic groups, patients from IMD quintile 1 comprised just 17% of those referred, suggesting a potential referral bias. There was no clear preference for listing patients who had a second causal aetiology for their liver disease. Very few patients were not listed based purely on social/psychological factors. This data should encourage clinicians to refer patients with a history of ArLD for transplant assessment, regardless of their socioeconomic background.

P093

TOLL-LIKE RECEPTOR 4 INHIBITION ACTS SYNERGISTICALLY WITH G-CSF TO PREVENT ORGAN INJURY AND INDUCE LIVER REGENERATION IN ACUTE-ON-CHRONIC LIVER FAILURE

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Background and Aims Acute-on-chronic liver failure (ACLF) is characterised by lack of regeneration. Granulocyte colony stimulating factor (G-CSF) carries pro-regenerative properties and has been shown to be of benefit in ACLF. However, the large trial of G-CSF (GRAFT study) in patients with ACLF showed no benefit and in certain groups mortality tended to be higher. This study was performed to define the mechanisms underlying the negative effect of G-CSF and determine whether its beneficial effect could be harnessed using a toll-like receptor 4 (TLR4) antagonist.

Method Two mouse models of ACLF were used: CCL4 (0.5mg/ml, 6w) to induce chronic liver injury followed by LPS i.p. (*Klebsiella*, 4mg/kg) (n=4–10) or Galactosamine (GalN) i.p. (1000mg/kg) as a second hit (n=8). 1h after, G-CSF 250µg/kg s.c. and/or TLR4-inhibitor TAK-242 10mg/kg i.p. were injected and continued every 24h. The treatment duration was 24h and 5d in the LPS model and 48h in the GalN model. Samples were stored and analysed for liver injury, inflammation, senescence and regeneration.

Results 6w CCL4 led to bridging fibrosis, TLR4 up-regulation and infiltration of G-CSFr expressing cells. LPS increased ALT levels, cell death (TUNEL+), enhanced hepatic infiltration of

neutrophils (Ly6G+), macrophages (F4/80+) and TNFα. G-CSF increased the 48h mortality from 0% to 66%, aggravated liver inflammation with macrophage and NK cell (CD45+, CD49b+, CD3-, CD19-) infiltration and IL6 expression. G-CSF +TAK-242 reduced the mortality to 0%, abrogated the liver injury (TUNEL) and liver inflammation (macrophages, neutrophils, TNFα, IL6) significantly. In the second model, GalN also induced a significant liver injury. Treatment with G-CSF +TAK-242 was significantly more effective than the individual therapies. G-CSF+TAK-242 was associated with increased liver regeneration evidenced by increased tissue expression of pSTAT3 and BCL2. CCL4+LPS induced a p53 and p16-dependent cell cycle arrest and lack of proliferation (CyclinA) in hepatocytes. G-CSF+TAK-242 mitigated senescence and significantly increased the rate of CyclinA expressing hepatocytes (figure) suggesting enhanced liver regeneration.

Conclusion The present study shows that G-CSF is deleterious in LPS-associated ACLF through further activation of inflammatory pathways and immune cell infiltration. TLR4 inhibition with TAK-242 prevented G-CSF driven tissue injury and induced liver regeneration showing evidence of synergy between the two molecules thereby providing a novel therapeutic strategy for ACLF patients.

P094

POTENTIAL MECHANISMS UNDERLYING THE PROTECTIVE EFFECT OF LONG-TERM ALBUMIN INFUSION IN CIRRHOSIS

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Background Long-term albumin administration has shown a reduction in mortality in hepatic decompensation, however the mechanism of this is unclear. The aims of this study were to determine (i) whether analbuminaemic (NAR) rats have greater liver injury and sensitivity to LPS (ii) whether albumin infusion is protective in NAR rats (iii) the impact of analbuminaemia and albumin infusion on the gut-liver interface and hepatic TLR4 signalling.

Methods 10 treatment groups of NAR and SD rats were studied (n=4–7); Naïve, cirrhosis (4-w after bile duct ligation (BDL)) and ACLF models (induced by lipopolysaccharide (LPS) to BDL) were studied. BDL groups: ±LPS, ±albumin infusion (1.5 g/kg i.p. for 2 weeks). Markers of liver injury: plasma ALT level and TUNEL staining; markers of gut integrity and permeability: DAB immunohistochemistry ZO-1 expression in ileum tissue; Hepatic TLR4 immunohistochemistry and related pathway genes RT2 PCR profiler were studied.

Results Liver injury: ALT levels and TUNEL positive areas were significantly higher in NAR compared with SD rats (p = 0.01 and p = 0.01), which were corrected with albumin infusion (p = 0.02, p = 0.047). Effect of LPS administration: coma-free survival was higher in SD rats than NAR rats (80% vs 40%). Effect of albumin administration: Administration of albumin to BDL rats reduced severity of liver injury and mortality after LPS administration [p = 0.001; 40% vs 100%, p = 0.04]. Markers of gut permeability: In NAR rats, the histopathological examination of the ileum and colon revealed a reduction in ZO-1 expression, which was restored with

Abstract P094 Figure 1 ZO-1 immunohistochemistry of ileum showed ZO-1 was downregulated in NAR naïve group. Albumin infusion restored ZO-1 expression

albumin supplementation (figure 1). Hepatic expression of TLR4 and associated pathways: Cirrhotic NAR animals had greater hepatic TLR4 expression which was reduced by albumin administration. Hepatic TLR4 gene array confirmed the activation of TLR4 dependent pathways in the cirrhotic NAR animals, which was abrogated by albumin infusion.

Conclusion NAR animals have significantly greater liver injury, increased sensitivity to LPS and mortality which is prevented by albumin administration. Our data show for the first time that the mechanism of the protective effect of albumin is consequent upon restoration of gut junctional proteins and reduction of hepatic TLR4 expression.

P095

IMPLEMENTATION OF DECOMPENSATED CIRRHOSIS DISCHARGE BUNDLE: A UNIVERSITY HOSPITAL EXPERIENCE

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Background Decompensated liver cirrhosis is a frequent reason for admission to acute medical and gastroenterology units. Over the last two decades, a significant rise in the prevalence of liver cirrhosis in the UK has been noted, with the major culprits being alcohol related liver diseases, hepatitis B & C, and non-alcoholic obesity related disease. It has been observed that re-admissions to the hospital are common following discharge of the patients with decompensated liver cirrhosis. In order to improve the quality of discharge and reduce the re-admissions a decompensated discharge bundle has been developed by BSG and BASL. We aimed to assess the practice in our hospital against BSG/BASL guidelines and the impact by the implementation of the said discharge bundle.

Methods All those patients who were admitted with decompensated cirrhosis were included for data collection. Standard Quality Improvement model was adopted using two PDSA cycles. In cycle 1, discharge letters of 40 patients were assessed retrospectively against the decompensated cirrhosis discharge bundle tool kit during the months of January, February and March 2021. In cycle 2, there was re-assessment of discharge letters for 40 patients during the months of April, May and June to look for any change or improvement.

Results In cycle 1, it was noted that only 20% of the decompensated cirrhotic patients had weight, urea and electrolytes, diuretic dose adjustment and communication with the patients regarding future plans recorded on the discharge letters. Hence, the bundle was introduced by displaying the awareness posters in the Gastro ward and discussed with the junior doctors in the board round. Additionally, emails were sent to

doctors of gastro unit regarding the discharge bundle introduction.

There was a significant improvement of results in cycle 2, where 60% of the patients with decompensated cirrhosis had the above mentioned parameters documented in the discharge letters respectively.

Conclusion There were inconsistencies in the discharge letters when assessed during cycle 1 and the documentation was sub-optimal. However, with the introduction of discharge bundle in the hospital has led to a significant improvement in the discharge letter documentations when compared against the decompensated cirrhosis discharge bundle in cycle 2. In order to get much better results and to continue the improvement, we would consider the incorporation of the bundle in the Trust E-Library and include in the junior doctor inductions.

P096

THE POTENT UREASE INHIBITOR FLUROFAMIDE EFFECTIVELY SUPPRESSES AMMONIA PRODUCTION BY THE COLONIC MICROFLORA

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Background Ureolysis by colonic microorganisms gives rise to a significant fraction of the portal vein ammonia load; colonic urease inhibition would therefore be a logical approach to reducing systemic ammonia in patients with hepatic encephalopathy. This was trialled in the 1960's in a small number of patients, using the urease inhibitor acetohydroxamic acid (AHA); disappointing clinical results led to the approach being abandoned. However, AHA is not a particularly potent inhibitor of urease; more potent inhibitors have since been developed, one of which is flurofamide. It is possible flurofamide might be more effective in this context, but no relevant work has been reported; we have conducted an initial laboratory study into the effects of flurofamide on ammonia production by the colonic microflora, in particular the flora of the right colon.

Methods Patients attending for routine colonoscopy who did not have inflammatory bowel disease or change of bowel habit were approached to take part. At colonoscopy, 50 mls sterile water was introduced into the right colon, and aspirated back into a polyp trap. These washings were transported to the laboratory for processing within 2 – 4 hours; a mechanical cell count was performed, and the samples were incubated for 22 hours in urea-containing culture medium with various concentrations of flurofamide, under both aerobic and anaerobic conditions. Following incubation, ammonia and urea levels in the medium were measured.

Results As expected, colonic washings produced ammonia when cultured in urea containing medium, although ammonia production did not correlate directly with the number of organisms in the inoculum. Lower concentrations of flurofamide had variable effects on ammonia production, but higher concentrations reduced levels to an average of less than 5% of the ammonia generated in the absence of flurofamide (figure 1). Results from aerobic and anaerobic cultures were very similar; there was no evidence for flurofamide toxicity. Urea levels were difficult to interpret due to assay variability and the high baseline level of urea