Oral presentations

BSG plenary

**OC-001** THE IMPACT OF THE INTRODUCTION OF FORMALISED POLYPECTOMY ASSESSMENT ON TRAINING IN THE UNITED KINGDOM
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**Introduction** Polypectomy is regarded as the most hazardous part of colonoscopy, accounting for the majority of procedure-associated morbidity and yet is a necessary skill for all colonoscopists. Training in polypectomy has, to date, been variable and poorly structured. Anecdotal evidence suggested poor exposure to polypectomy during training. A novel assessment tool, the Directly Observed Polypectomy Skills (DoPYS), was introduced nationally in the United Kingdom in October 2011 with the intention of both improving training and facilitating documentation of competency.

**Methods** The aim was to assess the impact of the mandatory introduction of the DoPYS as part of the formal colonoscopy certification process. Applications for certification in the year prior to the introduction of DoPYS were analysed retrospectively and compared with data collected prospectively for those in the following year.

Data were collected on the total lifetime number of colonoscopies performed, the number of assessments for both colonoscopy and polypectomy and whether applicants had any evidence of performing polypectomy before certification in competence in colonoscopy.

**Results** There were 175 applicants for certification in the first year. The median number of procedures per candidate was 287. Thirty-two per cent of candidates had evidence of any observed polypectomy with 7 per cent of candidates referring to training in endoscopic mucosal resection (EMR). The median number of formative colonoscopy assessments was 3 (range 0–16).

In the year since DoPYS was introduced there were 150 applications for certification. The median number of procedures per candidate was 206. All of these candidates had evidence of polypectomy assessment with a median number of DoPYS of 7 (range 3–27). 89 per cent of applicants had evidence of assessed EMR. The median number of formative colonoscopy assessments in this cohort was 32 (range 9–199).

There was a significant increase in the number of logged polypectomy assessments (p < 0.001), experience of EMR (p < 0.001) and formative colonoscopy assessments (p < 0.001). There was no significant difference in the total number of colonoscopy procedures performed.

**Conclusion** These data—the largest in the literature to date—show that structured polypectomy assessment improves trainees’ documented exposure to therapeutic endoscopy as well as providing formal evidence of skills acquisition. As polypectomy plays an increasing role globally in colorectal cancer prevention, the DoPYS provides an effective means of assessing and certifying polypectomy in order to minimise the well-recognised risks associated with this technique.

**Disclosure of Interest** None Declared.

**OC-002** SELECTIVE ALPHA V INTEGRIN DELETION IDENTIFIES A CORE, TARGETABLE MOLECULAR PATHWAY THAT REGULATES FIBROSIS ACROSS SOLID ORGANS
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**Introduction** Myofibroblasts are the major source of extracellular matrix components that accumulate during tissue fibrosis, and hepatic stellate cells (HSCs) are the major source of myofibroblasts in the liver. To date, robust systems to genetically manipulate these cells have not existed. The paucity of tools that allow reliable, specific inactivation of genes in myofibroblasts in vivo has greatly hindered progress in understanding the underlying biology of fibrotic diseases.

**Methods** Mouse models of organ fibrosis: Chronic carbon tetrachloride injection (liver fibrosis), intratracheal bleomycin instillation (lung fibrosis) and unilateral ureteric obstruction (kidney fibrosis). Fluorescent reporter mice: mTmG (TdTomato/EGFP) and Ai14 (Rosa-CAG-LSL-tdTomato-WPRE) mice were crossed with PDGFR<sup>β</sup>-platelet derived growth factor receptor beta-Cre mice. Integrin knock-out mice: Itgα<sup>β</sup>Cre (Itgα<sup>β</sup>/Cre and Itgα<sup>β</sup>-/- mice were maintained on C57BL/6 background and itgα<sup>β</sup>-/- and itgα<sup>β</sup>-/- mice were maintained on a 129x129 background. Fluorescent cell sorting: TdTomato positive cells from Ai14; PDGFR<sup>β</sup>-Cre mice were sorted using a FACSaria.

**Results** We report that PDGFR<sup>β</sup>-Cre (platelet derived growth factor receptor beta-Cre) inactivates genes in murine HSCs with high efficiency. We used this system to delete the integrin α<sub>v</sub> subunit because of the suggested role of multiple α<sub>v</sub> integrins as central mediators of fibrosis in multiple organs. Deletion of the α<sub>v</sub> integrin subunit in HSCs protected mice from CCl<sub>4</sub>-induced hepatic fibrosis, whereas global loss of α<sub>v</sub>β<sub>3</sub>, α<sub>v</sub>β<sub>5</sub> or α<sub>v</sub>β<sub>6</sub> or conditional loss of α<sub>v</sub>β<sub>8</sub> on HSCs did not. PDGFR<sup>β</sup>-Cre effectively targeted myofibroblasts in multiple organs, and deletion of α<sub>v</sub> integrins using this system was also protective in bleomycin-induced pulmonary fibrosis and renal fibrosis induced by unilateral ureteric obstruction. Critically, pharmacological blockade of α<sub>v</sub> integrins by a novel small molecule (CWHM 12) attenuated both liver and lung fibrosis, even when administered after fibrosis was established.

**Conclusion** These data identify a core cellular and molecular pathway that regulates fibrosis, and suggest that pharmacological targeting of all α<sub>v</sub> integrins may have clinical utility in the treatment of patients with a broad range of fibrotic diseases.

**Disclosure of Interest** N Henderson: None Declared, T. Arnold: None Declared, Y. Katamura: None Declared, M. Giacomini: None Declared, J. Rodriguez: None Declared, J. McCarty: None Declared, P. Runinski Shareholder of: Ante grin Therapeutics, LLC, D. Griggs Shareholder of: Antegrin Therapeutics, LLC, J. Maher: None Declared, J. Iredale: None Declared, A. Lacy-Hulbert: None Declared, R. Adams: None Declared, D. Sheppard: None Declared.

**Liver free papers**

**OC-003** MULTICENTRE RANDOMISED CONTROLLED STUDY COMPARING CARVEDIOL WITH ENDOSCOPIC BAND LIGATION IN THE PREVENTION OF VARICEAL REBLEEDING
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**Introduction** Rebleeding after an initial oesophageal variceal haemorrhage remains a significant problem despite therapy with...
band ligation ± non-selective β-blockers. Carvedilol is a vasodilating non-selective β-blocker with alpha-1 receptor and calcium channel antagonism. It has a greater portal hypotensive effect than propranolol and has been shown to be effective in the prevention of a first variceal bleed. Our aim was to compare oral carvedilol with band ligation in the prevention of rebleeding following a first variceal bleed.

Methods Patients who were stable 5 days after presentation with a first variceal haemorrhage and had not been taking (or had contraindications to) β-blockers, were randomised to oral carvedilol (6.25 mg daily then 12.5 mg daily after one week if tolerated) or a band ligation programme. Patients were followed up at clinic after one week, monthly, then 3-monthly. The primary end-point was variceal rebleeding, on intention-to-treat analysis.

Results 65 patients were randomised, 32 to carvedilol and 31 to banding. Fifty-six (89%) patients had alcohol related liver disease. There was no difference in baseline mean age (51 years ± 10.9 and 50 years ± 13.0) or median Childs Pugh score (9, IQR 6–11 and 9, IQR 8–11) for patients randomised to carvedilol or banding respectively. Mean follow-up was 29 months. Compliance was 72% and 90% for carvedilol and banding respectively (p = 0.14) and there was no difference in the number of serious adverse events between the two groups. Variceal rebleeding occurred during follow-up in 12 (37.5%) and 9 (29.0%) patients in the carvedilol and banding groups respectively (p = 0.72), with mortality 25.0% and 31.0% respectively (p = 0.658). The differences in outcome between the groups were similar using per protocol analysis. This interim analysis indicates that to show a significant difference in rebleeding, 452 patients would be required in each group.

Conclusion Carvedilol is not clearly superior to band ligation in the prevention of variceal rebleeding. However there appears to be a survival benefit for patients taking this drug compared with those undergoing banding, which requires further exploration.

Disclosure of Interest None Declared

OC-004 | IN VITRO STEROID SENSITIVITY ACCURATELY PREDICTS 6 MONTH MORTALITY IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS

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Introduction Severe alcoholic hepatitis (SAH) has a high mortality especially in those who fail to respond to steroid treatment. Early identification of steroid resistant patients may allow rapid implementation of other therapies, which may improve patient outcome. An early change in bilirubin has prognostic value but would be required in each group.

Results 65 patients were randomised, 32 to carvedilol and 31 to banding. Fifty-six (89%) patients had alcohol related liver disease. There was no difference in baseline mean age (51 years ± 10.9 and 50 years ± 13.0) or median Childs Pugh score (9, IQR 6–11 and 9, IQR 8–11) for patients randomised to carvedilol or banding respectively. Mean follow-up was 29 months. Compliance was 72% and 90% for carvedilol and banding respectively (p = 0.14) and there was no difference in the number of serious adverse events between the two groups. Variceal rebleeding occurred during follow-up in 12 (37.5%) and 9 (29.0%) patients in the carvedilol and banding groups respectively (p = 0.72), with mortality 25.0% and 31.0% respectively (p = 0.658). The differences in outcome between the groups were similar using per protocol analysis. This interim analysis indicates that to show a significant difference in rebleeding, 452 patients would be required in each group.

Conclusion Carvedilol is not clearly superior to band ligation in the prevention of variceal rebleeding. However there appears to be a survival benefit for patients taking this drug compared with those undergoing banding, which requires further exploration.

Disclosure of Interest None Declared

OC-005 | THE EARLY EXPANSION OF INTRAHEPATIC NK CELLS IS ASSOCIATED WITH CLEARANCE OF HCV AFTER IFN-ALPHA -BASED TREATMENT

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Introduction Chronic hepatitis C virus (HCV) infection is a major cause of liver failure, cirrhosis and hepatocellular carcinoma. Current treatments are evolving but still largely rely on IFNα in combination with ribavirin +/- protease inhibitors. IFNα can activate Natural killer (NK) cells: large granular lymphocytes that can target virally-infected cells. NK cells may play a role in the immune response to chronic HCV. We examined whether the kinetics of NK cell expansion and activation affected long-term treatment success.

Methods Repeated matched blood and intrahepatic (IH) NK cells were obtained from 9 patients before treatment and on days 1, 3, 7, 14, 28 and 86 of treatment. IH samples were obtained by fine needle aspirations. NK cell phenotype (CD16, NKp30, NKp46 & NKG2D) and functional markers (CD107a, IFNg & granzyme B) were assessed by flow cytometry. Rate of viral clearance (k) was calculated from serial serum viral loads during treatment.

Results Multiple IH samples were obtained from 9 subjects. 5 of the 9 patients achieved viral clearance i.e. SVR4 failed treatment. The proportion of IH lymphocytes that were NK cells increased from mean 10% (+/−0.97% SEM) at baseline to 16.1% (+/−2.45% SEM) after 24 hours (p = 0.021) and 17.9% (+/−4.75% SEM) after 72 hours (p = 0.023). The proportions returned to baseline levels from day 7 onwards. The proportion of IH NK cells was greater in patients who achieved SVR (18.6%) than those who failed treatment (11.9%). The rate of viral clearance correlates with IH NK cells at day 1 (p = 0.086). IH NK cells at 24 hours demonstrated an increase in activation i.e. increase CD107a externalisation, decreased granzyme B and CD16 expression.

Conclusion IH NK cells are cytotoxically active during the early phase of treatment when reduction in viral load is most pronounced. The rate of expansion of these activated NK cells in the first 24 hours indicates treatment success or failure. These findings suggest that strategies to improve early NK cell migration to the liver during treatment may lead to better treatment outcomes.

Disclosure of Interest None Declared

REFERENCE
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