colonoscopic technique from Taiwan which facilitates easier placement of the snare thereby achieving en-bloc resection.

Methods A 67 year old lady presented to our institute with an altered bowel habit and was found to have a flat polyp in the sigmoid colon on colonoscopy.

Results Standard injection as per conventional endoscopic mucosal resection was initially performed. Then a suitably sized snare was selected and the snare tip was used to make a single incision with cut current lateral to the polyp. The snare tip was then anchored at the site of the incision and then the snare was slowly opened and simultaneously positioned around the polyp. Once the snare was adequately placed the polyp was resected. Histology revealed a tubulovillous adenoma with low grade dysplasia which was excised completely.

Conclusions This technique provides an easy and safe way to resect en-bloc flat, large and challenging colonic polyps.

PTH-079 FULLY COVERED METAL STENT INSERTION FOR THE TREATMENT OF REFRACTORY POST ENDOSCOPIC SPHINCTEROTOMY BLEEDING

Yasmin Kassir*, Alvin Ochieng, Phillip Berry, Terence Wong. *Guy's and St Thomas' NHS Foundation Trust, London, UK*

10.1136/gutjnl-2018-BSGAbstracts.102

Introduction Bleeding is a common complication of endoscopic sphincterotomy (ES), occurring in 4% of cases. Fully covered metal stents (FCMS) are mainly indicated in the treatment of biliary strictures, bile ducts leaks and biliary stones. Recent studies have shown the value of fully covered metal stent placement in the management of post ES haemorrhage after failure of primary endoscopic interventions.

Treatment options have previously been limited to arterial embolisation or surgery in cases where conventional endoscopic therapy has failed. FCMS placement provides a less invasive means of achieving haemostasis through mechanical tamponade and may be a suitable option in patients whose bleeding has not been controlled with first line endoscopic management.

Methods We report a case of post ES bleeding refractory to conventional therapy, where haemostasis was achieved through placement of a temporary FCMS. A 27 year old man underwent therapeutic ERCP for choledocholithiasis in which precut sphincterotomy (with needle knife) resulted in bleeding. Initial management with local injections of adrenaline, endoclips and heater probe therapy were unsuccessful in achieving prolonged haemostasis and the patient became haemodynamically unstable, with melaena and Hb drop from 103 g/L to 56 g/L. The patient underwent a repeat ERCP in which a fully covered (10 mm/6 cm) metal stent (Wallflex, Boston) was inserted across the ampulla to tamponade the site of bleeding. The stent remained in situ and was removed 6 weeks post initial insertion, with no residual bleeding. Of note, the patient developed acute cholecystitis 48 hours post stent insertion, requiring urgent cholecystectomy. There were no post-operative complications.

Results Our case demonstrates the successful management of post ES bleeding with the use of FCMS placement, avoiding the need for arterial embolisation or surgery. Despite achieving haemostasis, our patient developed acute cholecystitis

following stent placement, requiring urgent cholecystectomy. This has been reported in up to 10% of patients with FCMS for all indications. The patient remained well post operatively and stent was removed with no residual bleeding.

Conclusion Our case supports the proposed use of FCMS placement as second line management in post ES bleeding refractory to conventional endoscopic therapy. In applying this technique we avoided the use of arterial embolisation and its associated risks and complications, of particular importance in a young patient such as ours. There is a risk of cystic duct outflow obstruction in the application of covered metal stents, as our case highlights, and it is important to recognise this when considering this treatment modality.

PTH-080 A MULTIMODALITY ENDOSCOPIC APPROACH FOR MANAGEMENT OF BURIED BUMPER SYNDROME

Nikolaos Lazaridis*, Alberto Murino, Andrea Telese, Nikolaos Koukias, Edward J Despott. *Royal Free Unit for Endoscopy, The Royal Free Hospital and University College London (UCL) Institute for Liver and Digestive Health, Hampstead, London, UK*

10.1136/gutjnl-2018-BSGAbstracts.103

Introduction Buried bumper syndrome (BBS) is a rare, long-term complication of percutaneous endoscopic gastrostomy (PEG) placement, occurring in 2%–6% of the cases. BBS is thought to occur due to prolonged compression of the tissue between the external and internal fixators, leading to 'burying' of the PEG bumper into the gastric wall. Consequences of BBS include tube obstruction and more rarely bleeding, abscess formation, and perforation. Several endoscopic techniques are described for the management of BBS and these may be complimentary when used in combination.

Methods A 32-year-old woman with diabetes, chronic kidney disease, a history of hypoglycaemic brain injury and gastroparesis, requiring a venting PEG, presented with abdominal pain. PEG tube obstruction led to the suspicion of BBS and abdominal computerised tomography confirmed this.

Results At upper gastrointestinal endoscopy under general anaesthesia, the internal bumper was found to be completely buried by granulation and fibrotic tissue. A 2.5 mm FlushKnife (Fujifilm, Saitama, Japan) was initially used to partially dissect the overgrown gastric tissue in order to achieve insertion of a biopsy forceps down the external aspect of the PEG tube and through the dissected orifice. This manoeuvre opened a track in the overgrown tissue for insertion of a sphincterotome mounted on a JagWire (Boston Sci., MA, USA) through the external PEG tube. The sphincterotome was then flexed completely and several radial incisions on the overgrown tissue were performed using external traction on the sphincterotome. Finally, a 6 mm endoscopic balloon dilator was passed through the scope and pulled into the PEG tube by the biopsy forceps inserted through the external end of the tube. The balloon was then fully inflated within the PEG tube and traction was applied to the balloon and endoscope for release of the buried bumper and PEG tube remnant from the dissected overgrown tissue into the stomach. The dissected orifice was then closed using endoscopic clips. The procedure was performed under antibiotic prophylaxis.

Conclusion To the best of our knowledge, this is the first use of a complimentary, multimodality endoscopic approach for the effective, minimally invasive, safe management of BBS.

IBD

OTU-001 IDENTIFICATION OF A NOVEL THERAPEUTIC AGENT FOR TREATING IBD GUIDED BY SYSTEMS MEDICINE

^{1,2}Michael Burkitt*, ²Kate Lloyd, ^{2,3}Stamatia Papoutsopoulou, ³Emily Smith, ⁴Philip Stegmaier, ²D Mark Pritchard, ⁴Alexander Kel, ³Werner Müller, ²Chris Probert. ¹Manchester University NHS Foundation Trust, Manchester, UK; ²University of Liverpool, Liverpool, UK; ³University of Manchester, Manchester, UK; ⁴GeneXplain GmbH, Wolfenbüttel, Germany

10.1136/gutjnl-2018-BSGAbstracts.104

Introduction There remains an unmet need in the treatment of IBD. The SysmedIBD project established a multi-disciplinary consortium to systematically investigate patients with inflammatory bowel disease, focusing on the dynamics of NF-κB signalling. Through this approach we identified an established drug with potential for repurposing to treat IBD, in selected patients.

Methods Novel targets with potential for impacting outcomes of IBD were identified *in-silico* by combining integrated promoter/pathway analysis of published microarray data and systematic text-mining of the published literature using the geneXplain software platform. An established drug with potential for repurposing was assessed as a proof-of-concept agent using a multi-step validation pipeline based on its effect on NF-κB dynamics *in-vitro* and *in-vivo*, and its ability to ameliorate murine experimental colitis.

Results 3191 pharmacological agents (Prestwick Chemical Library) were assessed *in-silico*. 36 agents were highly significantly predicted to influence NF-κB and other IBD target activity. Amongst the highest ranked agents were the macro-lide antibiotics. Clarithromycin (CLA) was selected as a paradigm for subsequent analyses.

The effects of CLA were investigated in 5 experiments:

1. NF-κB mediated transcription was investigated using peritoneal macrophages and enteric organoids from a mouse expressing firefly luciferase under the control of the human TNF promoter: CLA suppressed responses in both tissues ($p < 0.05$).
2. NF-κB(p65) protein shuttling dynamics were characterised in enteric organoids cultured from a mouse expressing human p65-dsRed: CLA suppressed TNF induced oscillation of p65 ($p = 0.0002$).
3. C57BL/6 mice were treated with intra-peritoneal LPS (0.125 mg/kg) to induce small intestinal NF-κB activation: CLA suppressed DNA binding of p65 ($p = 0.002$).
4. The effect of CLA on DSS colitis was studied: mice treated with CLA lost significantly less weight ($p < 0.05$), and had less severe histology than mice treated with vehicle ($p = 0.004$).
5. The effect of CLA on TNF induced nuclear localisation of p65 in human enteric organoids was studied: CLA suppressed p65 nuclear localisation ($p < 0.0001$).

Conclusions Using a systems biology approach, we have identified an agent with potential for repurposing to treat IBD. Outcomes of earlier clinical trials of clarithromycin were discordant: we are developing a biomarker of NF-κB responsiveness that may enable precise selection of patients for a personalised medicine trial.

OTU-002 HLA-DQA1 CONTRIBUTES TO THE DEVELOPMENT OF ANTIBODIES TO ANTI-TNF THERAPY IN CROHN'S DISEASE

¹Aleksejs Sazonovs, ²Nicholas A Kennedy*, ²Claire Bewshea, ¹Loukas Moutsianas, ²Gareth J Walker, ¹Katrina De Lange, ²James R Goodhand, ¹Carl Anderson, ¹Jeff Barrett, PANTS investigator consortium, ²Tariq Ahmad. ¹Wellcome Trust Sanger Institute, Hinxton, UK; ²IBD Pharmacogenetics, University of Exeter, Exeter, UK

10.1136/gutjnl-2018-BSGAbstracts.105

Background Immunogenicity to anti-TNF therapy is a major cause of loss of response, treatment discontinuation and hypersensitivity reactions and currently cannot be predicted prior to treatment. A number of factors have been associated with the risk of immunogenicity, but knowledge of the cellular and molecular mechanisms remain limited. Our aim was to investigate genetic susceptibility to immunogenicity.

Methods The PANTS (Personalised Anti-TNF Therapy in Crohn's disease) study is a 3 year prospective observational UK-wide study investigating primary non-response, loss of response and adverse drug reactions to the anti-TNF drugs infliximab and adalimumab. Anti-drug antibodies (ADAs) were measured serially at trough using the IDKmonitor total ADAb ELISA assay. Immunogenicity was defined as (a) ADA titre ≥ 10 AU/ml and (b) ADA titre ≥ 10 AU/ml with no detectable drug. A genome-wide association study (GWAS) was carried out on imputed genotype data using a Cox proportional hazards model incorporating the anti-TNF used and presence of concomitant immunomodulator as covariates (SurvivalGWAS_SV v1.3.1).

Results After quality control, we had genotype data for 1284 patients followed prospectively for a minimum of 12 months since starting anti-TNF therapy. Using a Cox proportional hazards model and an immunogenicity definition of ADAs titre ≥ 10 AU/ml we identified a genome-wide association on chromosome 6 (top SNP rs74291249 with $p = 5.6 \times 10^{-13}$). We imputed the HLA alleles at 2- and 4-digit resolution using the HIBAG package and demonstrated that this signal was driven by HLA-DQA1*05 for both infliximab and adalimumab. No additive effect of having two DQA1*05 was seen. Figures 1 and 2 show immunogenicity-free survival stratified by HLA-DQA1*05 genotype and concomitant immunomodulators at baseline.

Abstract OTU-002 Figure 1 Immunogenicity by immunomodulator and HLA-DQA1*05 for infliximab and adalimumab.