

On multivariate analysis, age, deprivation status, co-morbidity, and hospital length of stay were associated with increased 3-year mortality in both study periods.

**Conclusion** The overall mortality after hospitalisation for CD has not altered, although mortality associated with emergency medical admission has decreased, and now does not differ from rates after emergency surgical admission.

#### REFERENCE

- <sup>1</sup> Kennedy NA, Clark DN, Bauer J, *et al.* Nationwide linkage analysis in Scotland to assess mortality following hospital admission for Crohn's disease: 1998–2000. *Aliment Pharmacol Ther* 2012;35:142–53

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#### PWE-085 AUDIT OF OUTCOMES OF A MANAGED 5 ASA SWITCHING PROGRAM

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**Introduction** 5-aminosalicylic acid (5-ASA) preparations are used to induce and maintain remission in ulcerative colitis (UC). The cost of the recommended maintenance dose for oral 5ASA preparations varies from 86p and 208p per day (MIMMS 2011). Switching to cheaper 5ASAs has been suggested as a possible drug cost saving. The BNF states that preparations are not interchangeable but with little direct evidence to support this statement. The aim of this pilot study is to gain preliminary data on a primary care based 5ASA switching programme.

**Methods** Salofalk granules (Dr Falk Pharma) and Pentasa (Ferring Pharmaceuticals) were identified as the cheapest 5ASA items prescribed in 31 GP practices. An initial pilot study in one practice revealed that only 5/21 patients responded to a written invitation alone and successfully switched to Salofalk. We therefore developed a managed programme utilising a community based gastroenterology nurse specialist in 4 other practices.

A written invitation detailing the rationale for switching 5-ASA was sent to all appropriate patients who were then phoned a week later. If patients agreed to the switch, the GP surgery was contacted by the Nurse Specialist to change the repeat prescription. Patients were switched to Salofalk in 2 practices and Pentasa in the other 2. GP and hospital records were then examined 6 months post-switch to assess for evidence of patient acceptability and tolerability.

**Results** 120 patients (56 male, 64 female) with a mean age of 50 years were identified as being on a 5-ASA preparation (oral or topical). 56 (47%) were under either virtual or hospital gastroenterology follow-up. 64 patients with ulcerative colitis were taking oral 5-ASAs. 21 (33%) were already taking Salofalk or Pentasa. Of the remaining 43 patients, 24 (56%) agreed to the switch, 10 (23%) declined, and 9 (21%) did

not respond to the invitation or telephone call. Of the 24 patients who agreed to switch, only 17 (71%) completed the process. 15 (88%) remained on the new 5-ASA for at least 6 months, with reasons for discontinuation cited as preference for the previous preparation or diarrhoeal symptoms.

**Conclusion** Conducting a managed 5ASA switching programme is feasible with 17/43 eligible patients successfully switched with 15/17 continuing on these preparations. Areas for development include following up patients who initially agreed but failed to switch, recording more robustly any flares, involving secondary physicians and assessing adherence and cost savings.

This study provides preliminary evidence to develop a large scale study in this important area.

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#### PWE-086 DETERMINING STEM CELL AND CRYPT DYNAMICS IN INFLAMMATORY BOWEL DISEASE

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**Introduction** Inflammatory bowel disease (IBD) confers a high risk of development of colitis-associated colorectal cancer (CACRC) in patients with extensive colitis. It is believed that a field effect, resulting from chronic inflammation and clonal outgrowth is present in ulcerative colitis (UC) patients, and this promotes the accumulation of protumourigenic clones via increased crypt fission rates. Increased rates of crypt fission may explain the mass expansion of protumourigenic mutations across the whole length of the bowel in a very short time period as observed in patients with CACRC (Leedham *et al.*, 2009; Galandiuk *et al.*, 2012).

**Methods** Fresh frozen normal colon (n = 15) and UC colon (n = 6) tissue samples were collected and sectioned in an *en face* orientation. Two-colour enzyme histochemistry for cytochrome c oxidase (CCO) activity was performed to identify clonal populations. Adjacent crypts completely deficient of CCO activity were recorded as a 'CCO deficient patch' and those with a fraction of the crypt that was CCO-deficient were designated as 'partial crypts'. The CCO-deficient clone fraction in partial crypts was estimated by recording the number of pixels within CCO-deficient (blue) and CCO-proficient (brown) areas. The number and size of clonal patches in colitis patients was compared to non-UC controls.

**Results** As in the healthy colon, CCO-deficient clonal patches accumulate in an age dependent fashion in the UC colon. The mean number of crypts within a CCO-deficient patch was statistically significantly larger (p < 0.05) in the UC colon than in the normal colon. In addition we observe a larger percentage of wholly and partially CCO-deficient crypts in the UC colon when compared to the normal controls.

**Conclusion** The proliferative drive induced by continuous inflammation and mucosal repair in UC appears to promote the expansion of CCO-deficient patches. The increase in the proportion of wholly and partially mutated crypts in UC could be explained by crypt hyperplasia with more stem cells present driving fission. This increased rate of clonal expansion may contribute to the

increased rate of tumorigenesis in the colitic bowel, however analysis of a larger patient cohort is needed.

#### REFERENCES

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**Disclosure of Interest** None Declared.

#### PWE-087 INTERLEUKIN-17A HOMODIMER REDUCES PRO-INFLAMMATORY CYTOKINE PRODUCTION BY INFLAMMATORY BOWEL DISEASE MUCOSA CULTURED EX VIVO

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**Introduction** Interleukin (IL)-17A, which is up-regulated in inflammatory bowel disease (IBD) mucosal lesions, and IL-17F are normally present as IL-17AA and IL-17FF homodimers and may occasionally form IL-17A/F heterodimers. The role of each IL-17 dimer in IBD is currently unknown. Therefore, we studied the effects of IL-17AA, IL-17FF and IL-17A/F in ulcerative colitis (UC) and Crohn's disease (CD) mucosa.

**Methods** Inflamed colonic biopsies from 17 IBD patients (6 UC and 11 CD) were cultured *ex vivo* for 24 h with IL-17AA, IL-17FF or IL-17A/F (1 ng/ml). Mucosal myofibroblasts isolated from the inflamed colon of 4 CD and 4 UC patients were cultured for 24 h with tumour necrosis factor (TNF)- $\alpha$  20 ng/ml or with increasing concentrations (1–100 ng/ml) of IL-17AA, IL-17FF or IL-17A/F. IL-6 and IL-8 were measured in culture supernatants by ELISA.

**Results** IL-17AA, but not IL-17FF, significantly reduced both IL-6 and IL-8 production by inflamed IBD biopsies cultured *ex vivo*, whereas IL-17A/F decreased IL-8 release by IBD mucosa. No difference was observed between CD and UC. Neither IL-17AA, nor IL-17FF, nor IL-17A/F exerted any effect on IL-6 and IL-8 production by IBD myofibroblasts. As expected, TNF- $\alpha$  stimulation significantly increased IL-6 and IL-8 production by both CD and UC myofibroblasts *in vitro*. No difference was observed between CD and UC myofibroblasts.

**Conclusion** IL-17AA exerts an anti-inflammatory action on inflamed IBD biopsies cultured *ex vivo*. The action of IL-17AA is not mediated by myofibroblasts, therefore further studies are underway to ascertain which cell type is the main target of IL-17AA in IBD mucosa.

**Disclosure of Interest** None Declared.

#### PWE-088 THE IMPACT OF THIOPURINE HYPERMETHYLATION ON CLINICAL OUTCOMES IN PATIENTS WITH IBD

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**Introduction** 15% of patients with inflammatory bowel disease (IBD) prescribed azathioprine (AZA)/mercaptopurine (MP) demonstrate a skewed drug metabolism with low thioguanine nucleotides (TGN) and unexpectedly high methylmercaptopurine (MeMP) levels. This predicts a lack of treatment efficacy and excess adverse events; however studies on the effect of thiopurine hypermethylation (TH) in adult IBD patients are lacking. Importantly, where identified TH can be circumvented with the use of low dose AZA/MP and allopurinol. The aim of this study is to characterise the impact of TH in IBD patients and determine if thiopurine metabolite profiles at week 4 of treatment can predict its occurrence to allow early combination treatment.

**Methods** 273 patients with IBD, who were anti-TNF- $\alpha$  therapy naïve and matched for red blood cell thiopurine-S-methyltransferase activity, were retrospectively identified. Of these 181 patients demonstrated average MeMP:TGN ratios <11 (at least 2 profiles between weeks 12 – 52) and were used as a control group that was compared to 92 patients with average MeMP:TGN ratios  $\geq$ 11. Clinical outcomes were recorded for the first 12 months of therapy. A failure of AZA/MP as monotherapy was determined by 3 gastroenterologists with expertise in IBD. Thiopurine metabolite profiles were measured in 139 patients at week 4 of therapy and were compared to average metabolite profiles between 12 – 52 weeks of treatment.

**Results** The average MeMP:TGN ratios in those with and without TH were 21.0 and 2.52 respectively ( $p = < 0.0001$ ). The normalised dose of thiopurine was higher in patients with TH (1.91 vs. 2.09 mg/kg;  $p = < 0.0001$ ). Patients with TH were more likely to fail AZA/MP monotherapy as first line treatment during the first 12 months of therapy, in comparison with patients with normal methylation profiles ( $p = 0.0088$ , Gehan-Breslow-Wilcoxon Test). The difference in the number of treatment failures at 12 months was 15.7%. There was no difference in the occurrence of gastrointestinal intolerance, myelotoxicity or pancreatitis between groups, however there was an excess of hepatotoxicity with TH ( $p = 0.0006$ ; OR = 8.058; 95% CI: 2.188 – 29.670; Fisher's exact). TH was demonstrated in 83.7% of cases by 12 weeks of therapy. A MeMP : TGN level > 6.17 at week 4 accurately predicted TH (ratio  $\geq$ 11) after 12 weeks of therapy (AUC = 0.839;  $p = < 0.0001$ ; sensitivity = 75.4%; specificity = 88.4%).

**Conclusion** TH is associated with an excess of thiopurine treatment failures as monotherapy immunosuppression during the first 12 months of treatment. We also confirm its association with hepatotoxicity. A MeMP:TGN >6.17 may be useful in early identification of patients likely to benefit from combination treatment.

**Disclosure of Interest** None Declared.

#### PWE-089 LONG TERM OUTCOMES FROM LEUCOCYTAPHERESIS IN ULCERATIVE COLITIS: A RETROSPECTIVE CASE SERIES

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**Introduction** Leucocytapheresis, the extracorporeal removal of leucocytes from patient's blood, has conflicting evidence of benefit in ulcerative colitis (UC). Numerous studies have recorded short term clinical remission rates while few have examined the long term end-points of colectomy, death and steroid free remission.