

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

REFERENCES

- 1 Leedham SJ, Graham TA, Oukrif D, McDonald SA, Rodriguez-Justo M, Harrison RF, Shepherd NA, Novelli MR, Jankowski JA, Wright NA. Clonality, founder mutations and field cancerization in human ulcerative colitis-associated neoplasia. *Gastroenterology* 2009 Feb;136(2):542-50
- 2 Galandiuk S, Rodriguez-Justo M, Jeffery R, Nicholson AM, Cheng Y, Oukrif D, Elia G, Leedham SJ, McDonald SA, Wright NA, Graham TA. Field cancerization in the intestinal epithelium of patients with Crohn's ileocolitis. *Gastroenterology* 2012 Apr;142(4):855

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)- α 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- α 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- α 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.