Abstract PMO-234 Table 1

Rutgeerts' score	No. of patients	No. of patients with clinical recurrence at last follow-up
i_0	5	0
i_1	10	1
i_2	5	2
i_3	9	6
i_4	5	4

Competing interests None declared.

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PMO-235 A RANDOMISED PLACEBO-CONTROLLED DOUBLE-BLIND STUDY OF OCTASA® 4.8 G/DAY (800 MG TABLETS 5-ASA) FOR THE INDUCTION OF ENDOSCOPIC REMISSION IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction High concentration 5-ASA formulations have potential to improve patient adherence and increase therapeutic efficacy in ulcerative colitis (UC). We conducted a multicenter, double-blind, randomised placebo controlled trial to assess the efficacy and safety of an 800 mg Octasa® tablet for induction of remission.

Methods The trial was conducted at 26 centres in Belarus, India, Turkey and Ukraine from November 2009 to May 2011. Eligible patients had active UC with a minimum disease extent of 15 cm from the anal verge, a modified UC disease activity index (UC-DAI) score of 4–10 with a sigmoidoscopic score of ≥2 and a rectal bleeding score of ≥1. Patients requiring other treatments for UC, those with severe disease or those who had previously failed treatment with >2 g/day of 5-ASA were not eligible. Eligible patients were randomly assigned to receive three Octasa® 800 mg tablets BID or matching placebo for 10 weeks. At Week 6 and Week 10, the proportion of patients in endoscopic remission, defined by a sigmoidoscopic score of ≤1, was compared by the χ^2 test. Patients who did not undergo sigmoidoscopy were analysed as not being in endoscopic remission.

Results 281 patients were randomised, 140 received Octasa® and 141 received placebo. Of the 281 randomised patients, 248 had an evaluable post-randomisation sigmoidoscopy. The baseline characteristics were similar between the treatment groups; the mean age was 42.4 and 40.1 years, disease duration was 54.3 and 51.8 months, UC-DAI was 6.7 and 6.6, respectively for Octasa® and placebo groups. At Week 6, endoscopic remission was achieved in 45.7% of Octasa® treated patients vs 24.8% of placebo treated patients (p<0.001; 95% CI of the between group difference, 9.7% to 31.3%). The corresponding values at Week 10 were 52.1% vs 36.9% (p=0.010; 95% CI of the between group difference, 3.6% to 26.3%). The mean decrease in the sigmoidoscopic score at the end of treatment was -0.8±0.8 vs −0.5±0.7 respectively for the Octasa® and placebo treatment groups (p=0.002). The most frequently occurring adverse events were gastrointestinal disorders. Worsening of UC was reported in 9.3% Octasa® treated patients and 23.1% placebo treated patients.

Conclusion The 800 mg Octasa® tablet was safe and more effective than placebo for inducing endoscopic remission in patients with active UC.

Competing interests B Feagan: Grant/Research Support from: Tillotts, Consultant for: Tillotts, U Mittmann: Consultant for: Tillotts, D Gilgen: Employee of: Employee of Tillotts, C Wong: Grant/Research Support from: Tillotts, E Mikhailova: Grant/Research Support from: Tillotts, O Levchenko: Grant/Research Support from: Tillotts, Y Marakhouski: Grant/Research Support from: Tillotts.

PMO-236 ARE GUIDELINES FOLLOWED IN HISTOLOGY REPORTING IN INFLAMMATORY BOWEL DISEASE (IBD)?

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Introduction IBD has 240 000 suffers in the UK. Diagnosis is made on consideration of clinical, macroscopic, microscopic and radiological findings to classify Crohns disease (CD), ulcerative colitis (UC) and IBD type unclassified (IBDTU) (previously indetermediate colitis). An accurate diagnosis to differentiate between the different types of IBD is important as evidence based treatment differs among the different types. An accurate histological classification of IBD increases diagnostic accuracy by 5%–41%. In line with the BSG 2011 IBD guidelines, histopathology should "attempt to define the type of IBD, mention other coexistent diagnoses, or complications and the absence or presence of any dysplasia and its grade". There are eight recognised histological features consistent with a UC diagnosis and two further criteria to differentiate between active, inactive or quiescent disease. That for CD includes nine features with a further three to mark active disease.

Methods To assess whether histopathology reporting in IBD are in line with BSG guidelines. Using the BSG guideline "A Structured Approach to Colorectal Biopsy" the histopathology reports of 60 IBD patients were scrutinised to see if they correlated with the guideline; examined for 8 histological features of UC, 9 for CD, disease activity, complications and presence and grade of dysplasia.

Results The cohort identified 60 patients (38 UC, 22 CD). The type of IBD was specified in 25% (IBDTU 3%, UC 10%, CD 4%) and not mentioned in 40%. 23% of UC specimens were labelled as such by the histolpathologist; in that cohort there was also 3% IBDTU, 37% "IBD", 0% CD. In the CD group; 0% IBDTU, 4% UC, 18% CD, 28% "IBD". 80% of specimens had no mention of complications/coexistent features. Of those documented CMV was noted in only 1 UC case, fistulae in 2 CD cases and infection in a total of nine across the groups. Dysplasia was not mentioned in 22% UC and 59% CD; listed as a relevent negative finding in 71% UC and 36% CD and identified as low grade dysplasia (tubuloadenoma) in 3 UC cases and 1 CD case. The features most frequently identified: In UC: (1) severe crypt architectural distortion; (2) severe widespread decreased crypt density, In CD it was (1) mucosal surface normal, irregular, villous; (2) crypt atrophy.

Conclusion In our study the majority of histology reports lack important information pertaining to and even attempting to classify IBD. On average for patients suffering from CD or UC, the histological reports only state two histological signs which are of immense importance in confirming either diagnosis. None of the

histological reports mentioned all the signs in UC or CD either as positives or relevant negatives. The importance of good histological reporting may help clinicians in differentiating between the different IBD types which in turn may help guide optimum evidence based management.

Competing interests None declared.

PMO-237 PREBOTICS AS PRIMARY PREVENTION OF CROHN'S DISEASE: IMPACT ON LUMINAL MICROBIOLOGY AND ELEVATED FAECAL CALPROTECTIN IS GREATER IN HEALTHY SIBLINGS THAN IN PATIENTS

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Introduction Inflammation in Crohn's disease (CD) is driven by the intestinal microbiota, however, microbial manipulation with prebiotics is ineffective in treating active disease.[1] Siblings of patients are at risk of developing CD, and some share aspects of the CD phenotype including raised faecal calprotectin (FC) and dysbiosis. Prebiotics may alter these risk markers.

Methods Patients with inactive CD (n=19, CD activity index <150) and 12 unaffected siblings ingested 15 g/d of fructo-oligosaccharide/inulin (FOS) for 3 weeks. FC (enzyme-linked immunosorbant assay) and faecal microbiota (quantitative PCR targeting 16S ribosomal RNA (rRNA) genes, quantified relative to representative bacterial 16S rRNA genes) were measured at baseline and follow-up. Non-parametric statistical analyses were performed, and values presented as medians.

Results In patients and siblings, Bifidobacteria and *Bifidobacterium longum* increased post-FOS. In siblings but not patients, *Bifidobacterium adolescentis* and *Roseburia* spp. also increased (Abstract PMO-237 table 1). Compared with patients, siblings had a greater median percentage point change in Bifidobacteria (+14.6% vs +0.4%, p=0.028), *B adolescentis* (+1.1% vs 0.0% p=0.006) and *Roseburia* spp. (+1.5% vs −0.1% p=0.004). Of those with raised FC at baseline, it decreased post-FOS in only 7/19 patients (37%), compared with 4/5 (80%) siblings (p=0.142). The change in FC was significantly negatively correlated with baseline FC in siblings (r=−0.715, p=0.009) but positively correlated with baseline FC in patients (r=+0.352, p=0.140).

Abstract PMO-237 Table 1 Microbiota at baseline and follow-up

Bacteria Concentration log_{10} /g dry faeces, median (IQR)		Baseline	Follow-up (post FOS)	p Values
Bifidobacteria	Patients	9.4 (2.0)	9.7 (1.3)	0.013
	Siblings	9.9 (0.6)	10.3 (0.5)	0.028
B longum	Patients	9.0 (3.4)	9.4 (2.1)	0.036
	Siblings	9.1 (3.5)	9.6 (2.8)	0.008
B adolescentis	Patients	5.2 (4.4)	5.2 (9.5)	0.831
	Siblings	9.0 (4.2)	9.1 (3.8)	0.012
Roseburia spp.	Patients	9.2 (1.9)	8.9 (4.3)	0.198
	Siblings	9.3 (3.2)	9.6 (0.8)	0.023

Conclusion In contrast to inflamed CD,[1] a prebiotic effect with FOS occurs to a limited extent in non-inflamed CD, and also occurs, more markedly, in at-risk siblings. Furthermore, FC decreased in siblings post-FOS, but did not change significantly (and even tended to rise) in patients with inactive CD. Prebiotics may best be employed in disease prevention rather than treatment.

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PMO-238 BLOCKADE OF THE B7 INTEGRIN PREVENTS ADHERENCE OF T LYMPHOCYTES TO MADCAM-1 IN AN IN VITRO MODEL OF VASCULAR MICROCIRCULATION POST-CAPILLARY SHEAR FLOW

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Introduction The intestinal vascular microcirculation plays a pivotal role in the immune cell dysregulation that drives inflammatory bowel disease. T lymphocyte recruitment, adherence and migration are dependent on the integrin heterodimer α4β7, which binds with high affinity to vascular endothelium expressing MAdCAM-1, prior to lymphocyte diapedesis into the lamina propria. This integrin therefore provides a potential therapeutic target.

Methods Using Cellix® technology, a dynamic in vitro model was created, testing the potential of β7 integrin blockade to impair lymphocyte adhesion to MAdCAM-1 under shear flow. The Cellix® system comprises a microfluidic platform and nano pump, with biochip channels that replicate the shear flow and stress found in post-capillary venules. Peripheral blood mononuclear cells (PBMC) were utilised, along with HuT78 T cells that constitutively express the α4β7 integrin and the chemokine receptor CXCR4, known to be upregulated in inflammatory bowel disease. Biochips were coated for 12 h at 4°C with 10 μg/ml MAdCAM-1 Fc, then blocked with 0.1% BSA for 30 min to prevent non-specific adherence to plastic. Adherence of T cells was quantitatively assessed by microscopy at a physiological flow rate of 1 dyne/cm^3. The effect of an anti-human β7 integrin monoclonal antibody (clone Fib504, BD Pharmingen) on lymphocyte adherence was measured. 3 nM of the chemokine CXCL12 (ligand for CXCR4) was added to the system to model the pro-inflammatory environment present in inflammatory bowel disease. Experiments were performed at 37°C.

Results HuT78 lymphocytes and PBMC (5×10^6/ml) provided consistent adherence to MAdCAM-1 under flow, mean ± SE adherent cells/hpf of 32.8±4.5 and 46.2±3 respectively. Adherence was significantly improved with the addition of 3 nM CXCL12 to 45.7±2.8 ($p<0.05$) and 78.5±1.5 ($p<0.001$). Incubating the cells with the Fib504 anti-β7 integrin antibody, led to a significant reduction in adherence of unstimulated cells to 17.8±2 ($p<0.001$) and 18±3.2 ($p<0.0001$). This reduction was maintained on stimulation with CXCL12, at 17.3±0.9 ($p<0.001$), and 5.3±0.9 ($p<0.0001$).

Conclusion This novel in vitro model, demonstrated significant modulation of α4β7 lymphocyte adhesion to the ligand MAdCAM-1 with an anti-β7 antibody. This highly controlled model system provides a more physiological representation of chemokine driven responsiveness than previously published chemotaxis or adhesion assays, and thus the Cellix® platform may serve as a useful tool for the development and validation of future anti-lymphocyte adhesion therapeutics. This research supports the clinical investigation of therapeutics targeting the β7 subunit or α4β7 heterodimer in this disease setting.

Competing interests None declared.