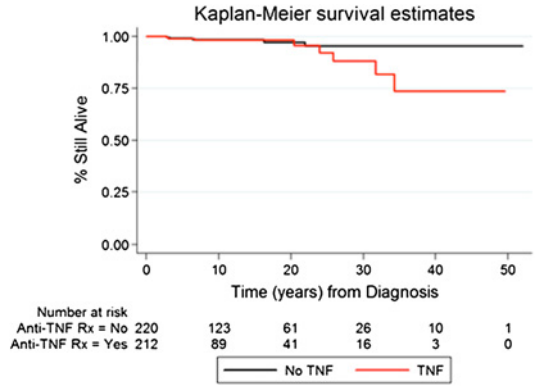
software. Proportional hazard regression model was used to assess mortality. Other SAE and OI were studied using logistic regression, t-test, and χ^2 with Fishers exact.

Results Cohort 1: 137 (64.5%) CD patients. 170 (80%) received Infliximab (IFX) as their only anti-TNF treatment, 34 (16%) IFX and Adalimumab (ADA) and 8 (4%) ADA only. Cohort 2: 220 patients comprising 88 (40%) CD. The mean age at drug initiation was 35.3 (SD 16.1) yrs in cohort 1, 45.7 (SD 15.9) yrs in cohort 2 ($p<0.0001$). Median follow-up after drug initiation in cohort 1 was 2.7 years (0—11.0), total 714.9 yrs, in cohort 2 6.4 (0—30.8) yrs, total 1524 yrs. There were 8 (4%) deaths in cohort 1 (1 cardiovascular (CVS), 3 sepsis, 3 solid organ malignancies, 1 haematological malignancy) and 5 (2%) deaths in cohort 2 (2 CVS, 2 sepsis, 1 haematological malignancy). Cohort 1 patients had a higher mortality when corrected for age at diagnosis (HR 3.4 95% CI 1.1 to 10.5) Abstract PWE-233 figure 1. In cohort 1 there were two cases of demyelination (1 suspected), 1 TB reactivation, 40 in-patient treated infections, 8 malignancies, seven cases of *Clostridium difficile* and no drug induced lupus. Hospital recorded SAE did not differ between cohorts 1 and 2 and no risk factors were identified. The mean number of primary care recorded OI was 5.8 (SD 5.8) in cohort 1 and 4.5 (SD 4.2) in cohort 2.



Abstract PWE-233 Figure 1

Conclusion The age at diagnosis adjusted mortality of IBD patients treat with anti-TNF is significantly greater than patients treated with thiopurines alone. Causality is unclear and may reflect underlying disease severity. Anti-TNF treated patients have similar rates of other SAE and primary care OI compared to patients treated with thiopurines alone.

Competing interests None declared.

PWE-234 OPTIMISING THE RESPONSE TO THIOPURINE THERAPY: A SEARCH FOR NOVEL EXPLANATIONS FOR THIOPURINE HYPERMETHYLATION

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Introduction Thiopurines are not effective in up to 1/3 of patients with inflammatory bowel disease (IBD) and 1/5 have to discontinue therapy due to side effects. An important cause of these problems is thiopurine hypermethylation. This is a catabolic process leading to an unfavourable thiopurine metabolite profile (high methylmercaptopurine (MeMP) to low thioguanine nucleotide (TGN) ratio; >11:1), which cannot be predicted by measurement of thiopurine-*S*-methyltransferase (TPMT) activity. Importantly thiopurine hypermethylation can be circumvented with the use allopurinol in combination with a low dose thiopurine. The aim of this study is to establish the mechanism of thiopurine hypermethylation and identify predictive genetic markers to allow early combination therapy. We hypothesised that thiopurine hypermethylation occurs as a result of genetic factors that affect methylation flux and the cellular transport of methylated metabolites.

Methods 168 age and dose-matched patients prescribed AZA/6-MP were identified. Genomic DNA was extracted from EDTA blood samples of 76 patients demonstrating thiopurine hypermethylation and 92 patients with normal methylation profiles. Polymorphic sequence variants in genes predicted to affect thiopurine methylation flux and cellular metabolite transport were identified from single nucleotide polymorphism (SNP) databases and genotyped by Taqman assay. Associations were tested using Fisher's Exact test.

Results We found a significant association between the haplotype of rs9332377 T and rs4646316 C, which encodes a low-activity synonymous Catechol-O-methyltransferase (COMT) variant, and protection from thiopurine hypermethylation (rs9332377 T, $p=0.0178$, rs4646316 C, $p=0.03$). A polymorphism in the nucleobase transporter, ABCB5, was significantly associated with thiopurine hypermethylation (rs2031641 G/G, $p=0.0098$). The association was strengthened when patients with MeMP levels >5000 pmol/l vs MeMP <5000 pmol/l were compared ($p=0.0065$).

Conclusion Changes in methylation flux due to the activity of methyltransferases other than TPMT affect the formation of thiopurine methylated metabolites, likely through direct competition for the essential co-factor S-adenosylmethionine. Furthermore, polymorphism in the ABCB5 gene, which affects the nucleotide-binding domain of this transporter, is associated with thiopurine hypermethylation, suggesting reduced cellular efflux of methylated metabolites. Further studies are now indicated to establish the role of these genetic markers in clinical practice.

Competing interests None declared.

PWE-235 SCREENING USING THE EUROPEAN CROHN'S AND COLITIS ORGANISATION (ECCO) GUIDELINES DEMONSTRATES HIGH STRONGYLOIDES SERO-PREVALENCE IN MIGRANTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction Strongyloidiasis can persist and cause hyperinfection years after acquisition when host immunity is impaired. European Crohn's and Colitis Organisation guidelines[1] on opportunisitc infections recommend that Inflammatory Bowel Disease (IBD) patients returning from endemic areas be screened. However, prevalence of intestinal helminths in migrant IBD patients is unknown. We investigated the sero-prevalence of Strongyloidiasis and factors associated with infection.

Methods Migrant patients attending IBD clinic over a 10-month period, with a diagnosis of Crohn's disease (CD) or Ulcerative colitis (UC), were tested for Strongyloides serology. Eosinophil count and inflammatory markers were measured. Ethnicity was used as a proxy for migrant status. Sero-positive patients were followed-up with a Strongyloides charcoal culture before treatment with Ivermectin. Repeat eosinophil count and inflammatory markers were performed 3 months later. T test and χ^2 analysis ($p<0.05$) were performed using SPSS for Windows.

Results 97 migrant patients (54 CD vs 43 UC) were tested. 13/97 patients were sero-positive. In both groups, over 70% of patients were from Asia. Mean eosinophil counts ($\times 10^9$/l) were not different between the two groups (0.29 vs 0.22, $p>0.05$). No significant

change was seen in eosinophil count or in inflammatory markers post treatment. In the sero-positive group 23% had past and current eosinophilia, but this was not statistically different from sero-negative patients. 9/13 reportable charcoal stool cultures were negative. No patients with Strongyloides were taking steroids, compared to 23% of sero-negative patients. In both groups, >40% were on two or more immunosuppressants.

Conclusion There is a high sero-prevalence of Strongyloides in migrant IBD patients. Patients from Asia demonstrated the highest prevalence. Eosinophilia and raised inflammatory markers were not predictive of positive serology, most likely due to the high rate of immunosuppression. We cannot confirm all sero-positive patients were infected; published data[2] supports the specificity of Strongyloides serology for current infection. We recommend ECCO guidelines and current British Society of Gastroenterology guidelines are adapted to include targetting IBD patients who originate from endemic areas and serological testing be first line. Follow-up of patients is required to assess the impact of treatment on IBD activity.

Competing interests None declared.

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PWE-236 WHITE CELL APHAERESIS (WCA) WITH ADACOLUMN IS EFFECTIVE IN SELECTED CASES OF CHRONIC REFRACTORY COLITIS WITH HIGH HISTOLOGICAL ACTIVITY

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Introduction Treatment options for patients with chronic refractory colitis are limited. White cell aphaeresis (WCA) is effective in inducing clinical remission in chronic refractory colitis in patients with a strong inflammatory burden at baseline and histologically active disease. Previous multinational sham controlled trials have demonstrated significant improvement when patients with high histological activity (modified Rileys score) are selected for treatment.

Methods A prospective study was conducted in 30 patients with severe steroid -dependent or steroid -refractory ulcerative colitis referred for WCA. Inclusion criteria were (i) High disease activity score (partial Mayo score ≥6) (ii) Intractable symptoms despite treatment with steroids and/or immunosuppressants (iii) Severe disease at endoscopy and histologically. The aim was to induce clinical and IBD-Q remission at 12 weeks. A Mayo score ≤3 defined clinical remission. The 32 item Inflammatory Bowel Disease questionnaire (IBD-Q) was used to assess quality of life prior to treatment and at 12 weeks.

Results Patient Characteristics: Prior to treatment 28 patients (93.3%) were prescribed 5-ASA compounds. 12 patients (40%) were prescribed topical therapies (5-ASA enemas or suppositories/steroids enemas). 27 patients (90%) were steroid dependent (Prednisolone mean dose 21.1 mg, median 20 mg). Three patients (10%) were steroid refractory (no response to high dose oral steroids). 13 patients (43.3%) were prescribed Azathioprine of the remainder all had documented intolerance or a contraindication. One patient (3.3%) was prescribed six Mercaptopurine. Five patients had failed Infliximab (16.6%) and in one patient (3.3%) it was contraindicated. 1 patient (3.3%) had failed intramuscular Methotrexate. **Outcomes**: At week 12 clinical remission (Mayo score ≤3) was achieved in 22 patients (73.3%), 18 patients (60%) were no longer prescribed oral steroids. IBD-Q remission at week 12 was achieved in 19 patients (63.3%). Of the remainder, five patients (16.6%) achieved an IBD-Q response. Of eight patients (26.6%) who failed to achieve clinical remission at 12 weeks, one achieved delayed remission at 20 weeks. Of the remaining seven treatment failures, five underwent colectomy (16.6%).

Conclusion WCA can be effective in inducing clinical remission and improving quality of life (IBD-Q) indices in chronic severe steroid refractory ulcerative colitis with highly active disease histologically. This data series suggests WCA should be considered before colectomy in this challenging patient group.

Competing interests None declared.

PWE-237 CICLOSPORIN IN ACUTE SEVERE ULCERATIVE COLITIS: A META-ANALYSIS

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Introduction The efficacy of intravenous Ciclosporin in the treatment of acute severe steroid refractory ulcerative colitis is variable in several small studies.[1 2] The benefit of immunosuppression in initial responders for preventing delayed colectomy is unclear and large randomised trials are not forthcoming. The primary aim of the meta-analysis was to evaluate the efficacy of intravenous Ciclosporin in steroid refractory acute colitis. Primary end points were immediate and delayed colectomy rates. Secondary end points were delayed colectomy rates in responders on immunosuppression vs no immunosuppression.

Methods MEDLINE (1966–2011), EMBASE and PubMed databases searched using keywords, "colitis" "acute colitis," "ciclosporin," "cyclosporin," "ulcerative colitis" and "fulminant colitis" from January 1965 to December 2011. Articles were selected/reviewed based on a pre-defined inclusion criteria and independently reviewed by three authors (RK, NG and TT) and data collected. Meta-analysis using random effects model was done.

Results 31 studies involving 1295 patients were included in the final analysis (692 males, average age 37.4 years, range 27–58.8 years). The average duration of colitis prior to admission (25 studies, 1062 patients) was 54 months and 660 patients (26 studies, 1148 patients) had pancolitis. The immediate colectomy rate was 23.6%, (95% CI 20% to >27.5%) and delayed colectomy 37.8% (95% CI 32.8% to 43.1%) at an average follow-up of 28.8 months. On meta-regression analysis the duration of colitis was the only confounding factor for delayed colectomy (p=0.05). On sub-group analysis, immunosuppression (Aza/6MP) in initial responders significantly reduced delayed colectomy rates by 20% (OR 0.36, 95% CI 0.61 to 0.81, p=0.014). The number need to treat to prevent one delayed colectomy was 5. There was a 13% increase in colectomy rates in the sub-group of patients (5 studies, 113 patients) who were on immunosupression (failed immunospression) prior to iv ciclosporin although this was not statistically significant (p=0.22).

Conclusion Intravenous Ciclosporin prevents immediate and delayed colectomy in 76.4% and 62% respectively. There is a non-significant increase in colectomy rates (13%) in patients who failed immunosuppression prior to Ciclosporin. Immunosuppression in initial responders significantly reduces delayed colectomy rates and should be considered unless contraindicated.

Competing interests None declared.

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