Results 100 patients, 58 female with a mean age of 49.2 (range 18–75), 42 male with a mean age of 47.1 (range 18–77). Mean disease duration was 12.8 (range 0–41). Mean and median scores for IBD patients were 10.15 (95% CI: 9.2–11.1) and 9 (95% CI: 8–11) respectively. CD (38) patients achieved a significantly higher score than UC (61), median scores of 10.5 and 9 respectively, p = 0.007. CCKNOW scores achieved were significantly lower with increasing age, p = 0.0006. Patient gender, ethnicity, disease duration or perceived disease activity had no significant effect upon CCKNOW score.

Conclusion Patient understanding of inflammatory bowel disease is no better now than when assessed in 1999, median scores being 9 and 10 respectively. There are persisting knowledge deficits regarding the subjects of fertility and the complications of IBD. Elderly patients performed significantly worse than younger counterparts and may therefore benefit the most from increased access to appropriate educational programmes and support.

REFERENCE
1 Quality Care Service standards for the healthcare of people who have Inflammatory Bowel Disease (IBD) IBD Standards Group. 2009 http://www.ibdstandards.org.uk/ (accessed 21.4.13)

Disclosure of Interest None Declared.

PWE-098 EARLIER USE OF AZATHIOPRINE IN ULCERATIVE COLITIS DOES NOT ALTER SUBSEQUENT NEED FOR HOSPITALISATION, BIOLOGIC THERAPY, OR COLECTOMY

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Introduction Azathioprine (AZA) is an established treatment for ulcerative colitis (UC). However, controversy exists regarding its efficacy in inducing and maintaining clinical remission, particularly with the advent of biologics which, unlike AZA, have been tested in large, rigorously designed randomised controlled trials. We studied the effectiveness of AZA as second-line therapy after failure of 5-aminosalicylates (5-ASAs) in a large cohort of UC patients, with particular emphasis on whether its earlier use alters the natural history of the disease course.

Methods All UC patients treated with AZA at our centre were identified from a prospective electronic database. We excluded individuals who had received either infliximab or ciclosporin as a bridge to AZA. The following demographic data were collected: gender, age at diagnosis, age at AZA commencement, concomitant therapy at AZA commencement, and duration of disease prior to AZA commencement.

Results In total, 255 patients were included (55% male, mean age at diagnosis 36.4 years). Mean age at commencing AZA was 42.3 years. Mean disease duration prior to AZA commencement was 70 months. Concomitant therapy at AZA commencement was oral 5-ASAs in 87%, topical 5-ASAs in 22%, and oral prednisolone in 77%. At 4 months, 207 (81%) of 255 patients were still on AZA (46 had discontinued due to adverse events and 2 due to non-response), and 163 (64%) had responded to therapy.

There were 165 (65%) patients still receiving AZA at last point of follow-up, of whom 153 (60%) were in remission (mean duration of therapy 64.5 months). 26 patients required admission to hospital for an exacerbation during AZA treatment, 20 patients ultimately required biologic therapy, and 21 underwent colectomy. Among 90 patients receiving AZA within 12 months of diagnosis, 21 (23%) patients experienced one of these endpoints, compared with 29 (19%) of 154 who commenced AZA >12 months after diagnosis (p = 0.40).

Serious adverse events included 6 cases of pancreatitis, 6 cases of cancer (3 non-melanoma skin cancers) and 1 case of neutropenic sepsis presenting within 1 month of AZA commencement.

Conclusion AZA is a safe and effective therapy for UC patients who fail 5-ASAs, and should continue to be used prior to instituting biologic therapies. However, earlier use does not seem to alter the natural history of the disease.

Disclosure of Interest None Declared.

PWE-099 DIRECT DETECTION OF THIOPURINE METABOLITES IN ERYTHROCYTES AND LEUKOCYTES USING A NOVEL LCMS/MS METHOD TO INTERROGATE DRUG RESPONSE AND IN VIVO METABOLISM

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Introduction One of the major issues hampering the understanding of metabolism and response to thiopurine drugs (azathioprine (Aza), mercaptopurine (MP) and thioguanine (TG)) is the indirect method for measuring their metabolites in red blood...
cells (RBC) after pre-analytical processing. RBC which lack inosine-monophosphate dehydrogenase, critical for bioconversion of thiopurines, do not reflect thiopurine metabolism in peripheral mononuclear cells (PMC) as exemplified by the poor concordance between metabolite levels and clinical response. To address this problem we have developed a 'direct method' of measuring thiopurine metabolites in both RBC and PMC.

Methods PMCs and RBCs were isolated from blood samples of thiopurine (low dose aza/allopurinol (LDAA), TG or MP) treated patients. They were separated by Lymphoprep, sonicated, centrifuged and 50 μL of supernatant injected for chromatographical separation of the metabolites and analysed on a API4000 triple quadrupole LC-MS/MS. Standard curves and controls validated and metabolite levels reported as pM of metabolites/mg of protein.

Results Concentrations of metabolites in both RBC and PMCs were determined from standard curves (7.8 -500 nM) and expressed relative to protein concentration. Comparison between these and results from commercially available RBC metabolite levels are shown below. Sum of methylated metabolites from the LCMS/MS includes methylated thioguanine nucleotides. Undetected metabolites listed as ND

Conclusion The metabolite profiles between patients on FDA, LDAA and TG are very different indicating that these treatments have distinct metabolic pathways. The direct and commercial methods are also different in metabolic profiles raising the suspicion that the commercial method is not an accurate reflection of true metabolic profiles in RBCs. The clinical implication from these data is that the choice of drug protocol (LDAA in "high methylators") is not based on reliable methods. To confirm this, these data and other markers of response and efficacy are being collected prospectively to facilitate a more informed and deeper understanding of how and why FDA, LDAA and TG treated patients respond to these different drug protocols, with an ultimate goal of individualisation of therapy and improvement of the use of these cheap and established drugs.

Disclosure of Interest None Declared.

PWE-100 INCREASING WEIGHT AND BODY MASS INDEX ADVERSELY AFFECT THIOGUANINE NUCLEOTIDE LEVELS IN INFLAMMATORY BOWEL DISEASE

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Introduction Inflammatory bowel disease (IBD) often requires long term immunosuppressive therapy with thiopurines such as azathioprine (AZA) or mercaptopurine (MP) and anti-tumour necrosis factor (TNF) agents. Despite the variable response to thiopurines and anti-TNF agents, few predictive factors of response have been identified. A lower body mass index (BMI) has been associated with a better outcome for azathioprine therapy, infliximab and adalimumab. Obese IBD patients are more likely to have active disease or be hospitalised. This study examined the association between weight and thiopurine therapy by examining 6-thioguanine nucleotide (6-TGN) levels.

Methods We conducted a retrospective analysis of patients who were treated at the Royal Liverpool University Hospital with a thiopurine. The dose of thiopurines was adjusted as tolerated to a maximum of 2.5 mg/kg for AZA and 1.5 mg/kg for MP. Eligible patients had a 6-TGN measurement with their height and weight recorded at the same time. Associations between 6-TGN, BMI, weight, patient demographics and biochemical indices were estimated using a multivariable linear regression model. Body fat index was calculated as described previously. All tests were declared statistically significant if p < 0.05.

Results 106 patients (48 male, 58 female) were included and contributed 133 measurements. 55% had Crohn’s disease and 45% had ulcerative colitis. 91% were on AZA and 9% were on MP. After adjustment, a one kilogram increase in weight was associated with a 1.62 unit decrease in 6-TGN levels (95% CI: 0.40 to 2.82, p = 0.0094). Body fat index correlated strongly with weight for both males and females (0.8345 and 0.8860 respectively) and a significant difference was found between BFI for each sex (p < 0.001) with females, on average, having a higher BFI. Weight, BMI and BFI differed significantly across sub-therapeutic, therapeutic and supra-therapeutic 6-TGN groups (Table 1).

Conclusion 6-TGN levels decreased significantly with increasing weight and BMI despite a similar weight based dosing. This may explain the previously noted adverse outcomes in obese IBD subjects and underscores the importance of thiopurine metabolite testing

Disclosure of Interest S. Subramanian Speaker bureau with: Speaker honoraria from Warner Chilcott, Shire, MSD, Abbvie and Amirall, Conflict with: Conference support from Abbvie, MSD and Warner Chilcott, S. Poon: None Declared, A. Kneebone: None Declared, R. Acher: None Declared, R. Jackson: None Declared, B. Gregg: None Declared, P. Collins: None Declared, C. Probert: None Declared, M. Dibb: None Declared.

PWE-101 IMAGING THE SMALL BOWEL IN ULCERATIVE COLITIS-RELEVANT OR STILL “UNCLASSIFIED”?

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Introduction It is widely accepted that Ulcerative Colitis (UC) is a mucosal inflammatory disease confined to the colon. Bolder