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 uL 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

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Abstract PWE-100 Table 1

	6TGN Level			
	Sub (<230 pg/ml) n = 63	Therapeutic (230–450 pg/ml) n = 48	Supra (>250 pg/ml) n = 22	*p*
Dose per kg:	1.71 (0.65)	1.62 (0.66)	1.84 (0.70)	0.4641
Weight	79.3 (26)	67.5 (14)	62.2 (14)	**0.0008**
Body Mass Index (BMI)	27.4 (9)	23.4 (4)	22.6 (5)	**0.0024**
Body Fat Index (BFI)	31.1 (12)	25.6 (9)	25.6 (11)	**0.0199**

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