bowel diseases (IBD), are typically dosed according to patient's body weight. A previous meta-analysis showed higher remission rates in patients with "therapeutic" levels of 6-thioguanine (6-TGN), but weight based dosing correlates poorly with 6-TGN levels (1). 6-TGN testing is not universally available, results are not available immediately and repeated measurements are necessary to ensure dose adequacy and adherence to therapy. Proxy measures such as mean corpuscular volume (MCV) and lymphocyte count (LC) have been advocated as markers of dose adequacy. We aimed to analyse the relationship between 6-TGN, patient demographics, MCV, LC and other putative surrogate markers of therapeutic 6-TGN levels.

Methods: This retrospective study was conducted at the Royal Liverpool University Hospital. All patients who had concurrent measurements of 6-TGN and full blood count were included in the analysis. 6-TGN levels were classified as sub-therapeutic (<230), therapeutic (230–450) or supra-therapeutic (>450). The association between 6-TGN, patient demographics, MCV, LC and other putative surrogate markers was estimated using a multivariable linear regression model for continuous 6-TGN and a proportional odds logistic regression model for the ordered 6-TGN levels. All results were declared statistically significant if p < 0.05.

Results: A total of 106 patients (48 male, 58 female) were included and contributed 133 measurements. Of these patients 58 (55%) had Crohn’s disease and 47 (44%) had ulcerative colitis. The mean azathioprine dose was 123.5 mg (SD 73.8) or 1.70 mg/kg (SD 0.67). After adjusting for other variables, a one unit increase in MCV, was associated with a 10.88 unit increase (95% CI: 4.31 to 17.45, p = 0.0001) and a one unit increase in ALT was associated with a 2.67 unit decrease in 6TGN levels (95% CI: 0.36 to 4.97, p = 0.0001) and a one unit increase in MCV, was associated with a 10.88 unit increase (95% CI: 4.31 to 17.45, p = 0.0001). There was no correlation between LC, NC, WCC or ALKPHOS and 6-TGN levels.

Conclusion: MCV and 6-TGN nucleotide levels increase together. If 6-TGN levels are not available, MCV can be used as a crude but imperfect surrogate marker of dose adequacy and toxicity.

REFERENCE
Osterman MT, Kundu R, Lichtenstein GR, Lewis JD. Association of 6-thioguanine nucleotide levels and inflammatory bowel disease activity: a meta-analysis. Gastroenterology 2006;130:1047–53

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