Abstract PTU-104 Figure 1 Proposed model of thiopurine hepatotoxicity.

allopurinol (ALLO) co-therapy (LDAA). The current opinion is that hepatotoxicity is secondary to high red cell methylated metabolites (MMPR/MMP). However, many patients develop hepatotoxicity without high MMP levels.² We report a series of patients who regardless of low MMP developed hepatotoxicity whilst on allopurinol co-therapy, 3 of which were TPMT heterozygotes.

Aim to determine outcomes of increasing the dose of Allopurinol from 100 to 200 mg in patients with hepatotoxicity to LDAA.

Methods Patient records and our IBD database were searched for patients on LDAA who developed hepatotoxicity whilst on LDAA (100 mg of ALLO). Liver function tests (LFTs), liver screen, ultrasound results and clinical outcomes were determined.

Results From the 2500 patients with IBD locally, 600 were exposed to thiopurines and 300 were on LDAA. Nine patients had sustained hepatotoxicity, 3 were TPMT heterozygotes. Seven of these patients responded fully to increased dose of ALLO to 200mg. Two had a suboptimal response (1 had PSC as a potential cause). All patients had asymptomatic abnormalities of LFTs, negative chronic liver screen apart from 2 who had ultrasound proven fatty liver disease without abnormal LFTs prior to LDAA. We observed that all patients had improvements in their LFTs, whilst 7 had complete correction of abnormal AST, ALP and bilirubin. Median time for treatment was 24 months (range 12–48 months), with full response to therapy in all 7 patients.

Conclusion This is the first series which reports improvement of LFTs by increasing ALLO dose for patients on LDAA. This subgroup of patients were unlikely to have high MMPR as 3 of them were TPMT heterozygotes and all were on LDAA therapy, therefore a different mechanism, of hepatotoxicity is proposed (Figure 1). It is possible that reactive oxygen species generated from the oxidation of metcaptopurine are responsible, and this can be further improved by adjusting the dose of ALLO. Further studies are required.

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Disclosure of Interest None Declared.

PTU-105 EXPRESSION OF MICRORNAS MIR-31, MIR-146A AND MIR-155 IS SIGNIFICANTLY ELEVATED IN ANTI-TNF-ALPHA TREATMENT FAILURE IN COLONIC CD

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Introduction Crohn's disease (CD) is a Th1/Th17 driven disease in which TNF- α and INF- γ play important roles. Anti-TNF- α drugs are used in moderate-severe CD to induce and maintain remission. Mucosal healing is an aim of therapy. MicroRNAs are noncoding RNAs which control translation of mRNA. MiR-31, miR-146a and miR-155 are involved in the regulation of immune responses and are deregulated in CD. Aim of this study is to evaluate the impact of medical treatment on microRNA expression in CD and to investigate microRNAs as biomarkers in CD.

Methods 37 patients with colonic CD undergoing colonoscopy were recruited. A partial Simple Endoscopic Score for CD (SES-CD) was assessed. Sigmoid biopsies were taken from 19 patients in remission (SES-CD=0) and 18 patients with active sigmoid CD (SES-CD $\geq$ 1). Remission (R) was defined as mucosal healing (SES-CD=0) and treatment failure (F) as an SES-CD $\geq$ 1 in the left colon. MicroRNA (miR-31, miR-146a and miR-155) and mRNA expression (TNF- α , INF- γ) were evaluated by qPCR. Sub-analysis compared treatment naïve patients (6 inactive/8 active) to patients on thiopurines (TP) (R= 5/F= 5) and anti-TNF- α therapy (R=6/F=7).

Results miR-31, miR-146a and miR-155 were significantly up-regulated as were TNF- α and INF- γ in active sigmoid CD compared to patients in remission. Patients on TP compared to treatment naïve patients showed significant down-regulation of TNF- α and INF- γ in remission, compared to treatment naïve patients with active CD. MicroRNA levels in TP failure were interestingly lower compared to patients in remission. In contrast, microRNA levels in the anti-TNF- α group in therapy failure were significantly elevated compared to active treatment naïve patients, behaving opposite to patients on TP. MicroRNA expression in remission showed levels similar to treatment naïve patients in remission. While TNF- α and INF- γ returned to base levels in remission on anti-TNF- α drugs, significantly lower compared to active treatment naïve CD, in therapy failure TNF- α remained elevated and INF- γ was significantly raised.

Conclusion Our data reveals a clear up-regulation of miR-31, miR-146 and miR-155 as well as of TNF- α and INF- γ in active colonic CD. TP and anti-TNF- α drugs significantly alter the expression of microRNAs miR-31, miR-146a and miR-155 compared to treatment naïve patients behaving in an opposing manner. MicroRNAs remain significantly elevated in patients with sigmoid CD failing to respond to anti-TNF- α treatment. MicroRNAs expression profiles may have a role as biomarkers in predicting treatment failure in CD.

Disclosure of Interest None Declared.

PTU-106 SUCCESSFUL PREGNANCIES WITH THIOPURINE-ALLOPURINOL CO-THERAPY FOR INFLAMMATORY BOWEL DISEASE

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Introduction Combination of low dose thiopurine with allopurinol can improve the clinical efficacy and bypass some of the adverse reactions of thiopurine monotherapy. Thiopurines can be used safely during pregnancy but there is scarce data regarding allopurinol. We report twelve cases of safe use of thiopurine and allopurinol co-therapy to manage IBD during pregnancy.