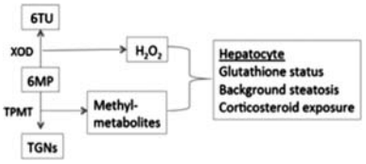

Abstract PTU-104 Figure 1 Proposed model of thiopurine hepatotoxicity.

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≥1). Remission (R) was defined as mucosal healing (SES-CD=0) and treatment failure (F) as an SES-CD≥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 interstingly 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.

Abstract PTU-106 Table 1 Pregnancy and fetal outcomes with thiopurine and allopurinol co-therapy

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Diagnosis	UC	UC	UC	UC	UC	UC	UC	Crohns
Dose thiopurine/allopurinol	AZA 50 mg, Allo 100 mg	AZA 25 mg 5d / 50 mg 2d, Allo 10 0mg	AZA 25 mg 5d / 50 mg 2d, Allo 100 mg	AZA 50 mg, Allo 200 mg	6MP 50 mg 5d, Allo 100 mg	6MP 50 mg 5d, Allo 100 mg	6MP 25 mg 3d, Allo 100 mg	6MP 50 mg 6d, Allo 100 mg
Duration of pre-pregnancy co-therapy (months)	6	19	1	12	14	6	15	24
Age at pregnancy (years)	21	24	34	31	32	36	32	29
Number of flares in pregnancy	0	1	0	0	0	0	0	0
Gestation at delivery (weeks)	41	38 +1	39 +4	40 +3	38	39	34	38
Mode of delivery	SVD	C-section	C-section	SVD	SVD	SVD	C-section	C-section
Fetal birth weight	3.5 kg	2.94 kg	3.42 kg	3.95 kg	3.75kg	3.0 kg	2.91 kg	3.51 kg

Methods Patients were retrospectively identified at two hospitals in the UK and in Australia, using our local IBD databases. All pregnancies of co-therapy patients were included. TPMT activity and pre-pregnancy weight were used to calculate thiopurine dosing. Data regarding pregnancy and fetal outcomes were collected from patient notes.

Results Eleven females on co-therapy became pregnant, totalling twelve pregnancies with eight live births (Table 1) and four ongoing pregnancies. There were no reported terminations, miscarriages or spontaneous pre-term deliveries (<37 weeks). Four patients gave birth by spontaneous vaginal delivery (SVD); four by Caesarean section (C-section). There were no low birth weight (<2.5kg) babies. The APGAR scores of all babies were normal and no congenital malformations were identified either on fetal ultrasound scans or on neonate checks. The median duration of follow-up of babies was 6.5 months with no indication of morbidity.

Conclusion All twelve cases were treated successfully with co-therapy without any adverse pregnancy related events or adverse fetal outcomes. Intrauterine exposure of the fetus to thiopurine metabolites is not greater with combination therapy compared with thiopurine monotherapy. There are only two reports of congenital malformations with maternal allopurinol use. The case for an association based on two cases is weak, moreover a negative publication bias with respects to successful maternal allopurinal use is suspected. Our study provides support for clinicians and patients wishing to continue thiopurine-allopurinol co-therapy during pregnancy.

Disclosure of Interest None Declared.

PTU-107 COMPARISON OF MORTALITY FOLLOWING HOSPITALISATION FOR ULCERATIVE COLITIS IN SCOTLAND BETWEEN 1998–2000 AND 2007–2009

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Introduction We have previously demonstrated concerningly high 3-year mortality following hospitalisation with ulcerative colitis (UC) between 1998 and 2000 in Scotland.[1] We have extended these studies by examining 3-year mortality following hospitalisation with UC in Scotland between 2007–2009, providing an opportunity for comparison with our earlier results.

Aim To compare 3-year mortality, and factors related to mortality, in Scottish patients hospitalised with ulcerative colitis (UC) between Period 1 (1998–2000) and Period 2 (2007–2009).

Methods The Scottish Morbidity Records and linked datasets were used to assess 3-year crude mortality, standardised mortality ratio (SMR) and multivariate analyses of factors associated with 3-year mortality. The 3-year mortality was determined after four admission types: surgery-elective or emergency; medical-elective or emergency. Age-standardised mortality rates (ASR) were used to compare mortality rates between periods.

Results The admission rate with UC increased from 10.6 per 100,000 of the Scottish population per year in Period 1 to 11.6 in Period 2 (p = 0.046). Among those admitted with UC, the proportion aged <30yrs increased (p = 0.009). Crude and adjusted 3-year mortality fell between time periods (Crude 12.2% [Period 1] to 8.3% [Period 2], adjusted OR 0.59, CI 0.42 to 0.81, p = 0.04). Following emergency medical admission, 3-year mortality was reduced in Period 2 (OR 0.58, p = 0.003). Within the >65 yrs age group crude 3-year mortality fell (38.8% to 28.7%, p = 0.02). The overall SMR in period 1 was 3.04 and 2.96 in Period 2.

Directly age standardised mortality decreased from 373 (CI 309–437) to 264 (CI 212–316) per 10,000 person years. On multivariate analysis, older age and co-morbid remained associated with 3-year mortality in Period 2.

Conclusion Although the mortality associated with admission remains high at 3 years, crude and adjusted rates suggest significant reductions over the last decade.

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PTU-108 CROHN'S DISEASE AND ANOGENITAL GRANULOMATOSIS PRESENTING WITH GENITAL OEDEMA

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