allopurinol (ALLO) co-therapy (LDA). 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. 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 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 heterozygous 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 metacaptopurine are responsible, and this can be further improved by adjusting the dose of ALLO. Further studies are required.

**REFERENCES**


Disclosure of Interest None Declared.

---

**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 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 = 3) 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**

M Sheikh*, 1C Nelson-Piercy, 1J Sterner, 1G Mackenzie, 1T Flower, 1A Ansari.
1Gastroenterology, East Surrey Hospital, Redhill; 2Women's Health Academic Centre, Guy's and St Thomas’ Foundation Trust, London, UK; 3School of Pharmacy, University of Queensland; 4Gastroenterology, Mater Health Services, Brisbane, Australia

**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.
**COMPARISON OF MORTALITY FOLLOWING A86 GUT EXTENDED STUDIES BY EXAMINING 3-YEAR MORTALITY FOLLOWING**

...premature hospitalisation during pregnancy. 1 We have previously demonstrated concerningly...hospitalised with ulcerative colitis (UC) between 1998 and 2000 in Scotland. 1 We have...of interest, non-declared. J. Satsangi. 1NT Ventham*, 1NA Kennedy, 2A Duffy, 2DN Clark, 3AM Crowe, 4AK...10.1136/gutjnl-2014-307263.181

**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 cases gave birth...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.

**Methods** The Scottish Mortbidity 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, 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.

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

**REFERENCE**
1 Nicholls RJ, Clark DN, Kelso L, et al. Nationwide linkage analysis in Scotland implicates age as the critical overall determinant of mortality in ulcerative colitis. Aliment Pharmacol Ther 2010;31:1310–21

**Disclosure of Interest** N. Ventham: None Declared, N. Kennedy: None Declared, A. Duffy: None Declared, D. Clark: None Declared, A. Crowe: None Declared, A. Knight: None Declared, J. Nicholls Grant/research support from: A grant was obtained from AbbVie Ltd to be administered by the North West London Hospital Trust (NWLHT) on behalf of Prof Nicholls, to allow funding of ISD and Corvus Communications for their work on the project. In the context of the work presented in this manuscript and in consideration of BMJ guidance, none of the authors have any competing or other conflict of interest, J. Satsangi: None Declared.

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

**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.


**METHODS** The Scottish Mortbidity 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, 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.

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

**REFERENCE**
1 Nicholls RJ, Clark DN, Kelso L, et al. Nationwide linkage analysis in Scotland implicates age as the critical overall determinant of mortality in ulcerative colitis. Aliment Pharmacol Ther 2010;31:1310–21

**Disclosure of Interest** N. Ventham: None Declared, N. Kennedy: None Declared, A. Duffy: None Declared, D. Clark: None Declared, A. Crowe: None Declared, A. Knight: None Declared, J. Nicholls Grant/research support from: A grant was obtained from AbbVie Ltd to be administered by the North West London Hospital Trust (NWLHT) on behalf of Prof Nicholls, to allow funding of ISD and Corvus Communications for their work on the project. In the context of the work presented in this manuscript and in consideration of BMJ guidance, none of the authors have any competing or other conflict of interest, J. Satsangi: None Declared.

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

**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.


**METHODS** The Scottish Mortbidity 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, 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.

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

**REFERENCE**
1 Nicholls RJ, Clark DN, Kelso L, et al. Nationwide linkage analysis in Scotland implicates age as the critical overall determinant of mortality in ulcerative colitis. Aliment Pharmacol Ther 2010;31:1310–21

**Disclosure of Interest** N. Ventham: None Declared, N. Kennedy: None Declared, A. Duffy: None Declared, D. Clark: None Declared, A. Crowe: None Declared, A. Knight: None Declared, J. Nicholls Grant/research support from: A grant was obtained from AbbVie Ltd to be administered by the North West London Hospital Trust (NWLHT) on behalf of Prof Nicholls, to allow funding of ISD and Corvus Communications for their work on the project. In the context of the work presented in this manuscript and in consideration of BMJ guidance, none of the authors have any competing or other conflict of interest, J. Satsangi: None Declared.
PTU-106 Successful Pregnancies With Thiopurine-allopurinol Co-therapy For Inflammatory Bowel Disease

M Sheikh, C Nelson-Piercy, J Stenner, G Mackenzie, J Duley, T Florin and A Ansari

*Gut* 2014 63: A85-A86
doi: 10.1136/gutjnl-2014-307263.180

Updated information and services can be found at:
http://gut.bmj.com/content/63/Suppl_1/A85.2

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**