are few explanations for the wide variation in inter-individual TPMT activities in the wild-type range. Bioavailability of the cofactor *S*-adenosylmethionine (SAM) and RBC age may play a role. The aim of this study was to determine if gender or anaemia influences RBC TPMT activity.

Methods We analysed a retrospective cohort of 6,496 RBC TPMT samples (n = 3804 females, n = 2692 males) measured in the PRL since 2004 and correlated enzyme activity with gender and haemoglobin concentrations.

Results A greater portion of females exhibited intermediate TPMT activity (13.46%) as compared to males (11.07%). The mean TPMT activity was also significantly lower in females (32.94 pmol/mg Hb/h) versus males (34.13 pmol/mg Hb/h; p = < 0.0001, 95% CI 0.7950–1.589). When separated by low, intermediate or normal TPMT activity, this relationship only remained in patients with normal TPMT activity. TPMT activity was significantly higher in female patients with an Hb < 10g/dl (n = 250, mean TPMT 38.06 pmol/mg Hb/h) versus females with an Hb > 12g/dl (n = 2192, mean TPMT 32.46 pmol/mg Hb/h; p = < 0.0001). Similarly TPMT activity was significantly higher in male patients with an Hb < 10g/dl (n = 123, mean TPMT 38.14) versus males with an Hb > 12g/dl (n = 1901, mean TPMT 33.76; p = < 0.0001).

Conclusion TPMT activity in the wild-type range is lower in females than males, suggesting a post-translational influence on TPMT activity related to gender. Lower levels of SAM have been reported in females, which may explain this observation[2]. Re-appraisal of the concordance between TPMT genotype and phenotype, adjusting for gender is therefore indicated. The finding of higher TPMT activity with anaemia may be due to a younger red cell population in this group. The difference in TPMT activities between patients with or without anaemia is clinically relevant, particularly where the TPMT activity is around the cut-off between intermediate (10–25 pmol/mg Hb/h) and normal (≥26 pmol/mg Hb/h) ranges. TPMT genotyping should be considered in such patients.

Disclosure of Interest None Declared

REFERENCES

1. Karas-Kuzelicki, *et al.* Pharmacogenomics 2009. 10:1309–22.
2. Poirier, *et al.* Cancer epidemiology, biomarkers & prevention 2001. 10:649–655.

OC-016 ELEVATED FAECAL CALPROTECTIN PREDICTS DISEASE PROGRESSION IN CROHN'S DISEASE

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Introduction Historical cohort studies have clearly demonstrated that over time the majority of patients with Crohn's disease (CD) will progress from inflammatory (B1) to stricturing (B2) or fistulating (B3) disease. Emerging data suggest that more intensive treatment targeted towards mucosal healing will help to prevent disease progression. Faecal calprotectin (FC) is an established surrogate biomarker for endoscopic mucosal healing. It has yet to be established whether tailoring therapy to FC levels prevents disease progression.

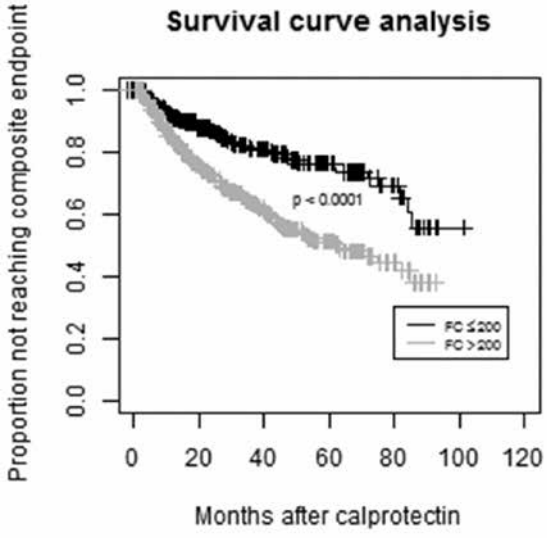
In the present study we aimed to determine whether FC levels in patients with established CD were predictive of disease progression.

Methods The Edinburgh Faecal Calprotectin Registry (EFCR) comprises data on 22,130 FC assays in 16,278 patients from 2005–2012. Detailed phenotypic information was obtained on patients with CD by retrospective casenote review. Data collected included demographics, disease location, disease behaviour over time, CD-related surgery, investigations, hospitalisations and drug therapy. Patients were included in the main analysis if they had at least 12 months' follow-up since first FC. The a priori primary endpoint was a composite of progression in Montreal luminal behaviour, hospitalisation for flare and resectional surgery.

Results There were 881 CD patients identified with at least one FC, of which 723 had at least one year's follow-up, with median follow-up time 40 months (IQR 25–60). The median age was 28y (IQR 20–42) at diagnosis and 40y (28–53) at time of first FC.

239 patients (33%) reached the primary endpoint, of whom 68 had had progression of their Montreal behaviour from B1 to B2 or B3, or from B2 to B3.

The median of the earliest FC was significantly higher in the group that reached the primary endpoint at 586 µg/g (IQR 210–1235) vs. 289 (75–1001) in those that did not (p < 0.0001). Survival analysis (Fig 1) revealed significant differences in time to progression, hospitalisation or surgery with calprotectin ≥ 200 (p < 0.0001).



Abstract OC-016 Figure 1

Conclusion This large single-centre study presents compelling evidence that measurement of FC can be used to predict disease course, which creates the opportunity for physicians to intervene earlier and perhaps alter the disease course.

Disclosure of Interest None Declared

OC-017 A DISCRIMINANT ANALYSIS DEMONSTRATES THAT SIBLINGS OF PATIENTS WITH CROHN'S DISEASE HAVE A DISTINCT MICROBIOLOGICAL AND IMMUNE PHENOTYPE COMPARED WITH HEALTHY CONTROLS: INSIGHTS INTO DISEASE PATHOGENESIS

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Introduction Crohn's disease (CD) is associated with genetic risk, intestinal dysbiosis, altered blood T-cell phenotype, increased faecal calprotectin (FC) and intestinal permeability (IP). Factors shared by CD patients and unaffected siblings may be implicated in CD pathogenesis.