Conclusion (1) A distinct subset of miRNAs is deregulated in the mucosa of actively inflamed sigmoid UC in patients who are on no treatment. (2) miR-31 and -223 are constitutionally expressed in sigmoid UC and could offer a potential diagnostic tool for patients who have no active inflammation at the time of endoscopy. (3) Manipulating miRNA expression offers promise as a potential new therapeutic pathway in active disease. (4) When investigating miRNA profiles and function it is essential to use an accurately phenotyped and homogeneous patient group. (5) We are the first to show a miRNA profile for sigmoid UC in treatment naive patients.

Competing interests None declared.

OC-166 PREDICTIVE FACTORS OF DISEASE RELAPSE FOLLOWING THIOPURINE WITHDRAWAL FOR SUSTAINED CLINICAL REMISSION OF IBD

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Introduction Thiopurine therapy is effective in maintaining clinical remission in IBD. However, long-term therapy is associated with an increased risk of lymphoma; therefore in clinical practice we aim to withdraw therapy after 4–5 years. Nevertheless, many patients will experience disease relapse within 12 months of drug withdrawal.1

Methods The aim of the present study was to retrospectively determine the relapse rate in ulcerative colitis (UC) and Crohn’s disease (CD) following azathioprine (AZA) or mercaptopurine (MP) withdrawal and to determine factors predictive of relapse. Patients were identified by electronic case note review of an IBD research database in Edinburgh. Major inclusion criteria were AZA and/or MP therapy for a minimum of 5 years, AZA/MP withdrawal due to sustained clinical remission with no steroid therapy for 6 months prior to drug withdrawal, and minimum 12 months follow-up. The primary outcome was disease relapse requiring AZA reintroduction, steroids or colectomy within 12 months of AZA/MP withdrawal, with secondary outcome assessed at 24 months. Clinical/laboratory predictors of relapse were sought. 1226 electronic records were reviewed (565 CD and 661 UC). 654 were treated with a thiopurine (348 CD and 286 UC). 74 met the strict study inclusion criteria (45 CD and 29 UC).

Results CD was associated with a significantly higher risk of relapse than UC on Kaplan–Meier analysis (Abstract OC-166 figure 1, p=0.026). The moderate–severe relapse rate for 12 months was 44% for CD and 14% for UC. For 24 months, relapse rates were 60% for CD and 48% for UC. Elevated platelet count (p=0.03) and elevated white cell count (p=0.03) were predictive of relapse for UC, while no predictive factors were identified for CD. Median (range) duration of thiopurine use was 6.2 (3.4–12.7) years for CD and 6.0 (3.1–18.0) years for UC. Median duration of follow-up was 32 months for CD and 45 months for UC. Retreatment with a thiopurine after relapse was successful in 7/7 cases for UC and 18/24 for CD.

Abstract OC-166 Figure 1 Survival curves for moderate to severe relapse following thiopurine withdrawal in Crohn’s disease and ulcerative colitis
Conclusion Relapse rates after withdrawal of a thiopurine are high, particularly for CD, and predicting this remains difficult. To help increase the power of this study, we are now expanding it across the UK.

Competing interests None declared.

REFERENCE

OC-167 CALCULATING THE "MISSED OPPORTUNITY" OF THIOPURINE MONOTHERAPY OVERCOME WITH THIOPURINE AND ALLOPURINOL COMBINATION THERAPY

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Introduction A proportion of patients preferentially methylate thiopurines, resulting in high levels of methylated metabolites and low levels of thioguanine nucleotides. This can result in hepatotoxicity and treatment non-response. Co-prescription of thiopurines (at 25%–50% of standard dose) with allopurinol, (which blocks xanthine oxidase) circumvents this problem, optimising metabolite profile and clinical outcome and additionally overcomes atypical side effects experienced on thiopurine monotherapy. Using data from a large cohort of patients receiving combination therapy, we aimed to establish what proportion of all patients starting thiopurines could benefit from combination treatment.

Methods Using data from a cohort of 109 patients recruited retrospectively, all receiving combination therapy in our clinic, Iyr clinical response rates were calculated by indication. Using data from a published prospective cohort and side effect rates from meta-analysis, we calculated the proportion of all patients starting thiopurines that could be salvaged from treatment failure to Iyr remission by combination therapy.

Results 10/17 (59%) of hyper-methylating non-responders to thiopurine monotherapy, 8/17 (47%) of those treated for atypical side effects and 11/15 (73%) switched for hepatotoxicity achieved remission at 1 year. Using these response rates, potential gain was calculated from a prospective cohort (n=207) from our centre. 60 patients discontinued thiopurine monotherapy due to non-specific side effects, eight due to hepatitis and 32 were hyper-methylating non-responders, a total of 100 patients with clear indications for combination treatment. Our results predict that 55/100 could have achieved 1-year remission, representing 26% of the original cohort. Using a more conservative published side effect rate of 10% (Prefontaine et al 2010, Cochrane Database of Systematic Reviews, CD000545) and excluding 2.8% due to side effects unsuitable for combination therapy (pancreatitis and myelotoxicity), 12% of all patients started on azathioprine could have their outcome on thiopurine therapy converted from treatment failure to 1-year remission by combination therapy.

Conclusion 12%–26% represents the “missed opportunity” of patients starting thiopurine monotherapy which can be realistically overcome by combination treatment with allopurinol, converting treatment failure to successful 1-year remission. Given that thiopurines remain a key part of most IBD treatment paradigms, this is an important opportunity for improved treatment outcomes in IBD.

Competing interests None declared.

OC-168 TOWARDS INDIVIDUALISED RISK PREDICTION FOR CROHN’S DISEASE

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Introduction Although the RR of developing Crohn’s disease (CD) is increased in first degree relatives (FDR) of probands by 13–27-fold, (1) it is difficult to apply this on an individual basis. Recently, risk models for complex disease using information from genome-wide association and epidemiological studies have been built. Potentially, such models could identify FDR at highest risk of CD, for screening and early intervention. A aim To generate a risk model for CD, and ultimately determine if such a model can predict presymptomatic or future development of CD.

Methods CD patients were contacted to identify asymptomatic FDR aged 18–55 who wished to participate in research into risk prediction and presymptomatic diagnosis of CD. (Recruitment target: 500 FDR) DNA was extracted from saliva. Genetic analysis used the Immunochip (Illumina), and genotypes were determined for disease susceptibility loci established by CD genome-wide meta-analysis. (2) A multiplicative risk model was generated using risk prediction software (REGENT) (3) based on genotype and smoking status, and CD RR determined for each FDR.

Results The first 100 FDR have been recruited. Demographics: 53% siblings, 36% offspring, 11% parents. Mean age 37, females 66%, smokers 25%, ex-smokers 33%. NOD2 genotype counts were not significantly different to their frequencies in the control population, but were significantly different to cases (15% heterozygous, 0% homozygous, p=0.64 for controls vs FDR, p=0.001 for cases vs FDR). CD RR ranged from 0.04 to 10.07 (median 0.96) and was significantly higher than that in the general population: 19% of FDR had a RR >2, compared to an expected proportion of 11% (p=0.02). Comparison of highest and lowest RR quartiles in FDR showed good separation of RR between the groups. More FDRs in the highest RR quartile had >2 CD-affected relatives compared with FDRs in the lowest RR quartile, but this was not significant (5 vs 1, p=0.19).

Conclusion Increased RR of CD is confirmed in FDR compared to the general population. Risk stratification is possible, but follow-up is required to determine if such risk scores can be used to predict presymptomatic CD or future development of CD. Additionally, risk awareness may encourage smokers to quit. Once recruitment to the study is completed, FDR in the highest and lowest risk quartiles will proceed to further tests including faecal and serum biomarkers, and capsule endoscopy. All those recruited will undergo follow-up for 10 years.

Competing interests None declared.

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