identified a significant association within the Class II MHC region.

Disclosure of Interest None Declared.

OC-005 NOVEL PATHWAY-CENTRIC ANALYSIS REVEALS VARIANTS ASSOCIATED WITH TOXICITY AND RESPONSE TO THIOPURINES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction Thiopurines remain the first line immunosuppressants recommended in the management of inflammatory bowel disease (IBD). Unfortunately, 30–40% of patients prescribed these agents develop adverse drug reactions or fail to derive therapeutic benefit. Candidate gene studies have identified loci that explain some of these treatment failures; however a substantial fraction of the genetic contribution remains undefined. Using whole thiopurine pathway analysis the aim of this study was to identify novel loci associated with toxicity and response to azathioprine (AZA)/mercaptopurine (MP) in patients with IBD.

Methods Genomic DNA was extracted from EDTA blood samples of 472 well-characterised IBD patients treated with AZA/MP. We examined exome array data using the Illumina HumanExome Beadchip and restricted the analysis to variants associated with the thiopurine pathway as defined by the KEGG database (100 genes, 639 single nucleotide polymorphisms). Using a case-control design we firstly tested for genetic associations between patients with ($n = 154$) and without ($n = 258$) adverse drug reactions, and secondly for polymorphisms differentiating patients with ($n = 188$) and without ($n = 141$) response to thiopurines after 12 months of treatment. One year intervention-free clinical response was defined by 3 investigators (PB, PI, JS).

Results Following adjustment for principal components, the minor alleles at *ADK* rs946185 ($p = 0.0078$; OR 1.675), *SLC28A1* rs2242046 ($p = 0.0168$; OR 1.600) and *ABCA1* rs4149268 ($p = 0.033$; OR 1.487) were associated with the development of drug toxicity, whereas the minor alleles at *ABCB5* rs2301641 ($p = 0.0170$; OR 0.608), *ABCC4* rs4148549 ($p = 0.027$; OR 0.652) and *AOX1* rs55754655 ($p = 0.038$; OR 0.549) protected against it. The minor allele at *RRM2* rs1130609 ($p = 3.80 \times 10^{-5}$; OR 0.461), which codes a subunit of ribonucleotide reductase involved in the conversion of thio-guanine nucleotide to deoxy-thioguanine nucleotide, and a higher normalised dose of AZA/MP were associated with protection from non-response. Conversely, the minor allele at *ABCA1* rs2230808 ($p = 0.008$; OR 2.585) and Crohn's disease ($p = <0.001$; OR 5.007) were associated with non-response to treatment at 12 months.

Conclusion High-throughput sequencing using exome array technology has revealed new loci, other than thiopurine-S-methyltransferase, explaining toxicity and response to thiopurines. Validation of these markers in separate cohorts will allow the development of biomarker panels to predict outcomes prior to the start of treatment.

Disclosure of Interest None Declared.

OC-006 SAFETY AND EFFICACY OF LOW DOSE AZATHIOPRINE AND ALLOPURINOL CO-THERAPY: A LARGE SINGLE CENTRE EXPERIENCE

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Introduction The effectiveness of full dose azathioprine (FDA) for inflammatory bowel disease (IBD) has been questioned in recent scientific literature. A popular strategy to improve its outcomes recommends the use of low dose azathioprine with allopurinol co-therapy (LDAA) for patients profiled as "hyper-methylators" (30% of non-responders). The aim of this study was to determine the safety and efficacy of LDAA without using thiopurine metabolite (TM) profiling.

Methods Records of IBD patients treated with LDAA were retrospectively analysed.

Patients who had poor response and/or side-effects to FDA were offered LDAA by all Consultants whilst a single IBD physician also offered LDAA to thiopurine-naïve patients. Azathioprine dose was reduced to 25% of the thiopurine methyl transferase (TPMT) adjusted dose (0.5 mg/kg for wild type and 0.25 mg/kg for heterozygotes) followed by conventional haematological monitoring. Non-adherence was assessed by TM measurements. Full response (FR) was defined as steroid free remission (Harvey Bradshaw index ≤ 3 , Truelove-Witts normal) for greater than 3 months after a 3 month induction period for LDAA.

Results Of 300 LDAA patients, adequate data was available for 295 cases. Group 1 (G1) were treated 1st line ($n, 105$) and Group 2 (G2) were switched from FDA to LDAA ($n, 190$). Overall, for both groups, there were 207 (70%) full responders (FR), 20 partial responders (PR) and 68 non-responders (NR). Full response rate was 78% in G1 and 66% in G2. The commonest indication for switching to LDAA was non-response to FDA ($n, 118$).

Analysis of haematological indices revealed significant changes ($p < 0.05$) in erythrocyte sedimentation rate, white cell count and platelet count after therapy induction.

Myelotoxicity occurred in 5 patients (all NR, WCC >2 and <3.5) and 12 patients had asymptomatic hepatotoxicity (ALT range: 100–700) which resolved by increasing allopurinol to 200 mg in 9 patients (all FR).

Time on treatment: 208 patients took LDAA for more than twelve months with a median length of therapy of 24 months.

Conclusion Appropriately dosed LDAA therapy delivers a therapeutically effective dose of azathioprine without the

Abstract OC-006 Table 1

Indication	Clinical response (n)			
	FR	PR	NR	Total
AZA/GMP Naïve (LDAA without FDA exposure)	82	7	16	105
Switched from FDA to LDAA	125	13	52	190
Poor response	81	10	27	
GI intolerance	16	n/a	11	
Hepatotoxicity	7	1	3	
Myelotoxicity	13	2	1	
"Flu-like" symptoms	3	n/a	1	
Other	5	n/a	9	

need for dose escalation. It appears to be more effective, better tolerated and safer (less haematological disturbance) than FDA. These results will serve to allay the fear of toxicity of LDAA and question the need for thiopurine metabolite level profiling prior to using this apparently superior therapeutic approach.

Disclosure of Interest None Declared.

OC-007 HAEMOPOETIC STEM CELL TRANSPLANTATION FOR SEVERE RESISTANT CROHN'S DISEASE: PRELIMINARY EVIDENCE FOR DURABLE BENEFIT

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Introduction The Autologous Stem Cell Transplantation International Crohn's Disease (ASTIC) Trial shows haemopoietic stem cell transplantation (HSCT) to be effective over one year in Crohn's disease, but its durability remains to be established.

Methods ASTIC is a multicentre parallel group randomised controlled trial in patients with impaired quality of life due to Crohn's Disease that is resistant to established treatments. All patients undergo stem cell mobilisation before HSCT given immediately (one month: early HSCT) or after a delay of thirteen months (late HSCT). This abstract describes currently available data over 2 years and includes the first report of changes occurring in the first year transplantation in the late HSCT group.

Results A full analysis of progress over one year has shown a reduction in Crohn's Disease Activity Index (CDAI) from 326 (range 163–512) to 162 (12–506) and in the SES-CD endoscopic score from 13 (5–33) to 3 (0–200) in patients following early HSCT (n = 23) compared to 354 (91–581) to 298 (70–589, active vs control p = 0.01) and 13.5 (0–36) to 7 (1–27, active vs control p = 0.02) respectively in the control group prior to transplantation (n = 22). The Table shows data for those patients (approximately 50%) with full data currently available to two years (one year after transplantation in the control group).

Scores for the IBD-Q quality of life index improved from 123 (103–144) to 165 (125–206) following early HSCT and were maintained at 157 (126–213). Scores rose from 108 (79–136) to 147 (108–188) in the year following delayed HSCT.

Conclusion If full data (available June 2014) confirm these preliminary results, it would support the notion that improvements in CDAI, endoscopic appearances and quality of life benefit persist and may possibly increase over the second year following transplantation. One year data in the delayed group show a similar magnitude of effect to that seen in patients undergoing early transplantation.

Disclosure of Interest None Declared.

Abstract OC-007 Table 1

	CDAI (n = 12 and 14)		SES-CD (n = 13 and 13)		EQ5D VAS (n = 9 and 10)	
	Early HSCT	Late HSCT	Early HSCT	Late HSCT	Early HSCT	Late HSCT
Baseline	338 (264–473)	354 (264–473)	13 (8.5–25)	14 (4.5–19.5)	56 (39–65)	35 (29–60)
1 year	162 (73–280)*	288 (209–368)	3 (1.5–10)*	6 (3–20)	80 (68–88)*	50 (21–70)
2 year	90 (36–231)*	155 (84–300)*	3 (0–10.5)*	2 (0–6.5)*	87 (64–91)*	74 (43–83)*

Values shown are median and interquartile range.

Asterisk data*: Post HSCT

Endoscopy section free papers

OC-008 ENDOSCOPIC SUBMUCOSAL DISSECTION CAN TRANSFORM THE MANAGEMENT OF PATIENTS WITH UPPER GASTROINTESTINAL SUBMUCOSAL TUMOURS: RESULTS FROM A UK SERIES

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Introduction It is very difficult to establish an accurate diagnosis for upper GI submucosal tumours. Biopsy during endoscopy cannot go deep enough. EUS is unable to give a tissue diagnosis. The risks of surgical resection are higher than the benefits as the lesion may very well be benign. As a result most of these patients keep having endoscopic surveillance as 'possible' GISTs.

Methods A retrospective cohort study of patients undergoing ESD for upper GI submucosal tumours. They were all referred to us as possible GISTs that were found to be growing in size on surveillance. ESD was carried out in all these cases. As these lesions are mostly bulky, gravity and patient positioning were utilised as traction during ESD to achieve deroofing and enucleation of these tumours. Any complications were recorded. Endoscopic follow up was performed to assess for incomplete resection or recurrence.

Results 21 submucosal lesions were resected by ESD between 2007 and 2013. 7 were oesophageal, 10 gastric and 4 duodenal. Sizes ranged from 10 to 35mm. Endoscopic clearance was achieved in all cases. Histology showed a wide range of diagnoses, mostly benign (table). There was 1 complication; a micro-perforation which was identified and clipped intraprocedurally, giving a complication rate of 4.7%. On follow up, there was 1 recurrence (recurrence rate 4.7%) which was managed

Abstract OC-008 Table 1 Histological diagnosis of submucosal tumours resected by ESD

Diagnosis	Number
Granular cell tumour	3
GIST	2
Leiomyoma	2
Pancreatic acinar tissue	1
Carcinoid	6
Lipoma	2
Inflammatory fibroid polyp, hyperplastic polyp	1+1
Synovial sarcoma	1
Gangliocytic paraganglioma	1