P132 — HOSPITAL RE-ADMISSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE – WHAT ARE THE RISK FACTORS?

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Introduction Early re-admission after hospitalisation for an inflammatory bowel disease (IBD) flare is a negative quality indicator and causes unnecessary healthcare expense. Scoring systems to predict IBD readmissions have been shown to be ineffective. We aimed to describe the IBD re-admission rate at our hospital and investigate the risk factors.

Methods Retrospective study of patients admitted to a London-based district general hospital under the gastroenterology team with a flare of inflammatory bowel disease between 2015 and 2018. Characteristic including but not limited to demographics, disease type, length of stay (LOS) during index admission, biochemistry and biologic use were recorded. Hospital software (Sunquest Integrated Clinical Environment, Medway) was used to identify patients re-admitted at 30 and 90 days after discharge. Multivariate logistic regression was performed.

Results 138 patients were admitted with an IBD flare during the study period (74 (53.6%) Crohn's disease (CD), 56 (40.6%) ulcerative colitis (UC), 8 (5.8%) IBD-U). Median age 33.5 (IQR 26 – 52), 71 (51.4%) female. Median LOS was 4.5 days (IQR 1.8 – 8). 36 (26%) patients were taking a biologic. Re-admissions occurred within 30 days in 19 patients (13.7%) and within 90 days in 30 patients (21.7%). Multivariate logistic regression showed that a raised CRP on discharge was associated with re-admission. For every increased unit of CRP by one there was an increased risk of readmission by 1.1 times (p=0.05). Patients aged 22–39 were significantly less likely to be readmitted (OR: 0.38, p=0.015). Male patients were significantly more likely to be readmitted (OR: 2.52, p=0.05).

Abstract P132 Table 1 Demographics and biochemistry associated with IBD re-admissions within 30 days of discharge.

	30-day Re-admission (n=21)	No Re-admission (n=117)	p value
Age, median (IQR)	31 (25.5 – 52)	34 (26 – 51)	0.44
Gender (F), n (%)	10 (47.6)	61 (52.1)	0.70
Type of IBD (CD), n (%)	10 (47.6)	64 (54.7)	0.55
LOS, days (median, IQR)	3 (0.5 - 11)	5 (2 -8)	0.35
CRP on discharge (median, IQR)	23 (5.5 – 59.3)	9 (2 – 25)	**0.005**
Albumin on discharge (median, IQR)	37 (31.5 – 41.5)	36 (31.3 – 41)	0.45
Biologic use, n (%)	6 (28.6)	30 (25.6)	0.78

Conclusion The 30 day and 90 day re-admission rate for our IBD population is just over 10% and 20%, respectively. CRP at discharge is significantly associated with both 30 and 90 day re-admission. After adjusting for confounders; CRP, age older than 40 and male gender were associated with re-admission to hospital. We advise caution in discharging IBD patients with raised inflammatory markers. Close follow up within a few days of discharge would be appropriate in this high risk sub-group.

P133 — AN ATLAS OF CANONICAL CYTOKINE REGULATED TRANSCRIPTIONAL NETWORKS UNVEILS A NOVEL MOLECULAR STRATIFICATION OF IBD

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Introduction The immune- epithelial interactions are central in our current understanding of inflammatory bowel disease (IBD) pathogenesis. Cytokines have been shown to play an integral part in this cross-talk, with some considered pro-inflammatory (e.g. IFNγ, TNFα) and others protective (e.g. IL22).

Methods We set out to define and compare the transcriptional programmes regulated by the canonical cytokines IFNγ(TH1), IL13 (TH2), IL17A(TH17), IL22 (TH22) and TNFα, as a pro-inflammatory control, in human colonic organoids (colonoids) and associate them to disease phenotypes and therapeutic trajectories in IBD.

Whole transcriptome profiling of cytokine treated human colonoids (n=4) was performed using the Illumina platform. Bioinformatic tools included: pathway analysis (Ingenuity database, interrogation of whole biopsy transcriptomic profiles of IBD patients (n= 423) using gene set variation analysis (GSVA) and weighted gene correlation network analysis (WGCNA).

Results A large functional overlap was found between IFNγ, IL22 and TNFα transcriptional programmes with key pathogenic pathways upregulated by all three cytokines (e.g. IL6, NF-kB, TREM1, TLR signalling, acute phase response, neutrophil chemotaxis). GSVA revealed enrichment of all cytokine regulated transcriptional modules in active inflammation while there was no difference in activated module number or type between UC and colonic CD. Intriguingly, patients with the same endoscopic activity had a gradient of activated cytokine regulated modules. Those with ≥2 modules enriched had a higher risk of non-response to anti-TNFα therapy in both IBD phenotypes [relative risk: 2.9,95%CI(1.7,6)]. A strong, positive correlation was seen between IL22, IFNγ and TNFα enrichment scores. WGCNA revealed a neutrophil chemotaxis chemokine module to be the pathway most strongly associated with anti-TNFα non-response. This module was primarily upregulated by both IL22 and TNFα.

Conclusions Our study provides novel insights into the human gut immune-epithelial interactome and paves the way for a more granular immunophenotyping of IBD. It highlights that the simultaneous activation of modules regulated by multiple canonical cytokines is associated with non-response to anti-TNFα. Targeting of these shared pathogenic pathways may hold the key to overcoming non-response to biological therapies.

P134 — THE INFLAMMATORY BOWEL DISEASE BIORESOURCE: FOCUS ON RESEARCH FACILITATION

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Introduction The Inflammatory Bowel Disease (IBD) BioResource is a UK-wide platform comprising >32,000 Crohn's

and colitis patients across >100 participating hospitals with a long-standing goal of fostering IBD Research to expedite clinical translation. For each patient recruited, clinical and self-reported phenotype data are collected, alongside plasma, serum and DNA samples for genetic analyses. The resulting data-rich panel is open to <u>any investigators</u> wishing to access data/samples or recall genotype-selected participants to donate further samples or trial novel therapies.

Methods <u>Building the IBD BioResource panel</u>: Patients' clinical data are collected at recruitment by the IBD team through a clinical data sheet based on the Montreal classification while health and lifestyle information are obtained via a patient questionnaire. All include demographics, smoking habits, general and IBD specific health questions, family history of IBD and non-IBD conditions, medication, treatment, surgery history and co-morbidities. The IBD BioResource panel also holds Whole Genome/Exome sequencing and GWAS data derived from its detailed biological samplings.

<u>Accessing the IBD BioResource panel</u>: The built-in panel of patients and their data is open to any investigators from science or industry. Following feasibility checks, submitted research applications are reviewed by the NIHR BioResource Scientific Advisory Board (SAB) based on scientific merits and projected benefit to patients. Upon study approval, patients meeting inclusion criteria are contacted by the NIHR BioResource team with a letter of invitation and a patient information leaflet. For volunteers willing to participate, appropriate arrangements are then made to gather information, collect fresh biological samples or engage patients in intervention studies.

Results To date 26 'Stage 2 studies' applied to utilise the IBD BioResource, 18 of which are currently active, 4 completed and 4 pending approval. Of the 26 applications, ~20% requested access to anonymised samples/data while the remaining ~80% required involvement of participants. Applications are national, with 7 from London, 6 from Cambridge, 4 from Oxford, 2 from Leeds. 2 from Pharma and 1 from Manchester, Exeter, Wolverhampton, Liverpool and Edinburgh. Field of studies include genetics, predictors and management of IBD; environmental, microbial and immunological contributors, fertility and well-being.

Conclusion The IBD BioResource and its network are on course to facilitating IBD Research through access to their panel and furthering knowledge/understanding of IBD for the benefit of Crohn's and colitis patients.

Introduction Ustekinumab (UST) is an anti-IL12/23 biologic licensed for the treatment of moderate to severe Crohn's disease (CD). The aims of this study were to establish the long-term real-world effectiveness and safety of UST for the treatment of CD in a large UK cohort.

Methods This was a multicentre retrospective cohort study including 8 NHS health-boards in Scotland. Patients treated with UST between Nov 2015 and Jun 2019 were identified. Inclusion criteria included: a diagnosis of CD; active symptoms attributed to CD with objective evidence of mucosal inflammation (CRP >5 mg/L or faecal calprotectin ≥250 µg/g or inflammation on endoscopy/MRI); completion of standard induction; week 8 review ± further follow up. Clinical assessments were performed based on physician global assessment (response was defined as ≥50% reduction in CD-related symptoms and remission defined as complete resolution of all CD-related symptoms). Mucosal healing was defined as absence of ulceration/erosions on ileo-colonoscopy or no inflammation on MRI if ileo-colonoscopy was not possible (eg. B2 disease). Deep remission was defined as clinical remission plus mucosal healing. Perianal response was determined by follow up MRI (reduction in enhancement, closure or fibrosis of tract compared to baseline MRI). Rates of serious adverse events (discontinuation of UST, hospitalisation or death) during follow up were described quantitively.
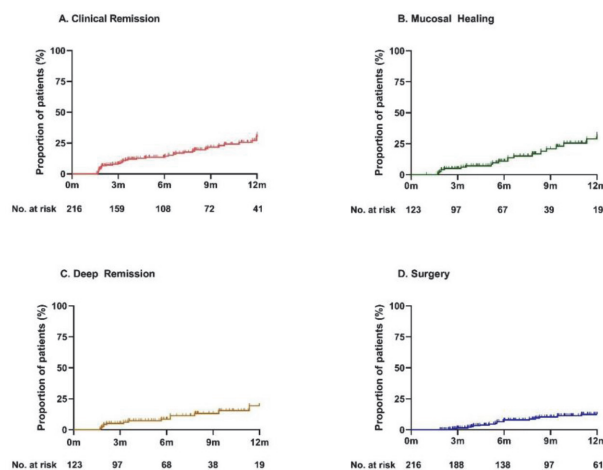
Results A total of 216 patients (57.9% female; median age 39.0 years, IQR 28.8–51.8; median disease duration 9.9 years, IQR 6.0–16.5) with a median follow up of 35.0 weeks (IQR 17.4–52.0) were included. The majority of patients had ileo-colonic disease (L1, 19.9%; L2, 23.1%; L3, 56.9%) and an inflammatory phenotype (B1, 43.1%; B2, 41.2%; B3, 15.7%). A total of 98.6% of patients had previously been exposed to a biologic and 55.1% had undergone previous surgery. Seventy-one percent of patients received 8-weekly maintenance dosing, whilst 25.5% and 40.7% of patients were also receiving an immunomodulator and/or steroids at initiation, respectively. At week 8, clinical response and remission rates were 45.4% and 6.0%, respectively. Twelve-month cumulative rates of clinical remission, mucosal healing (n=123) and deep remission (n=123) were 32.0%, 32.7% and 19.3%, respectively (figure 1). In patients with active perianal disease at initiation (n=37), 12-month cumulative rates of perianal response were 53.1%. During 140 patient years of follow up

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Abstract P135 Figure 1