Abstract HMO-2 Figure 1 Probability of 5-ASA discontinuation in the first year of therapy

proportion of days covered (PDC) in the first year of treatment was calculated. Multivariable Cox and linear regressions assessed predictors associated with 5-ASA discontinuation and adherence, respectively.

Results We identified 694 AYA initiated on oral 5-ASA treatment. The median time to 5-ASA discontinuation was 176 days (95% CI 153-204). A quarter of AYA stopped after a month of treatment and by a year 2 out of 3 individuals had discontinued. The proportion with continuous use of 5-ASA in the first year of treatment varied by age at initiation (10-14 years: 49%, 15-17 years: 52%, 18-24 years: 32% - Figure 1). The mean PDC was 73% (S.D. 0.31) in the first year of therapy and was lowest amongst individuals aged between 18 to 24 years, at 69% (S.D. 0.32), compared to 81% (S.D. 0.27) in 10 to 14 year olds and 79% amongst 15 to 17 year olds (S.D. 0.30). Starting treatment between 18 and 24 years of age and socioeconomic deprivation increased the risk of discontinuation and lower adherence, while early corticosteroid use, a proxy marker of disease severity, was associated with a lower risk of discontinuation and better adherence.

Conclusion AYA diagnosed with UC and initiated on oral 5-ASA medication are at risk early discontinuation and poor adherence. Clinicians should be vigilant regarding the higher risk following the first month of treatment, particularly in young adults and those living in deprived postcodes. Targeted interventions are needed to improve 5-ASA adherence among these high risk groups.

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HMO-3 MAPPING FIELD CANCERISATION AND CLONAL EVOLUTION IN IBD COLONS WITH DYSPLASIA AND CRC

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Introduction In Inflammatory Bowel Disease (IBD), clonal evolution and field cancerisation precedes the development of colitis-associated colorectal cancer (CA-CRC), however the extent and spread of pre-cancerous clones in the IBD colon remains incompletely determined and consequently clinical practice is poorly informed of how best to detect these clones by endoscopy and accurately predict future cancer risk. This study aims to quantify the number and size of mutant clones arising across the length of the colitic bowel, reveal the mechanism of how they arise and spread, and through this gain a detailed molecular understanding of the evolutionary dynamics of progression to CA-CRC.

Methods Three IBD patients undergoing a total panprocto-colectomy for multifocal dysplasia or CA-CRC were recruited prospectively. Fresh-frozen biopsies were taken at regularly spaced intervals (~2cm) across the entire colon (rectum to caecum, comprising 118, 108 and 25 biopsies respectively). Epithelial tissue was isolated from each biopsy using laser capture microdissection and DNA was extracted. Low pass whole genome sequencing (lpWGS) was performed to generate genome-wide copy number alteration (CNA) profiles.

Results Analysis from the first 45 samples from colon 1 show; 1) Multiple CNA events occur in macroscopically 'normal' parts of the colon. 2) Recurrent CNAs were shared between biopsies, revealing clonal expansions in multiple areas of the colon, both proximal and distal to the cancer, and comprising normal, inflamed, dysplastic and cancer-adjacent tissue. 3) Clonal expansions ranged from 2-14cm in size, and were separated by distances of 4-30cm. 4) Certain CNA events occur more commonly across the colon, both independently and from within different clonal patches, such as a gain on chromosome 7 and 20, and losses on chromosomes 5, 8 and 17. 5) Whole genome doubling events within clonal clades.

Conclusions These data show that across the IBD bowel, CNAs occur and expand in ostensibly 'normal' cells, demonstrating evidence of field cancerisation. Moreover, the fact that similar and independent patterns of CNAs are seen throughout the whole colon provide evidence to suggest both convergent and independent evolutionary events occurring respectively. Further work is needed to more precisely quantify clonal and sub-clonal distribution across the IBD colon, in addition to deriving measures of intra-colon, intra-lesion and intra-clade genomic diversity to complement the above measures of evolvability.

HMO-4 IMMUNOGENICITY TO SECOND ANTI-TNF THERAPY (IMSAT): IMPLICATIONS FOR SEQUENCING OF BIOLOGIC THERAPY

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Introduction Anti-TNF treatment failure in patients with IBD is common. International guidelines recommend switching out of class when anti-TNF drug levels are therapeutic and within class with an immunomodulator when anti-TNF drug levels are suboptimal and associated with antibody development.

We sought to define the: 1) risk of immunogenicity to a second anti-TNF stratified by immunogenicity to first anti-TNF, 2) rates of drug persistence following failure to first anti-TNF drug and 3) strategies to mitigate development of immunogenicity.

Methods We performed a retrospective cohort study across 38 UK hospitals. 1058 patients [532 (51%) male, 755 (71%) Crohn's disease] had both infliximab and adalimumab therapeutic drug monitoring performed by our service from May 2013 to October 2020 were identified. Drug and antibody levels were measured using the IDKmonitor® drug-tolerant ELISA assays. Treatment failure included primary nonresponse, secondary loss of response, adverse drug reactions and IBD-related surgery, and patients were identified by case note review. Immunogenic failure was defined as treatment failure with suboptimal drug levels (infliximab level <2 mg/L, adalimumab level <6 mg/L) with an antibody concentration ≥ 10 AU/ml. Pharmacodynamic (PD) failure was defined as treatment failure despite adequate drug levels.

Results Patients who developed immunogenicity to adalimumab (first) were more likely to develop immunogenicity to infliximab (second) (64% vs 40%, $p < 0.001$), and patients who developed immunogenicity to infliximab (first) were more likely to develop immunogenicity to adalimumab (second) (34% vs 20%, $p = 0.002$). Patients who developed: antibodies and undetectable drug, low drug levels, or low drug levels with immunogenicity to infliximab (first), were more likely to develop these outcomes to adalimumab (second) (all $p < 0.001$).

There was no difference in drug persistence to second anti-TNF in patients with pharmacodynamic and immunogenic treatment failure to first anti-TNF ($p = 0.86$). In patients with immunogenic (but not pharmacodynamic) failure, commencing an immunomodulator at the time of switching to second anti-TNF drug was associated with longer drug persistence than in patients treated with an immunomodulator throughout or not at all (Figure 1).

Abstract HMO-4 Figure 1 Drug persistence to second anti-TNF in patients stratified by immunomodulator use

Conclusions Immunogenicity to the first anti-TNF was associated with immunogenicity to the second anti-TNF, irrespective of drug sequence. Commencing an immunomodulator at the time of switching to second anti-TNF was associated with improved drug persistence in immunogenic, but not pharmacodynamic, failure. However, 50% of patients remained on second anti-TNF at 5 years in both groups, suggesting switching in-class may be appropriate, irrespective of the cause of treatment failure to first anti-TNF.

HMO-5 ASSOCIATION OF ANTI-INFLIXIMAB ANTIBODIES AND HLA-DQA1*05 VARIANT IN ULCERATIVE COLITIS: A RETROSPECTIVE SINGLE CENTRE STUDY

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Introduction The genetic variation HLA-DQA1*05 has been reported to be associated with anti-Infliximab antibody in CD. The relevance in UC patients receiving infliximab is uncertain.

Aim To evaluate the association of HLA-DQA1*05 and infliximab antibody formation, treatment changes and infliximab persistence in a real world setting of single centre cohort

Methods Infliximab treated UC patients (n=94) were retrospectively screened for HLA-DQA1*05. The risk of anti-infliximab antibody formation, absent drug levels in presence of antibody, change in therapy from infliximab were assessed in variant carrying patients in comparison to those without the variants. The proportion of patients needing dose optimisation of infliximab also evaluated.

Results Anti-infliximab antibodies were detected in 41.5% of patients in a median follow up of 14.75 (IQR 9-29) months. HLA-DQA1*05 was positive in 39.13% of patients. 52.2% of patients were on concomitant immunomodulators. Higher proportion of patients with HLA-DQA1*05 developed anti-Infliximab antibodies (59% Vs 24%, $p=0.002$). Eighty per cent of patients who had anti Infliximab antibodies with

Abstract HMO-5 Figure 1 Antibody formation in infliximab treated patients

Abstract HMO-5 Figure 2 Infliximab persistence