Methods A prospective database of all IBD patients starting biologics was interrogated to select patients initiating on anti TNF agents. We excluded patients Crohn's disease perianal fistula who had specific indication for combo therapy, patients with acute severe UC receiving accelerated induction those who were already on imunomodulators prior to initiation of anti TNF agents. Data was collected on demographics, disease characteristics, HLA DQA1*05 status, drugs levels and antidrug antibody status at week 6, week 14 and at least one time point during a 1 year maintenance period. The primary outcome was drug persistence at 12 months.

Results One hundred and fifty six patients were initiated on anti TNFs during the study period. HLA DQA1*05 was positive in 59 (37.8%) of patients. These patients received combination therapy (Infliximab + thiopurines in 42, Infliximab plus methotrexate in 9, adalimumab plus azathioprine 6, Adalimumab plus methotrexate in 2). All patients negative for HLADQA1805 received monotherapy with infliximab (78) or adalimumab (19). Primary non response was identified in 30 patients (overall 19%, Monotherapy 17(17.5%), combo therapy 13 (22%) and were switched to a non anti TNF agent Further 9% of patients had dose escalation due to suboptimal drug levels and partial response among whom 6 patients were switched to another class. Eleven patients stopped anti TNFs (4 and 7 in mono and combo therapy group respectively) due to intolerance and five patients discontinued immunomodulators in the combo therapy due to adverse effects.

Anti-drug antibodies was detected at week 6 in 2 patients in the monotherapy group and 3 patients in combo therapy group (p=NS). There was no difference in rates of antidrug antibody development during maintenance period between the two groups. One hundred and twelve patients remained on anti TNFs across both groups at 12 months follow up. The overall drug persistence rates was similar in the mono and combination therapy group (66.1% vs 72.2%, p=NS).

Conclusions HLA DQA1*05 status incorporated anti TNF treatment strategy may alleviate the need for combination therapy in IBD patients with no impact on development of anti-drug antibodies and drug persistence. A biomarker stratified randomised trial is recommended.

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WITHDRAWAL OF IMMUNOMODULATORY THERAPY IS FEASIBLE IN ANTI-TNF TREATED PATIENTS WITH NEGATIVE HLA-DQA1*05 – AN OBSERVATIONAL STUDY

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Background Combination therapy with immunomodulators and anti-TNFs were recommended following the results of the SONIC study. It was determined the main benefit for combination therapy was due to reduction in the risk of anti-drug antibodies. The PANTS study indicated that patients at higher risk of antidrug antibodies to anti-TNF agents could be identified with HLADQA1*05 allele carriage. A HLADQA1*05 stratified withdrawal of immunomodulators has not been evaluated before.

Methods We included IBD patients on combination immunomodulaotrs and anti TNF agents from a prospective database who had HLADQA1 *05 status determined retrospectively after treatment of minimum 12 months. Patients with Crohn's disease -perianal fistula or those on immunomodulators due to non-IBD indications were excluded. Immunomodulator with-drawal was offered to all patients in clinical and biomarker remission with a negative HLADQA1805 status. Patients were followed up with structured clinical and biomarker assessment. Therapeutic drug monitoring was performed at 3–6 month intervals. The primary outcome was development of anti-drug antibodies.

Results Three hundred and eighteen patients on anti-TNF agents had HLA-DQA1*status determined. Among these 248 patients were on combination therapy. Withdrawal of immuno-modulaotrs was suggested to 146 (59%) of the HLA-DQA1*05 negative patients. None of the patients declined attempt at withdrawal but five patients preferred dose reduction rather than complete cessation and these were not included in analysis. Median follow up among the remaining 141 patients was 13 months (range 3–27 months). Antidrug antibodies developed in 11 patients (7.8%) including in three patients with undetectable drug levels necessitating switch of agent. An additional 16 patients lost clinical response without development of antibodies.

Conclusion In anti TNF treated IBD patients in long-term remission, withdrawal of immunomodulators is feasible in majority of patients not carrying HLA-DQA1*05 with limited risk of development of antidrug antibodies.

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LUMENEYE DIGITAL PROCTOSCOPY IS SAFE AND STREAMLINES MANAGEMENT OF IMMUNE CHECKPOINT INHIBITOR INDUCED COLITIS

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Introduction Immune checkpoint inhibitors (CPI) have transformed cancer outcomes, but at the cost of inducing CPI-colitis in up to 46%, frequently leading to morbidity and CPI discontinuation. Diagnosis is via endoscopy, with >90% exhibiting inflammation involving the distal colon. The rising prevalence of CPI-colitis has increased pressure on endoscopy services, delaying patient management. Use of the Lumeneye, a low-cost GI digital proctoscope with biopsy ports, may be valuable in streamlining patient pathways.

Methods A single centre, prospective observational feasibility study (Royal Marsden Hospital, London UK). Consecutive patients with CPI-induced diarrhoea underwent Lumeneye proctoscopy and rectal biopsy sampling in the outpatient clinic. Digital photographs +/- video recordings were captured, and clinical data obtained from the electronic patient record. Patient reported comfort scores were assessed using the Modified Gloucester Comfort Scale (MGCS) and where applicable, compared to standard lower GI endoscopy.

Results Twenty-two Lumeneye procedures were performed on 18 patients (11 males, 7 females, median age 64 years). Cancers included melanoma (n=8), renal (n=2), upper GI (n=1), head and neck (n=1), prostate (n=2), pancreatic (n=1) or lung cancer (n=3). Nine received anti-PD-1/PD-L1 monotherapy, 9 received combination anti-CTLA-4/anti-PD-1.

The mean time from referral to either Lumeneye examination or lower GI endoscopy was 5 (IQR 3-7) and 28 days (IQR 18-34) respectively (p<0.001). The mean procedure time was 3 (IQR 2-4) minutes. Lumeneye was well tolerated

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Abstract P92 Figure 1 Lumeneye findings in CPI-colitis. Normal mucosa (A, B), erythema and oedema (C) suspected melanoma deposits (D)

and associated with a significantly lower MGCS score compared to standard lower GI endoscopy (2 -minimal discomfort vs 3-mild discomfort, respectively, p<0.05).

Endoscopic findings included normal mucosa in 11, with the remainder exhibiting varying degrees of oedema, erythema and erosions (figure 1). Four patients had lower GI endoscopy within 3 weeks of Lumeneye, with excellent concordance between endoscopic and histological findings.

In 2 patients awaiting flexible sigmoidoscopy, Lumeneye expedited a diagnosis of severe CPI-colitis that necessitated escalation to anti-TNF therapy. In another 6, presence of macroscopically normal mucosa informed the rationale for a rapid corticosteroid taper with administration of topical corticosteroids (Clipper).

Conclusion Examination of patients with CPI-colitis in the physician's office using Lumeneye was safe, well tolerated and reduced the burden on endoscopy services. Lumeneye streamlined the patient pathway by facilitating early diagnosis allowing timely escalation or de-escalation of immunosuppressive therapy.

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POSITIONING TOFACITINIB FIRST LINE FOR MODERATE TO SEVERE ULCERATIVE COLITIS: IMPACT ON EFFECTIVENESS OF SUBSEQUENT TREATMENTS

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Introduction Tofacitinib, a pan-Janus kinase inhibitor, has several advantages that make it an attractive first line advanced agent for the treatment of moderate to severe ulcerative colitis (UC), including its oral formulation and rapidity of onset. The study aim was to firstly assess tofacitinib effectiveness in bionaive patients and secondly, its impact on the effectiveness of subsequent advanced therapies after tofacitinib discontinuation, which has not previously been reported.

Methods A retrospective observational study was performed at a tertiary inflammatory bowel disease referral centre, including all adult patients who received at least one dose of tofacitinib. Data collected included patient demographics, tofacitinib persistence, discontinuation reasons, and adverse events. For the group that required a switch to another advanced therapy, we assessed rates of clinical response and remission, which were defined as a reduction in SCCAI of >3 and ≤2, respectively.

Results A total of 138 patients with UC were treated with tofacitinib until November 2022. of these, 74 received tofacitinib first line (53% male, median age 35 years, IQR 17) and were treated for a median duration of 17 months (IQR 20) (table 1). In total, 55 patients (74%) persisted with tofacitinib, and 19 patients (26%) discontinued therapy for the following reasons; non-response, 6/19 (32%), loss of response 6/19 (32%) and 2/19 (11%) for safety concerns related to their age. Adverse events leading to drug discontinuation occurred in 5/19 (26%) patients, including one patient who developed a colorectal cancer not thought to be drug-related.

Of those that discontinued tofacitinib, 18/19 (95%) were switched to another advanced therapy; 12/19 to anti-TNF, 3/19 to ustekinumab, 2/19 to filgotinib, and 1/19 to guselkumab, with rates of response (%)/remission (%) at 54/36, 100/

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