P93 FAECAL MICROBIOTA TRANSPLANT FOR REFRACTORY CHECKPOINT INHIBITOR IMMUNOTHERAPY-RELATED COLITIS

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Introduction Immune checkpoint inhibitors (ICIs) have revolutionised the treatment of various cancers. They improve survival but this comes at the cost of immune-related adverse events like ICI-colitis. First line treatment is steroids and refractory cases can be treated with infliximab, vedolizumab or faecal microbiota transplant (FMT). We describe our experience of FMT, alongside cytometric/transcriptomic analysis of the GI immune response, and whole stool metabolomic analysis pre- and post-FMT.

Methods 150 ml FMT was delivered to the caecum by colonoscopy. 5 pairs of colon pinch biopsies were collected pre- and week 6 post-FMT. Gut mononuclear cells (GMNC) were isolated from the biopsies by enzymatic/mechanical digestion. GMNC were analysed using a 21-parameter flow cytometry panel on the Cytek Aurora Spectral Analyser and a 780-plex Nanostring panel. Stool pre- and post-FMT, and that of the FMT donor, was subjected to whole metabolome analysis.

Results Two patients with refractory ICI-colitis were treated with FMT (same donor). Characteristics are shown in Table 1:

Patient 1's symptoms of diarrhoea and abdominal pain resolved fully. Week 6 sigmoidoscopy and biopsies were normal. Pre-FMT, there were high levels of activation (as measured by co-expression of HLA-DR and CD38) on CD4, CD8 and MAIT cell subsets as well as high Ki-67 and low expression of Bcl-2. Post FMT, there was reduced expression of HLA-DR and CD38 and lower expression of Ki-67 with high/homeostatic levels of Bcl-2 and an increased proportion of Tregs.

The bowel frequency of patient 2 demonstrated some clinical improvement, but week 6 sigmoidoscopy showed an unchanged UCEIS score and Nancy histological index. Pre FMT, there were similar levels of activation as seen in patient 1, but post-FMT responses were muted.

We will present an analysis of the GI immune response and of the stool whole metabolome, in these two patients with dichotomous clinical outcomes.

Conclusions We report the first use of FMT to treat ICI-colitis in the UK, demonstrating that it is effective in a subset of patients. Although both patients received stool from the same donor, they experienced contrasting treatment responses. We will present the salient GI immune and stool metabolomic differences to reveal mechanistic insights.

Abstract P93 Table 1

Patient	Age	Sex	Cancer	ICI	ICI-colitis treatment before FMT	UCEIS pre FMT	Nancy index pre FMT
1	63	F	Melanoma	Ipilimumab/ nivolumab	Steroids, infliximab, vedolizumab	4	3
2	61	M	Lung	Pembrolizumab	Steroids, infliximab	5	3

P94 VEDOLIZUMAB FOR INFLAMMATORY BOWEL DISEASE IN PRE AND POST LIVER TRANSPLANT

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Introduction The association between inflammatory bowel disease (IBD) and autoimmune liver disease (AILD) is well established. Vedolizumab (VDZ) is a gut-specific anti-α4β7 integrin antibody used to treat IBD. VDZ is favoured for AILD patients on additional immunosuppression. This retrospective observational study at a tertiary liver transplant centre aims to review VDZ use in IBD-AILD pre and post liver transplant (LT).

Method An electronic database of IBD patients treated with VDZ from November 2014 to February 2020 was used to identify those with AILD. Data on the nature of AILD, response to VDZ, complications or reason for cessation of VDZ was recorded.

Results 36 patients with IBD-AILD have been treated with VDZ, with 18 patients receiving ongoing therapy. Demographics are shown in table 1.

Of the 18 pre-LT patients, 1 had septic shock from cholangitis at the onset of VDZ therapy, 1 was diagnosed with breast cancer and cholangiocarcinoma a month after VDZ cessation for primary non response. 2 patients underwent LT whilst on VDZ with no post-operative complications.

Of the 18 post-LT patients, several complications were seen. There was a single case of: recurrent pharyngitis,

Abstract P94 Table 1 Vedolizumab (VDZ), Ulcerative colitis (UC), Crohn's disease (CD), IBD-unspecified (IBDU), autoimmune sclerosing cholangitis (AISC), primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH)

	Current VDZ	Discontinued VDZ
Number	18	18
Gender		
Female	4	5
Male	14	13
Age: years		
Mean	31.6	37.2
Range	19–62	18–71
Diagnosis		
UC	13	14
CD	3	2
IBDU	2	2
Duration of treatment: days		
Mean	540	345
Range	8–1241	41–1024
Liver disease		
AISC	3	3
PSC	5	3
AIH	1	3
OLT	9	9

Clostridium difficile infection, leukocytoclastic vasculitis, renal cell carcinoma and post-transplant lymphoproliferative disorder (PTLD) in the colon. 5 patients had cholangitis prior to and post VDZ. None of these complications were felt to be related to VDZ and therapy was continued long term in IBD responders.

2 patients have died, 1 due to cholangiocarcinoma and the cause is unknown for the other. 18 patients have stopped VDZ due to: primary non response in 13 cases, cancer in 3 (cholangiocarcinoma, rectal cancer, PTLD), remission in 1 and failure to attend appointments in 1.

Conclusion Our experience of VDZ use in IBD-AILD pre and post LT has demonstrated VDZ is a safe treatment option in this cohort. Complications including infections were treatable and patients continued on VDZ. The cessation of VDZ was predominantly due to lack of response and the causal relationship between the cancers and VDZ is not established in this observational study. Prospective multicentre studies would help elucidate further on the use of VDZ in this cohort.

P95 INFLAMMATORY BOWEL DISEASE DIAGNOSIS: CHOOSING THE RIGHT PATH

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Introduction Patients presenting to their GP with symptoms of undiagnosed inflammatory bowel disease (IBD) frequently meet criteria for secondary care referral on a two week wait (2ww) cancer pathway. IBD patient outcomes are improved when treatment is commenced early in the course of disease (Berg *et al,* 2019), and NHS operational standards recommended that 92% of routine GP referrals to secondary care should receive treatment within 18 weeks. Our aims were to determine the volume of new IBD diagnoses made following 2ww referral, and to understand whether this cohort were effectively triaged to initiate therapy in a timely manner.

Methods Details of adult (>18 years) patients with a new IBD diagnosis made at Guy's and St Thomas' NHS Trust (GSTT) were collected prospectively between 1st January 2019 and 31st December 2020. Patient demographics, IBD subtype, date of referral, referral pathway, and date of IBD treatment initiation were documented. Patients were excluded if they had an IBD diagnosis made elsewhere, or if they were diagnosed during inpatient admission. Data were analysed in Prism (version 8.0) using the Wilcoxon signed rank test.

Results 114 diagnoses of IBD were made during the study period, of which 60 were via 2ww referral (52.6%). 52.6% were male, with a median age of 45.0 years. 76 patients were diagnosed with ulcerative colitis (UC, 66.7%), 34 with Crohn's disease (CD, 29.8%), and four with IBD unclassified (IBDU, 3.5%). Patients referred on the 2ww pathway were significantly older than those diagnosed via routine GP referral (figure 1a, median age 45.0 vs. 30.5 years, $p<0.0001$). Treatment was commenced earlier for patients referred on the 2ww pathway than those referred routinely (figure 1b, median 2.9 vs. 13.2 weeks, $p<0.0001$). This was accounted for exclusively by the longer time between referral and colonoscopy in the standard vs. the 2ww cohorts (median 10.6 vs. 2.0 weeks). Time from referral to treatment initiation was greater for patients diagnosed with CD than those diagnosed with UC (median 10.4 vs. 5.0 weeks, $p<0.0001$). Of patients referred on a 2ww pathway, 85.0% commenced treatment within 18 weeks of referral, compared to 61.1% of those referred routinely.

Conclusions Most IBD diagnoses were made following 2ww pathway referral. Despite uncertainty about whether this would permit access to the most appropriate specialist, patients on the 2ww pathway had a shorter referral to treatment time than those referred routinely due to access to earlier diagnostic colonoscopy. The longer wait for treatment in Crohn's disease may reflect a reluctance or difficulty in starting steroids or immunomodulators in this cohort. A substantial proportion of patients referred on both pathways are not being treated within the recommended 18 week window.

P96 FACTORS INFLUENCING TREATMENT PREFERENCES IN STEROID RESISTANT ULCERATIVE COLITIS – A QUALITATIVE INTERVIEW STUDY

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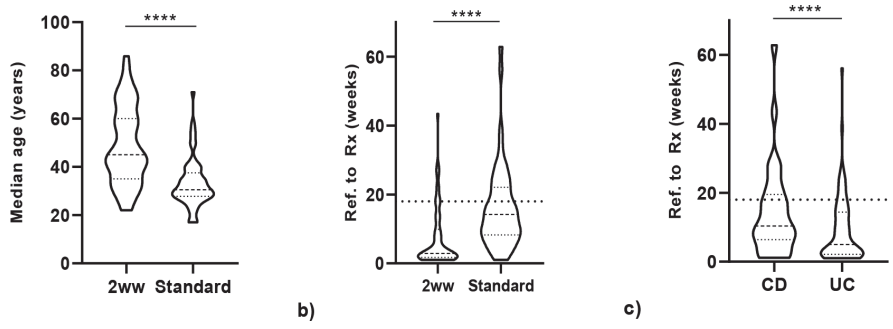
Background The best treatment option for people whose ulcerative colitis (UC) is resistant to steroids is not clear. Importantly, understanding of patient preferences for available treatments in this setting is also limited. Therefore, the objective of this study was to explore patient experiences of different treatment options, their approaches to decision making, and preferences for available treatments for steroid resistant UC.



Abstract P95 Figure 1