Conclusions VDZ is associated with reduced hospitalisation and steroid use over 1 year. Steroid free remission rates and safety profile is in keeping with the published literature.

PWE-046 TH17 CELLS DOMINATE THE COLONIC MUCOSAL IMMUNE RESPONSE IN PRIMARY SCLEROSING CHOLANGITIS ASSOCIATED COLITIS

^{1,2,3}Mohammed Quraishi*, ⁴Animesh Acharjee, ²Evaggelia Liaskou, ⁵Amanda Rossiter, ^{2,3,4}Subrata Ghosh, ¹Chris Tselepis, ⁴Georgios Gkoutos, ²David Withers, ^{2,3,4}Gideon Hirschfield, ^{1,2,3,4}Tariq Iqbal. ¹Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, UK; ²Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK; ³University Hospital Birmingham, Birmingham, UK; ⁴Institute of Translational Medicine, Birmingham, UK; ⁵Institute of Microbiology and Infection, University of Birmingham, Birmingham, UK

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Introduction Primary sclerosing cholangitis (PSC) is an idiopathic chronic cholestatic liver disease associated with ulcerative colitis (UC). PSC is thought to be a consequence of a genetically predisposition, dysregulated immune response and unknown factors including the gut microbiome. The colonic mucosal immune response in PSC associated colitis (PSC-UC), however, has been poorly defined. In this study, we analysed the characteristics of colonic mucosal CD4 T cells in patients with PSC-UC.

Methods Colon biopsies were collected from patients with PSC-UC (n=13), UC (n=10) and controls (n=20). One patient with PSC-UC and one patient with UC was on biologics. Three patients with PSC and three with UC had colonic inflammation. Lamina propria mononuclear cells were analysed by flow cytometry.

Results PSC-UC and UC were characterised by a significantly higher frequency of colonic mucosal CCR6 +CD161+Th17 cells compared to controls (17.5% vs 11.1%; p=0.009% and 21.02% vs 11.1%; p=0.01 respectively). CCR6-CXCR3 +CCR5+Th1 cells were significantly lower in PSC-UC compared to controls (15.46% vs 24.50% respectively; p 0.01). CD127-CD25+FoxP3+T regulatory cell frequencies was elevated and CCR6-CCR5-CXCR3- Th2 frequencies were reduced only in UC compared to controls (7.6% vs 4.38%; p=0.007% and 14.84% vs 8.77%; p=0.02 respectively). Significantly increased frequencies of IL17 producing CD4 cells were observed in both PSC-UC and UC compared to controls (7.75% vs 4.7%; p<0.001% and 7.251% vs 4.70%; p=0.006 respectively). Although there were no differences in TNF α and IFN γ producing CD4 cells, patients with PSC-UC had a

significantly higher frequency of IL17/IFN γ dual producing CD4 cells compared to controls (2.79% vs 1.76% respectively; p=0.03). Correlation analysis of PSC-UC and controls demonstrated that Th17 frequencies positively correlated with increasing frequencies of IL17 producing cells and negatively with Th1 (p<0.05).

Conclusions Our study demonstrates for the first time that the colonic mucosal immune response in PSC-UC is characterised by significantly higher Th17 cells and lower Th1 cells compared to controls. Patients with PSC-UC have higher IL-17 and IL17/IFN γ dual producing CD4 cells. Our findings highlight the need to explore the role of key players such as the gut microbiome in mucosal T cell homeostasis and Th1/Th17 plasticity in PSC.

PWE-047 THERAPEUTIC DRUG MONITORING FOR INFLIXIMAB & ADALIMUMAB IN IBD: PRACTICE PATTERNS, UNDERSTANDING & INTERPRETATION

¹Mark Samaan, ²Zehra Arkir, ¹Peter Irving, ³Charlotte Chuter*. ¹IBD Centre, Guy's and St Thomas' NHS Foundation Trust, London, UK; ²Vaiphath, St Thomas' Hospital, London, UK; ³York Teaching Hospital, UK

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Introduction The use of therapeutic drug monitoring (TDM) for infliximab and adalimumab in the treatment of inflammatory bowel disease (IBD) is becoming increasingly commonplace. In cases of non-response (primary or secondary) TDM can provide a clearer understanding of the cause of treatment failure and offer a rationale for steps taken to recapture response. However, several factors regarding its use remain uncertain such as minimum therapeutic thresholds, the relevance of antidrug antibodies found in the presence of detectable drug, and the benefits of TDM during remission.

Methods We designed a survey that included 5 TDM-based clinical scenarios, for which the 'most appropriate' responses were based on the Building Research in IBD Globally (BRIDGE) groups 'Anti-TNF Optimizer' (<http://www.bridgeibd.com/anti-tnf-optimizer>). This resource combines available TDM evidence with expert consensus. A link to our online survey tool was sent to various IBD clinician groups in June 2017 including members of the British Society of Gastroenterology, Royal College of Nursing IBD Network and the gastroenterology special interest group of the UK Clinical Pharmacy Association.

Results We received 142 responses. Of these, 110 (77%) were complete, comprising 50 (45%) consultants, 30 (27%) trainees,

Abstract PWE-047 Figure 1 Lower therapeutic thresholds selected by respondents for IFX and ADA

25 (23%) IBD nurse specialists and 5 (5%) gastroenterology pharmacists, and were used for analysis.

Over half (61, 55%) only carry out TDM in non-response. The remainder use TDM routinely, during stable maintenance therapy for patients in remission. Only 15 (14%) respondents reported being clear and confident in their understanding of the difference between drug-sensitive and drug-tolerant assays. Moreover, most (82, 75%) were unsure as to which type their laboratory uses. Lower therapeutic thresholds used by clinicians were variable (figure 1).

Consultants, high-frequency TDM users (>3 requests/month) and clinicians with larger anti-TNF cohorts (>100 patients) were significantly more likely to select the 'most appropriate' answer to at least 1 of the 5 TDM scenarios (figure 2).

Conclusions These results demonstrate marked heterogeneity in the practical use, understanding and interpretation of biologic TDM in IBD. Biologic decision-making, informed by TDM, should involve consultation with experienced clinicians who are frequent TDM users, ideally, as part of a multidisciplinary, biologics-focused IBD meeting.

Scenario	Respondents selecting 'most appropriate' answer (%)									
	Overall	Consultant (n=50)	Non-Consultant (n=60)	p	Anti-TNF cohort >100 (n=65)	Anti-TNF cohort <100 (n=40)	p	TDM used >3/month (n=65)	TDM used <3/month (n=45)	p
1	65	64	67	0.84	66	65	>0.99	68	62	0.68
2	52	66	40	0.008*	54	48	0.55	52	51	>0.99
3	45	58	33	0.012*	42	45	0.84	51	36	0.12
4	36	42	32	0.32	46	23	0.022*	45	24	0.043*
5	30	32	28	0.68	37	20	0.083	38	18	0.022*

Abstract PWE-047 Figure 2 Percentage of respondents selecting the 'most appropriate' answer to each scenario, overall and after diving by subgroup (NB: 5 respondents were unsure of the size of their anti-TNF cohort and were not included in that analysis)

PWE-048 THE NATURE OF CHECKPOINT INHIBITOR-ASSOCIATED LOWER GASTROINTESTINAL TOXICITY: A SINGLE CANCER CENTRE EXPERIENCE

^{1,2,3}Amit Samani*, ^{2,3}Zayd Tippu, ²Shuai Zhang, ²Sophie Merrick, ^{1,2}Hajir Ibraheim, ^{1,2}Nicholas Powell, ^{1,2}Debra Josephs, ^{1,2}Sophie Papa. ¹King's College London, London, UK; ²Guy's and St Thomas' NHS Foundation Trust, London, UK

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Introduction Immune checkpoint inhibitors (CPI) are a standard of care for various cancers however can cause unpredictable toxicity, notably of the lower gastrointestinal (GI) tract. As continued expansion of their use is anticipated, we sought to investigate the 'real world' frequency and characteristics of such toxicity.

Methods We conducted a retrospective case-note review of patients treated with ≥one dose of either nivolumab monotherapy (N), pembrolizumab monotherapy (P), sequential pembrolizumab/ipilimumab (P-I) or combination nivolumab +ipilimumab (n+I) between 01/03/2016 – 28/02/2017. Toxicity (tox) was graded using NCI Common Terminology Criteria for Adverse Events v4.03. Statistical comparisons used Student's T-test or Chi Squared tests with Bonferroni corrections.

Results 141 patients were treated (49 female, 34.8%), mean age of 64.6 years. 71, 33 and 37 (50.3%, 23.4% and 26.2%) had melanoma, lung and renal cancers respectively.

83 received P (58.9%) while 39 (27.7%) received N with only 11 (7.8%) and 8 (5.7%) receiving n+I or P-I respectively.

Of these, 29 had any grade GI tox. Their mean age (65.7 years), female proportion (34.4%) and proportion with melanoma, lung or renal cancers (55.2%, 20.1% and 24.1% respectively) did not significantly differ from the 112 patients with no GI tox.

However, 6 (20.6%) vs 2 (1.8%) received P-I and 5 (17.2%) vs 6 (5.4%) received n+I in the GI and no-GI tox cohorts respectively which was significantly different (p=0.001 and 0.036 respectively). Only 2 (7.1%) in the GI tox cohort had initial progressive disease compared to 47 (46.1%, p<0.001).

In the GI tox cohort, 17 had grade 1 (G1) tox, 5 G2 and 7 G3/4. When comparing the G3/4 to G1 cohort there was a trend towards younger age (54.3 vs 67.7 years), treatment with P-I or n+I (71.5 vs 17.8%) and higher CRP (100 vs 62 mg/L).

The rate of G3/4 toxicity was similar to the reported literature. For n+I, 5/11 (45.5%) had any grade GI tox with 3/11 (27.3%) having grade 3/4.

Finally, of those with G3/4 tox, 4 had documented fever at presentation, only 1 had haematochezia and all had diarrhoea of ≥5 x/day. All required IV methylprednisolone but 3 received alternate routes initially (2 oral, 1 rectal). Three patients required infliximab with only 1 requiring ≥1 dose.

Conclusions A significant proportion of patients develop lower GI tox with CPI. They were more likely to have been treated with ipilimumab containing regimens and to have a favourable response to therapy although this may have been confounded by the higher use of n+I in this cohort. The rate of G3/4 toxicity was similar to the literature. Some patients are initially treated with oral/rectal steroid; they may benefit from earlier IV therapy. Infliximab as a single dose is usually effective.

PWE-049 ASSESSMENT OF SYMPTOMATIC HYPOPHOSPHATEMIA WITH IRON ISOMALTOSIDE IN INFLAMMATORY BOWEL DISEASE PATIENTS

¹Walter Reinisch*, ²Jens Frederik Dahlerup, ³Richard Derman. ¹Medical University of Vienna, Vienna, Austria; ²Aarhus University Hospital, Aarhus, Denmark; ³Thomas Jefferson University, Philadelphia, USA

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Introduction Patients with inflammatory bowel disease (IBD) often need intravenous (IV) iron but some IV irons have been associated with hypophosphatemia in as many as 47%–70% of patients with iron deficiency anaemia (IDA) without chronic kidney disease with severe hypophosphatemia seen in up to 13% of the patients. Hypophosphatemia has been linked to acute symptoms such as pain, nausea and muscle weakness, and more long term complications such as development of osteomalacia with bone pain, fractures and pseudo fractures. Transient hypophosphatemia