Abstract PTU-001 Table 1 Summary of safety and efficacy in the OLE study

	Tofacitinib 5 mg BID (N=156)	Tofacitinib 10 mg BID (N=758)	Total (N=914)
Discontinuations, n (%)			
AEs due to study drug	4 (2.6)	19 (2.5)	23 (2.5)
Due to insufficient clinical response ¹	7 (4.5)	276 (36.4)	283 (31.0)
TEAEs, n (%)			
AEs	101 (64.7)	562 (74.1)	663 (72.5)
SAEs	11 (7.1)	84 (11.1)	95 (10.4)
Severe AEs	7 (4.5)	64 (8.4)	71 (7.8)
Infections AEs (SOC)	62 (39.7)	317 (41.8)	379 (41.5)
GI AEs (SOC)	38 (24.4)	270 (35.6)	308 (33.7)
Serious infections AEs	4 (2.6) ²	14 (1.8) ²	18 (2.0)
Malignancies excluding NMSC ³	0 (0)	9 (1.2) ³	9 (1.0)
NMSC ³	1 (0.6)	6 (0.8)	7 (0.8)
Efficacy endpoints (FAS, as observed)			
Remission at Month 2, n/N1 (%)	119/146 (81.5)	183/665 (27.5)	302/811 (37.2)
Remission at Month 12, n/N1 (%)	59/72 (81.9)	235/382 (61.5)	294/454 (64.8)
Remission at Month 24, n/N1 (%)	7/8 (87.5)	93/134 (69.4)	100/142 (70.4)
Mucosal healing at Month 2, n/N1 (%)	135/150 (90.0)	272/679 (40.1)	407/829 (49.1)
Mucosal healing at Month 12, n/N1 (%)	67/73 (91.8)	285/391 (72.9)	352/464 (75.9)
Mucosal healing at Month 24, n/N1 (%)	8/8 (100.0)	112/141 (79.4)	120/149 (80.5)

¹AEs of worsening of UC leading to discontinuation were designated as insufficient clinical response²All causities³Two cases were reported as severe (one appendicitis, one gastroenteritis norovirus)⁴Four cases were reported as severe (two appendicitis, one arthritis bacterial, one atypical pneumonia)⁵Aggravated events⁶Malignancy (number of cases): cervical dysplasia (1), hepatic angiosarcoma (1), essential thrombocythemia (1), acute myeloid leukaemia (1), cholangiocarcinoma (1), cutaneous leiomyosarcoma (1), Epstein-Barr virus associated lymphoma (1), renal cell carcinoma (1), adenocarcinoma of colon (1)Remission was defined as a Mayo score ≤ 2 with no individual subscore >1 , and rectal bleeding subscore of 0. Mucosal healing was defined by a Mayo endoscopic subscore ≤ 1

AEs, adverse event; BID, twice daily; FAS, full analysis set; GI, gastrointestinal; n, number of patients with the specified response within the given category; N1, number of randomised patients in the total population; N1, number of patients in the specified category with non-missing values; NMSC, neo-melanoma skin cancer; OLE, open-label, long-term extension; SAEs, serious adverse events; SOC, system organ class; TEAEs, treatment-emergent adverse events; UC, ulcerative colitis

REFERENCE1. Sandborn WJ, et al. *N Engl J Med* 2017;**376**:1723–36.**PTU-002 ACHIEVING BIOCHEMICAL REMISSION IN CROHN'S DISEASE WITH ADALIMUMAB THERAPY UTILISING THERAPEUTIC DRUG MONITORING**

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Introduction Adalimumab (ADA) is a well-established treatment for Crohn's disease (CD). Despite this limited data are available regarding the relationship of serum ADA levels, and antibodies to ADA (ATA) with clinical outcomes.

Methods We performed a prospective cross-sectional study to investigate the association of serum ADA levels and ATA on clinical outcomes. Inclusion criteria were a diagnosis of CD and minimum of 12 weeks therapy. Patients were written to in advance of their next clinic visit and advised to omit their ADA dose if due within 72 hour from their appointment. Harvey Bradshaw Index (HBI), serum ADA levels/ATA, CRP and faecal calprotectin (FC) were simultaneously collected at clinic. Biochemical remission was defined as FC <200 $\mu\text{g/g}$ in addition to CRP <5 mg/L.

Results At the time of drug level testing, 259 patients were on ADA maintenance therapy. A total of 195 samples were available for analysis from 178 patients; matched HBI, FC and CRP were available for 171 patients. Median duration of

ADA therapy was 2.4 years (IQR 1.2–4.3) with 37/178 (20.8%) patients receiving concomitant immunosuppression. Median ADA levels were higher in patients receiving weekly (n=55) (14.0 $\mu\text{g/ml}$, 8.0–17.4) vs. fortnightly dosing (n=123) (11.0 $\mu\text{g/ml}$, 7.0–14.5, $p=0.0095$). 29/178 (16.3%) patients were positive for ATA. A clear negative correlation was observed between ADA levels and ATA (Spearman's $r=-0.567$, $p<0.0001$). Median ADA levels were 11.4 $\mu\text{g/ml}$ (8.0–15.0), 5.0 $\mu\text{g/ml}$ (4.0–6.6) and 1.0 $\mu\text{g/ml}$ (0.8–2.0) at ATA of <10 AU/ml, 10–50 AU/ml and >50 AU/ml, respectively ($p<0.0001$). Patients in biochemical remission (n=81/171; 47.4%) had significantly higher ADA levels (12.0 $\mu\text{g/ml}$, 10.0–15.7) than those with active disease (8.0 $\mu\text{g/ml}$, 4.8–12.5, $p<0.0001$). ROC analysis revealed a positive correlation between ADA levels and biochemical remission [AUC (95% CI) 0.71 (0.63–0.79), $p<0.0001$]. An optimum ADA level of >8.8 $\mu\text{g/ml}$ was identified for predicting biochemical remission (82.7% sens, 55.6% spec, positive LR 1.86). ADA levels but not ATA independently predicted biochemical remission in a multivariate logistic regression model.

Conclusions Higher ADA levels were independently associated with biochemical remission; levels of >8.8 $\mu\text{g/ml}$, higher than previously suggested, might be an appropriate target in the maintenance treatment of CD.

PTU-003 FILGOTINIB DECREASES INFLAMMATORY MARKERS ASSOCIATED WITH ENDOSCOPIC IMPROVEMENT IN MODERATE TO SEVERELY ACTIVE CROHN'S DISEASE

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Introduction Filgotinib (FIL) is a JAK1-selective inhibitor currently in Phase III development for the treatment of ulcerative colitis and Crohn's disease (CD). In a Phase II study in patients with moderately to severely active CD (FITZROY, ClinicalTrials.gov ID#NCT02048618), 10 weeks of treatment with FIL 200 mg once daily demonstrated significantly higher clinical remission rates compared with placebo. Here, we report treatment-induced changes in serum cytokines, C-reactive protein (CRP) and faecal calprotectin (FC) and investigation of the association of these biomarkers with endoscopic changes.

Methods Serum samples were acquired at baseline (BL), and Weeks 2, 4, and 10 and stool samples collected at BL and Week 10. Serum cytokines were measured by chemiluminescence, CRP by immunoturbidimetry and FC by Calprest[®]. Percent change of biomarkers from BL at post-treatment visits were compared between placebo (PBO) (n=44) and FIL-treated (n=128) patients using an ANCOVA model adjusting for BL biomarker levels and stratification factors (steroid use, prior anti-TNF exposure and BL CRP). Association of % change in biomarkers with Week 10 endoscopic response ($\geq 50\%$ decrease from BL in SES-CD score) was assessed by AUROC.

Results Biomarker levels at BL were comparable between PBO and FIL treatment groups, except IL-17A and VEGF-A which were higher in PBO (medians at 3.2 and 547.2 pg/ml) vs. FIL

group (1.3 and 389.6 pg/ml, $p < 0.05$). FIL treatment induced reductions in FC (median% change of -30% to -35%), serum IL-6 (-11% to -20%) and serum VEGF-A (-8% to -12%) were observed at all time points. Decline in FC, CRP and VEGF-A in FIL-treated patients was observed at Week 2 and was significant compared with PBO-treated patients ($p < 0.05$). No significant change was observed for IL-10, IFN- γ , and IL-8. No significant changes were observed in PBO-treated patients. In FIL-treated patients, a significant association was observed between the decrease in both systemic (serum CRP and IL-6) and mucosal (FC) biomarkers and endoscopic response.

Conclusions Filgotinib treatment led to an early reduction in markers of systemic and mucosal inflammation that correlated significantly with endoscopic response.

PTU-004 ASKING ABOUT BOWEL CONTROL PROBLEMS IN IBD: RESULTS OF FACE-TO-FACE SCREENING VERSUS SELF-REPORTING

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Introduction Patients with IBD have difficulty revealing concerns about bowel control problems to clinicians,¹ who do not actively ask about this symptom² despite clinical guidelines recommending active-case finding in high-risk populations.³ With no available evidence to advise clinicians on how to ask, we aimed to determine the results of face-to-face or self-reported screening to identify faecal incontinence (FI) in IBD patients. We also asked about patients' desire for interventions to improve continence. FI was defined in this study as: 'ever having accidental passing of stool, faeces, poo into your underclothes, that you are either unaware of at the time, or unable to control'.

Methods This cross-sectional survey used a study-specific questionnaire to screen participants at either face-to-face interview (by clinician/researcher) or anonymously (participant self-completed). Eligibility criteria: 18 to 80 years of age, confirmed diagnosis of IBD, no current fistula, no stoma, any level of disease activity. Disease activity was measured using the Harvey Bradshaw Index or the Simple Clinical Colitis Activity Index.

Results Of 1336 participants, 48% were male; mean age 43 years (range 18–80); 55% had Crohn's Disease (CD), 41% ulcerative colitis (UC), 4% IBD unclassified. FI (occurring ever) was reported by 63% of 772 screened face-to-face and 56% of 564 self-report participants ($p = 0.012$). A total of 38.7% of all respondents expressed interest in an intervention for FI. Patients with CD were more likely to report FI than those with UC ($p \leq 0.05$). FI was reported by 49% of participants in remission, and by 59%, 83% and 93% of participants with mild, moderate and severe relapse of IBD respectively ($p \leq 0.001$).

Conclusions Bowel control problems are very common in patients with IBD (including in remission) and these symptoms can be identified by face-to-face interview and postal screening. Interest in interventions for FI is expressed by 38.7% of patients with IBD.

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PTU-005 INFLIXIMAB USE IN IMMUNE-RELATED DIARRHOEA/ COLITIS (IRD/C)

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Introduction Immune checkpoint inhibitors (ICIs) such as ipilimumab (ipi), nivolumab (nivo) and pembrolizumab (pembro) and the combination of ipi + nivo have improved response rates and survival in patients (pts) with advanced melanoma. Nivo was recently approved by the FDA as an adjuvant therapy. Responses may be durable, however associated immune-related adverse events may result in significant morbidity. Current treatment algorithms suggest that pts treated with ICIs who develop corticosteroid (CS)-refractory (CSrefr) irD/C are prescribed anti-TNF alpha antibodies such as infliximab (IFX). Little is known about the clinical features and outcomes of pts who receive IFX.

Methods Pts with advanced melanoma from the Royal Marsden NHS Foundation Trust who received CS and IFX were identified from an ethically approved irD/C database (pts treated with ICIs from 2011–2016) and their medical records were reviewed, including flexible sigmoidoscopy (FS) results. Descriptive statistics and percentages were used to summarise the features of the CSrefr versus CS-responsive (CSresp) groups.

Results Rates of all-grade irD/C by course of treatment were as follows: ipi 77/285 (27%), nivo or pembro 17/166 (10%), ipi + nivo 23/68 (34%). CS were prescribed in 72 (62%). 17 (15%) received IFX; 9 received 2 doses and 3 received 3 doses. 76% responded to IFX within a week; median time to improvement was 4 days (range 1–28). Table 1 outlines clinical information for the CSrefr and CSresp groups. Infection occurred in 10 episodes of IFX prescription (59%), 9 requiring antibiotics, including 2 cases of Pneumocystis jirovecii pneumonia.

Conclusions 35% of irD/C due to ipi + nivo is CS-refractory. In the CSrefr group, CS duration was longer, macroscopic colitis was more common and most pts developed an infection. Interestingly time to progression of disease was longer in the CSrefr group. Prospective clinical trials are warranted to evaluate whether early IFX may reduce the burden of CS in the management of irD/C without compromising disease control.