Abstract PTU-001 Table 1 Summary of safety and efficacy is 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†	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)§	14 (1.8)§	18 (2.0)
Malignancies excluding NMSC*	0 (0)	9 (1.2)††	9 (1.0)
NMSC*	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)

†AEs of worsening of UC leading to discontinuation were designated as insufficient clinical response
‡All causalities
§Two cases were reported as severe (one appendicitis, one gastroenteritis norovirus)
¶Four cases were reported as severe (two appendicitis, one arthritis bacterial, one atypical pneumonia)
*Adjudicated events
††Malignancy (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; N, number of randomised patients in the total population; N1, number of patients in the specified category with non-missing values; NMSC, non-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

REFERENCE

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PTU-002 ACHIEVING BIOCHEMICAL REMISSION IN CROHN'S DISEASE WITH ADALIMUMAB THERAPY UTILSING 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 µg/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 µg/ml, 8.0–17.4) vs. fortnightly dosing (n=123) (11.0 µg/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 µg/ml (8.0–15.0), 5.0 µg/ml (4.0–6–6) and 1.0 µg/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 µg/ml, 10.0–15.7) than those with active disease (8.0 µg/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 µg/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 µg/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, ClinicalTrial.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 (≥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