proportional hazards model survival analyses were performed.

Results 460 patients met the inclusion criteria and were followed up for a median of 4.1 years (2,2201 patient-years). 77% of patients had CE surveillance. Complete endoscopic resection was achieved in 94% and 64% of the polypoid and non-polypoid LGD respectively. Incidence rate of AN per 100 patient-years was 1.0 (95% CI 0.6–1.7) after endoscopic resection of polypoid LGD, 2.5 (95% CI 1.3–4.4) after resection of non-polypoid LGD resection and 8.9 (95% CI 6.0–12.6) if the LGD was unresected. Figure 1 demonstrates the cumulative incidence of AN according to LGD visibility and resectability. On multivariate analysis, predictors of AN progression were visible LGD of 1 cm diameter or more [Hazard ratio (HR) 2.5; 95% CI 1.4–4.45; p=0.002], multifocality [HR 1.8; 95% CI 1.1–3.2; p=0.046] and incomplete endoscopic resection, including invisible dysplasia [HR 5.8; 95% CI 3.3–10.1; p<0.001].

Conclusions This is the largest study this century to examine prognosis of LGD based on endoscopic features. Incidence of AN is low if visible LGD is endoscopically resected but large size, multifocality and co-existent invisible LGD increase this risk and should be considered when decision-making.

P116 EFFECTS OF FILGOTINIB ON CIRCULATING CYTOKINES AND WHOLE-BLOOD GENES/PATHWAYS IN PATIENTS WITH ACTIVE CROHN'S DISEASE

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Introduction A Phase 2 study of filgotinib (FIL), a Janus Kinase (JAK) 1-selective inhibitor, in moderate-to-severe Crohn's disease (CD; FITZROY) demonstrated significantly higher clinical remission rates compared to placebo at 10 weeks (Vermeire S. Lancet. 2017;389(10066):266–275), and an early decrease in systemic and mucosal inflammation biomarkers, which was more pronounced in endoscopic responders (Roblin X. ECCO, Vienna, Austria, 2018). We investigated the baseline (BL) correlation of whole-blood transcriptome pathway activities with clinical disease indices and circulating cytokines. The effect of FIL on changes in disease-related pathways in responders and nonresponders was also explored.

Methods PAXgene blood samples were collected from 104 patients with CD at BL and Week 10 (W10). RNA was sequenced (Illumina HiSeq 2500) after globin depletion (ThermoFisher GlobinClear). Differential gene expression analysis was performed using limma R package and hallmark pathway activity scores were calculated using single sample gene set enrichment analysis. All correlations were performed using the Spearman method.

Results At BL, pathways with activity scores positively correlated with Simple Endoscopic Score for Crohn's disease (SES-CD) were immune (IL-6/JAK/STAT3, inflammatory response), metabolic, and reactive oxygen species (ROS). These were also positively correlated with markers of systemic inflammation (CRP, SAA, IL-6, and OSM) and epithelial turnover (IL-22, C4M2, and C3M). Ten weeks of FIL treatment led to significant decreases of these pathways in endoscopic responders (50% reduction in SES-CD), whereas there were no significant changes following placebo treatment. While interferon (IFN) response pathway scores showed weak correlation (rho < 0.2) with SES-CD at BL, they were significantly reduced by FIL treatment, particularly in FIL responders.

Conclusions In whole blood, inflammation, metabolic and ROS pathways were reduced by FIL in endoscopic responders at W10, while reductions in IFN response pathways were observed in all patients regardless of endoscopic response.

P117 FILGOTINIB REDUCES MARKERS OF JAK1 SIGNALING IN CROHN'S DISEASE: CONCORDANCE WITH ENDOSCOPY AND HISTOPATHOLOGY

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Introduction Filgotinib (FIL) is a JAK1 inhibitor under phase 3 clinical evaluation for treatment of IBD. We conducted a post hoc analysis in patients (pts) with moderately to severely active Crohn's disease (CD) to assess the effect of FIL on markers of JAK1 signaling (STAT1/3 phosphorylation [pSTAT1/3]) within intestinal mucosa and their correlation to histologic/endoscopic indices (NCT02048618).

Methods Baseline (BL) and Week 10 (W10) biopsies were collected from predefined bowel segments. Within-subject matched biopsies (FIL, n=42; placebo [PBO], n=18) were scored for histologic and endoscopic disease activity. Machine learning (Visiopharmv.2019.06) was used to quantify%pSTAT1 and%pSTAT3 positive nuclei within epithelium (Ep) and non-Ep regions. Basal pSTAT levels from 182 non-diseased

Abstract P117 Table 1

pSTAT	BL MDA	W10 change	Ep			Non-Ep		
			FIL	PBO	P	FIL	PBO	P
pSTAT1	Low	Worsen	−0.168	−0.348	<0.05	−0.173	−0.394	<0.05
	High	Improve	0.436	0.286	NS	0.390	0.327	NS
pSTAT3	Low	Worsen	−0.115	−0.375	<0.005	−0.109	−0.382	<0.005
	High	Improve	0.449	0.241	<0.05	0.442	0.232	<0.05

segments were used to classify segments as low or high molecular disease activity (MDA). Agreement between endoscopy/histology and MDA was evaluated by Cohen's kappa coefficient ([]) and% agreement.

Results In segments with BL GHAS activity subscore ≥2, Ep (10–30%) and non-Ep (25–35%) MDA were elevated and correlated to histologic activity. Table 1 shows the effect of FIL on MDA in the intestinal mucosa: significantly fewer low BL MDA segments showed MDA worsening, and significantly more high BL MDA segments showed MDA improvement (pSTAT3 only) with FIL vs. PBO. Agreement for MDA and endoscopy was fair to moderate (κ 0.3–0.5), and for MDA and histology was moderate to good (κ 0.4–0.8).

Conclusions FIL improved JAK1-related MDA within the mucosa of pts with CD. Agreement between MDA and clinical indices was highest with histology.

P118 POSITIVITY THRESHOLDS OF TOTAL INFLIXIMAB AND ADALIMUMAB ANTI-DRUG ANTIBODY ASSAYS AND IMPACT IN CLINICAL PRACTICE

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Introduction Anti-drug antibodies can affect biopharmaceutical pharmacokinetics by increasing or decreasing drug clearance. Drug-tolerant (total), unlike drug-sensitive (free), antibody assays permit antibodies to be measured in the presence of drug.

We aimed to confirm the positivity threshold of our total anti-tumour necrosis factor (TNF) antibody ELISA assays in healthy volunteers and to use this threshold to report the prevalence of clearing and transient antibodies in patients treated with infliximab and adalimumab.

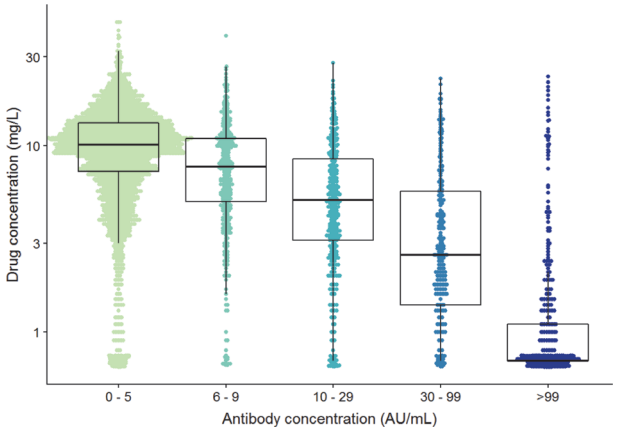
Methods Serum was obtained from 498 anti-TNF-naïve healthy adults recruited to the Exeter 10,000 study and tested for total anti-drug antibodies to infliximab and adalimumab. We used bootstrapping to calculate the 80% one-sided lower confidence interval [CI] of the 99th centile recommended by the FDA to define assay thresholds.

We used paired drug and anti-drug antibody levels derived from our national therapeutic drug monitoring service to report the distribution of clearing (antibody positive, drug negative) vs non-clearing (antibody positive, drug positive) antibodies. In patients with at least two test results, antibodies were classified as transient (single positive test with subsequent negative test) or persistent (at least two positive tests).

Results The 80% one-sided lower CI of the 99th centile titre for total anti-drug antibody to infliximab and adalimumab were 8.7 AU/mL and 5.9 AU/mL, respectively.

Using these thresholds, at the time of last testing, of 7,428 and 4,043 patients treated with infliximab and adalimumab; 21.1% and 8.3% had clearing antibodies and 27.9% and 20.0% had non-clearing antibodies, to infliximab and adalimumab, respectively.

Amongst patients with at least two tests, most developed persistent antibodies. Irrespective of anti-TNF drug, or threshold used, less than 10% patients developed transient antibodies.



Abstract P118 Figure 1 Relationship between adalimumab drug and anti-drug antibody levels in national TDM cohort

Across both our national TDM cohort and the PANTS study, there were significant associations between anti-drug antibody and drug levels (figure 1). In PANTS, higher anti-drug antibody levels were associated with poorer outcomes at weeks 14 and 54.

Conclusions We report lower positivity thresholds for the IDK-monitor® total anti-TNF antibody ELISA assays than the manufacturer, in particular, for adalimumab. Transient antibody formation is uncommon: most patients develop persistent anti-drug antibodies that lead to drug clearance.

P119 RISK OF FURTHER SURGERY AND ADHERENCE TO COLONOSCOPY GUIDELINES FOLLOWING RIGHT HEMICOLECTOMY FOR CROHN'S DISEASE

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Introduction The risk of further surgery following right hemicolectomy (RH) for Crohn's disease (CD) is high (~40%). Recent guidelines advise colonoscopy 6–12 months following RH to reduce the risk of further surgical intervention through medical therapy. We examined the risk of further surgery and use of colonoscopy following index RH.

Methods Hospital Episode Statistics were used to identify subjects with CD and RH between 2007 and 2016 in England. Adherence to post resection colonoscopic assessment guidance and risk of further surgery at the same site were investigated. Cox regression models examined the risk factors associated with further surgery and funnel plots demonstrated the colonoscopy practice of providers.

Results 12,230 CD subjects (55% female, median age 36 (IQR 26–49) years) had a RH during the study period. 1,367 (11%) had further surgery at the anastomotic site during follow up. 40% of Index surgery and 50% of further surgery was performed during an elective admission. 9% (747/8,293) of those with 5 year at follow up had further surgery as and 17% (366/2,163) of those with 10 years at follow up. Age over 54 compared to 18–24 years had a reduced risk of further surgery (adjusted Hazard ratio 0.81 (95%CI 0.67–0.97),