maintenance therapy, secondary loss of response is common affecting approximately 10%–15% of patients/year. Increasing drug levels, whether by doubling the dose or decreasing the interval, recaptures response in approximately 75% of patients. However, both of these strategies have cost implications. Anecdotal reports suggest that in patients losing response on maintenance infliximab (IFX) 5 mg/kg, a temporary increase to double doses (DD; 10 mg/kg) can lead to subsequent recapture of response at the lower dose. In a small cohort, we have previously shown that this strategy was not viable in the majority of patients. We now present an extended cohort across two centres with longer follow-up.

**Methods** We performed a retrospective review across two tertiary centres of all patients with Crohn's disease who had received temporary increases to DD of IFX for loss of response. Demographic data, HBI prior to the first infusion at the higher dose and prior to the first infusion at the lower dose, and ability to continue on IFX at 5 mg/kg were recorded.

**Results** 34 patients (18M:16F, median age 24 (range 12–51)) received DD IFX for loss of response. Median disease duration was 3 years (range 0–32) and the median time to dose increase from starting IFX was 12 months (range 3–60). All had received standard induction doses of IFX at 5 mg/kg on weeks 0, 2 and 6 and were on scheduled maintenance therapy. The dose interval prior to dose increase was 8 weeks for 24 patients, 7 weeks for 1, and 6 weeks for 9. 26 patients were on concurrent immunomodulators and 8 were not. One patient received 4 DD, 27 received 2 DD and six patients 1 DD. Dose increase was effective in the short term with the median HBI falling from 6 (range 0–27) prior to the first infusion at 10 mg/kg, to 1 (0–7) prior to the first infusion back at the standard dose (5 mg/kg) (p=0.003). However, only seven patients remained on IFX at the end of follow-up (median 13 months (range 8–25)). The median interval to discontinuing IFX was 4 months after the first DD (1–19). Of those who discontinued, four had infusion reactions while the others failed to maintain a response to IFX.

**Conclusion** Because of the limited treatment options available in Crohn's disease, attempting to recapture response in patients on IFX is appropriate. However, while temporary double-dosing is effective in the short term, it does not deliver long term disease control after subsequent dose reduction. Whether dose reduction is possible after prolonged dose increase remains to be answered.

**Competing interests** None declared.

## PTU-129 INITIAL EXPERIENCE WITH INFLIXIMAB LEVELS IN A TERTIARY IBD CENTRE

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**Introduction** Biologic use in the UK is increasing in patients with Crohn's disease (CD). While highly effective at inducing and maintaining remission, secondary loss of response occurs in approximately 15% of patients on maintenance treatment with biologics every year. There is some preliminary evidence that drug levels may play a role in this. However, measurement of anti-TNF levels has not been routinely available in the UK until very recently.

**Methods** We performed a service evaluation of a CE marked kit measuring serum levels of infliximab (IFX) as well as anti-drug antibodies (BMD, Marne La Vallee, France). Samples were taken immediately prior to infusion of IFX in patients attending for infusions over a 9-week period (March–May 2011). Results were not used in clinical management. A retrospective notes review was undertaken in January 2012 to see how drug levels related to clinical activity and to outcome. Only patients with CD on stable maintenance therapy were included and if repeated samples were taken, only the first measurement was used.

**Results** 52 samples were taken on 41 patients. Eight were excluded either because they did not have CD or because they were still in the induction phase of treatment. 33 patients (17 male) were, therefore, included in the analysis. Seven had subtherapeutic levels (SL) of IFX (<2 μg/ml). Patients with SL had a higher median Harvey Bradshaw index (HBI) (5 (range 0–7)) and C reactive protein (CRP) (8 (0–50)) at the time the sample was taken than those with therapeutic levels (TL) (HBI (1 (0–8) p=0.03: CRP 0 (0–8) p<0.05). The highest HBI and CRP recorded during subsequent follow-up was also higher in those with SL than TL but not significantly so (HBI SL 4 (2–11) vs TL 2 (0–12): CRP SL 11 (0–56) vs TL 0 (0–21)). Patients with SL were also more likely to require dose escalation of IFX (SL 2/7: TL 0/26 (p<0.04)) and intervention (change of drug therapy or surgical/endoscopic intervention) (SL 3/7: TL 2/27 (p=0.05)).

**Conclusion** Subtherapeutic IFX levels were associated with increased disease activity defined by biomarkers (CRP) and disease activity scores (HBI). Subtherapeutic levels were also predictive of a worse disease course over the following 6–8 months. Measuring anti-TNF drug levels in patients with IBD is promising and the utility of these tests in every day practice should be investigated further.

**Competing interests** None declared.

## PTU-130 MUCOSAL MRNA EXPRESSION PROFILING FROM THE TERMINAL ILEUM AND COLON REVEALS UNDER EXPRESSION OF CLAUDIN 8, A TIGHT JUNCTION MOLECULE, AS POTENTIALLY CAUSAL IN ULCERATIVE COLITIS

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**Introduction** Intestinal barrier dysfunction plays an important role in the pathogenesis of ulcerative colitis (UC). We investigated mRNA profiles of mucosa from the colon and terminal ileum, in patients with UC and controls (HC) to identify genes that might be implicated in the pathogenesis of the disease.

**Methods** Mucosal biopsies were taken from 24 quiescent UC patients (Mayo score <3) and 33 HCs undergoing colonoscopy. Patients were on no treatment or on 5-aminosalicylates ± azathioprine. HCs were patients without organic disease. Parallel biopsies were taken for RNA extraction and histology from macroscopically non-inflamed mucosa in the terminal ileum (TI), ascending, descending and sigmoid colon, and rectum. cRNA was hybridised to Illumina HumanHT v12.0 Expression Beadchips. Expression data were log transformed and normalised. Probes with a detection p value <0.01 were analysed. Comparing 85 biopsies from HCs and 68 biopsies from UC patients across the colon, the data for each bowel location were adjusted to the mean HC rectal expression level. Where multiple biopsies were taken from the same individual, the adjusted data across all biopsies for that individual were averaged. T tests between groups and outlier analysis (p<0.005, fold change (FC) ≥1.5) were performed using proprietary software.

**Results** Of the ~30K probes analysed, the two most significantly under-expressed in UC in the colon were those of claudin 8 (CLDN8) with FCs 2.94 ($p=1.29\times10^{-5}$) and 3.45 ($p=3.92\times10^{-5}$). The expression of claudin 8 increased distally in the colon, whereas claudins 3, 7 and 23 were highly, and uniformly, expressed throughout the colon and were normal in UC. Outlier analysis between HC and UC showed CLDN8 to be significantly under-expressed in 25%>40% of UC patients at all 4 colonic sites. There were no CLDN8 UC outliers in the TI. Most of these outlier patients demonstrated consistent levels of under-expression