P378. Predictors of sub-therapeutic infliximab or adalimumab trough levels and anti-drug antibodies and their influence on therapeutic decisions

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Background
Patients in Australia have restricted access to anti-TNF antibody therapies with little ability to dose adjust. We assessed predictors of anti-TNF drug levels and anti-drug antibodies (Ab) in a real world Australian IBD cohort and factors for sub-therapeutic anti-TNF levels and anti-drug Ab.

Methods
All patients who had infliximab (IFX) or adalimumab (ADA) trough levels and antibodies tested from three major Melbourne IBD centers were included. Clinical variables and a qualitative physician global assessment (PGA) of the disease activity at the time of testing (active or remission) were analysed along with biomarkers. IFX and ADA levels were measured by ELISA (Matriks Biotek). For both anti-TNFs, <3 μg/ml was considered sub-therapeutic. Anti-drug Ab were tested by ELISA, but only when anti-TNF levels were below 0.33 μg/ml. Performance characteristic including area-under-the-curve receiver-operator characteristics (AUROC) were determined.

Results
Of 114 patients tested, 69 (61%) were assessed due to loss of response (LOR), 40 (35%) in routine monitoring, 3 (3%) due to adverse effects and 2 (2%) for other. Median levels were similar in LOR vs monitoring (IFX 2.4 vs 3.6 μg/ml, $p = 0.27$; ADA 3.0 vs 3.6 μg/ml, $p = 0.72$, respectively; Mann–Whitney). CRP levels inversely correlated with IFX (Spearman $r = -0.38$; $p = 0.0004$) and ADA levels ($r = -0.51$; $p = 0.02$). Bivariate analysis demonstrated 45 of 92 (49%) treated with IFX and 9 of 22 (41%) with ADA had sub-therapeutic levels. Sub-therapeutic levels were best detected by a combination of disease activity assessed by both PGA and elevated CRP for both IFX (AUROC 0.75, sensitivity 90%, specificity 37%) and ADA (AUROC 0.80, sensitivity 83%, specificity 63%). PGA or CRP alone did not predict therapeutic levels. 21 of 70 patients with sub-therapeutic levels of IFX changed therapy (10 escalated dosage, 5 added immunomodulator, 4 switched in class, 2 surgery), compared with 10 of 43 with therapeutic levels ($p = 0.05$) There was a similar trend for ADA. Anti-drug Ab were detected in 8 patients. There was a tendency for fewer patients on concomitant immunomodulators to have anti-drug Ab (3 of 8) compared with those on monotherapy (5 of 8; $p = 0.08$). CRP and duration of therapy were not predictive for the presence of anti-drug Ab. 5 of these patients had a change in therapy (escalating dosage in 3, switching drug in 2).

Conclusion
Sub-therapeutic anti-TNF levels were associated with disease activity when present on both PGA and elevated CRP, and with subsequent change in therapy. Anti-drug Ab were uncommonly detected and only sometimes influenced treatment decisions. In contrast, drug levels did seem to influence clinical decision-making, but whether this improved outcomes needs to be determined.