

H Kerr<sup>1</sup>, T Lukose<sup>1</sup>, D Cheriyan, G Harewood, SE Patchett, A O'Toole<sup>1,2</sup>, K Boland<sup>1,2</sup>



Beaumont Hospital  
Ospidéal Beaumont

1. Department of Gastroenterology, Beaumont Hospital, Dublin,
2. School of Medicine, Royal College of Surgeons in Ireland, Dublin 2

## BACKGROUND

Ustekinumab is licensed for induction and maintenance therapy of moderate-severe inflammatory bowel disease (IBD). However, there are few data on the association between ustekinumab trough concentrations and mucosal healing<sup>1</sup>.

AIM: To identify maintenance target ustekinumab trough concentrations associated with mucosal healing in IBD.

## METHODS:

Trough ustekinumab levels and antibody titres were analysed in patients on maintenance drug using a drug-tolerant assay. Patients on maintenance subcutaneous ustekinumab for >16 weeks were included with levels drawn within a 1-week window to achieve trough level. Mucosal response was determined using combination of faecal calprotectin, endoscopy and radiology. Mucosal Healing identified as faecal calprotectin < 250 microg/ml or Global SES-CD score < 5 or Segmental Mayo score =1. Mucosal response was defined as reduction in faecal calprotectin, reduction in segmental Mayo score by 1 Mayo point or reduction in segmental SES-CD score. Clinical remission was defined as partial Mayo (pMayo) score <2 or Harvey-Bradshaw index score <5. Clinical response was defined as a reduction in segmental Mayo score by 1 point or a reduction in Harvey-Bradshaw score of 2 points.

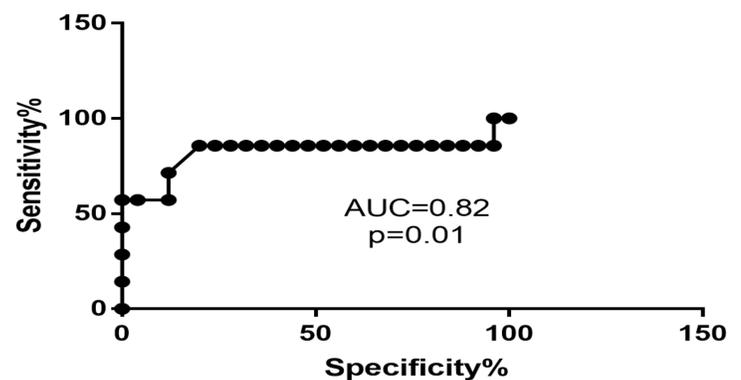
Median trough levels were analysed using Kruskal-Wallis test and logistic regression was used to construct a probabilistic model to determine sensitivity and specificity of levels predicting mucosal response.

## RESULTS:

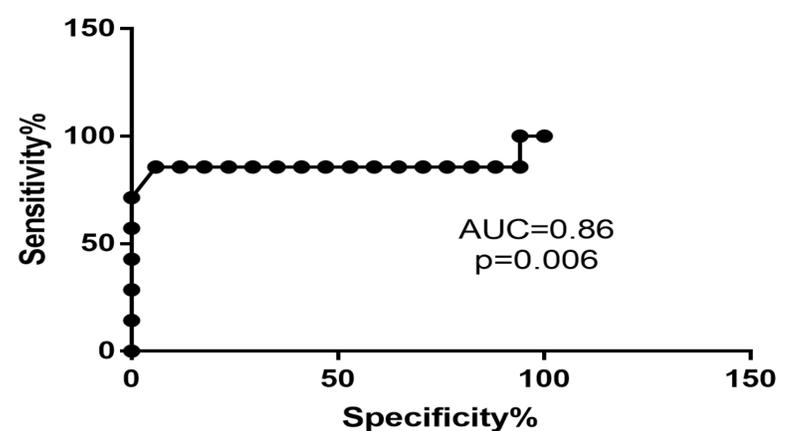
Table 1. Personal and Disease-specific Characteristics of Patients on Ustekinumab Maintenance Therapy Included in Analysis.

Variable	n (%)
Male	11 (34.3%)
Median (years)	39
Crohn's disease	29(90.6%)
UC/Indeterminate	3(9.3%)
No. on gomg/8WE	15(46.8%)
TNF experienced	26 (81.2%)
TNF naïve	6 (18.7%)
Clinical response	22(68.7%)
Clinical remission	5 (15.6%)

### Mucosal response vs non-response



### Mucosal healing vs non-response



Thirty-two patients on maintenance ustekinumab have been included to date (n = 29 CD, n = 3 IBD-U). 27 (84.37%) patients had previously failed TNF treatment. Clinical remission was recorded in 53.1% of patients (n=17) and a further 25% of patients (n=8) achieved mucosal response. After calculating a receiver operating characteristic (ROC) curve for mucosal response vs non-response, a trough level of 2.35 µg/mL was associated with mucosal response with 86% sensitivity and 90% specificity, AUC 0.86 (95% CI 0.62-1.1), P = 0.01. For mucosal healing vs non-response, a trough level of 2.35 µg/mL was associated with mucosal healing with 86% sensitivity and 94% specificity, AUC 0.82 (95% CI 0.6-1.1), P = 0.0063. No patients had detectable anti-drug antibodies.

## CONCLUSION:

A target trough ustekinumab level of 2.35 µg/mL was associated with mucosal response and remission in this real-world analysis of maintenance ustekinumab levels. This study is limited by patient numbers and recruitment is expanding to strengthen this analysis. Prospective studies on target ustekinumab levels should be carried out to facilitate patient-centred dosing targets.