# Clinical Validation of a Point of Care Test For Therapeutic Drug Monitoring of Infliximab

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## BACKGROUND

Infliximab (IFX) is a chimeric monoclonal antibody against tumor necrosis factor that is approved for the treatment of inflammatory bowel disease (IBD). Therapeutic drug monitoring (TDM) of IFX is widely used to ensure adequate serum concentrations in an attempt to maintain clinical benefit. The purpose of this study was to examine the clinical utility of a point of care (POC) IFX assay for TDM.

## METHODS

**CLINICAL STUDY DESIGN –** Retrospective observational clinical study using stored frozen serum specimens from a nested cohort from a prospective registry collected over 24 months.

**INCLUSION CRITERIA –** Adult patients with an established diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) who received maintenance IFX treatment.

**IFX POCT MEASUREMENT –** 20µL of thawed serum was mixed with pre-measured buffer in a reagent cartridge and read in the analyzer device, producing results within 3 minutes. IFX assay measuring range: 1.7 – 50.0 µg/mL.

**ENDPOINT –** Loss of response (LOR) defined as any of the following: **(i)** disease flare defined by documented worsening symptoms and abnormal endoscopy, imaging, or biomarker findings leading to discontinuation of IFX; **(ii)** disease activity leading to change in IBD medication; **(iii)** increase in fecal calprotectin ≥150 mg/Gr; **(iv)** IBD surgery or **(v)** new or recurring actively draining fistula. To be evaluable LOR patients were required to have provided a study specimen ≤60 days prior to the LOR event.

**STATISTICS –** LOR and No LOR groups were compared based on IFX concentration. Receiver-operating characteristic (ROC) curve analysis was done to identify IFX levels associated with LOR, and clinical cut-offs were evaluated by relative risk of LOR. Proportions of patients with LOR across IFX quartiles were compared by Fisher's exact test.

## RESULTS

A total of 92 IBD patients (LOR=55, No LOR= 37) were included in this study. IFX trough cut-off value that optimized sensitivity and specificity was 3 µg/mL **(Table 1)**. Area-Under-the-ROC Curve (AUC) value for loss of response was 0.818 **(Figure 1)**. Median IFX trough levels were lower in patients who experienced loss of response compared to patients who did not: median IFX 2.4 µg/mL vs 6.5 µg/mL, **(P < 0.001, Figure 2-A)**. Quartile analysis of IFX concentrations shows significant differences in percentage of patients suffering LOR **(P<0.001) Figure 2-B)**.

| Statistic | 3.0 µg/mL IFX | | 4.0 µg/mL IFX | | 5.0 µg/mL IFX | | 6.0 µg/mL IFX | |
|---|---|---|---|---|---|---|---|---|
| | Value | 95% CI | Value | 95% CI | Value | 95% CI | Value | 95% CI |
| Sensitivity (%) | **63.6** | 49.6 - 76.2 | **72.7** | 59.0 - 83.9 | **80.0** | 67.0 - 89.6 | **87.3** | 75.5 - 94.7 |
| Specificity (%) | **89.2** | 74.6 - 97.0 | **78.4** | 61.8 - 90.2 | **62.2** | 44.8 - 77.5 | **54.0** | 36.9 - 70.5 |
| Relative Risk of LOR | **5.89** | 2.28 - 15.2 | **3.36** | 1.78 - 6.34 | **2.28** | 1.44 - 3.59 | **1.90** | 1.32 - 2.73 |

**Table 1.** Shows clinical performance of Procise IFX for the detection of LOR at various IFX concentrations.

### ROC of 20IBD04 IFX

The Procise IFX assay sensitivity and specificity for the range of cut-offs is expressed in the ROC curve shown in **Figure 1**. The area under the ROC curve (AUC) is 0.818 showing very good assay performance in detection of LOR.

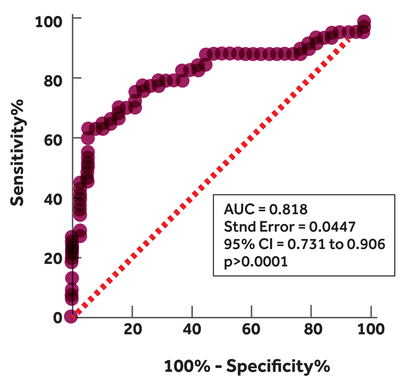


**Figure 1.** Shows ROC curve analysis of the Procise IFX test for the detection of LOR.

**Figure 2-A** Patients Suffering LOR vs. No LOR

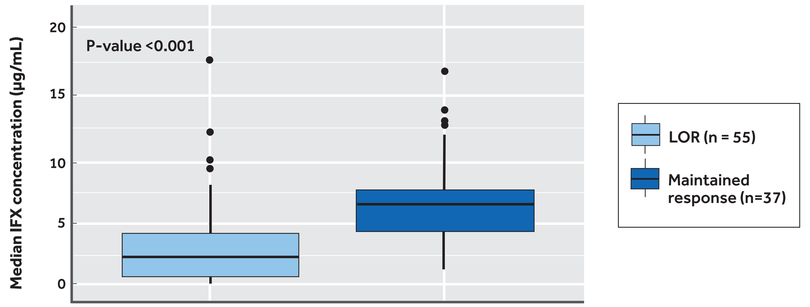


**Figure 2-B** IFX Concentration Quartiles

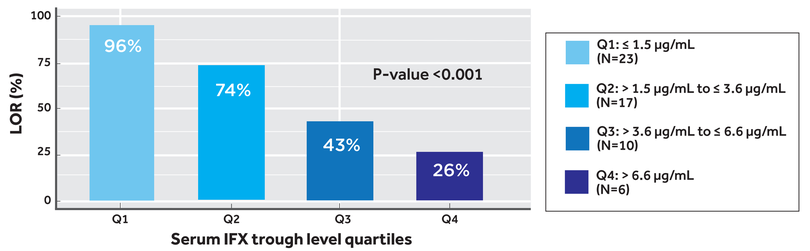


**Figure 2-A** shows patients losing response to IFX had serum levels significantly lower than those maintaining response. Horizontal lines correspond to medians and boxes to 25th - 75th percentiles. **Figure 2-B** shows significant differences across IFX concentration quartiles in percentages of patients with LOR.

## CONCLUSION

IBD patients in disease remission on maintenance IFX therapy with IFX levels below 3.0 µg/mL had a 5.89-fold increased risk of LOR compared to those above.

The ability to identify patients at highest risk of loss of response with a convenient POC format test enhances the clinical utility of TDM by enabling faster treatment response.