

Clinical Validation of a Point of Care Test For Therapeutic Drug Monitoring of Adalimumab



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BACKGROUND

Adalimumab (ADL) is a fully human monoclonal antibody against tumor necrosis factor that is approved for the management of inflammatory bowel disease (IBD). Therapeutic drug monitoring (TDM) of ADL is widely used to ensure adequate blood levels for maintenance of the clinical benefit. This study examined the clinical utility of a point of care (POC) ADL assay to facilitate 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 ADL treatment.

ADL 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. ADL assay measuring range: 1.3 – 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 ADL; (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.

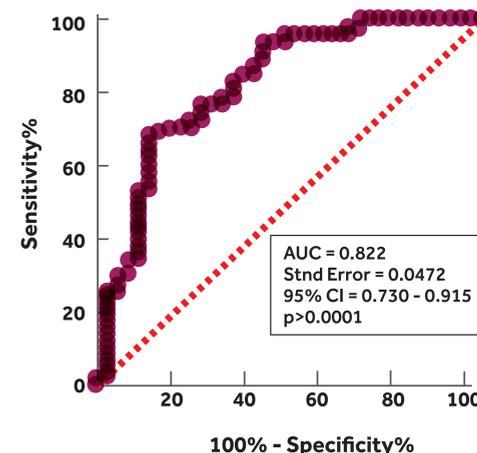
STATISTICS – LOR and No LOR groups were compared based on ADL concentration. Receiver-operating characteristic (ROC) curve analysis was done to identify ADL levels associated with LOR, and clinical cut-offs were evaluated by relative risk of LOR. Proportions of patients with LOR across ADL quartiles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

RESULTS

A total of 84 IBD patients (LOR=37, No LOR= 47) were included in this study. ADL trough cut-off value that optimized sensitivity and specificity was 8 µg/mL (**Table 1**). Area-Under-the-ROC Curve (AUC) value for loss of response was 0.822 (**Figure 1**). Median ADL trough levels were lower in patients who experienced loss of response compared to patients who did not: median ADL 6.0 µg/mL vs 13. µg/mL, (**P < 0.001, Figure 2-A**). Quartile analysis of ADL concentrations shows significant differences in percentage of patients suffering LOR (**P < 0.001, Figure 2-B**).

Statistic	≤6.0 µg/mL ADL		≤8.0 µg/mL ADL		≤10. µg/mL ADL		≤12. µg/mL ADL	
	Value	95% CI						
Sensitivity (%)	37.8	22.5 - 55.2	56.8	39.5 - 72.9	64.9	47.5 - 79.9	86.5	71.2 - 95.5
Specificity (%)	95.7	85.5 - 99.5	89.4	75.9 - 96.4	78.7	64.3 - 89.3	65.9	50.7 - 79.1
Relative Risk of LOR	8.89	2.15 - 36.7	5.34	2.22 - 12.8	3.05	1.68 - 5.55	2.54	1.57 - 3.86

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



The Procise ADL 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 0.822 showing very good assay performance in detection of LOR.

Figure 2-A Patients Suffering LOR vs. No LOR

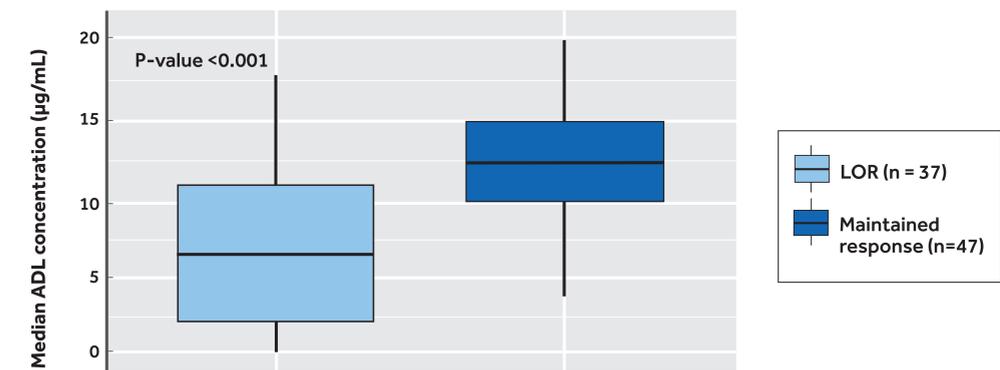


Figure 2-B ADL Concentration Quartiles

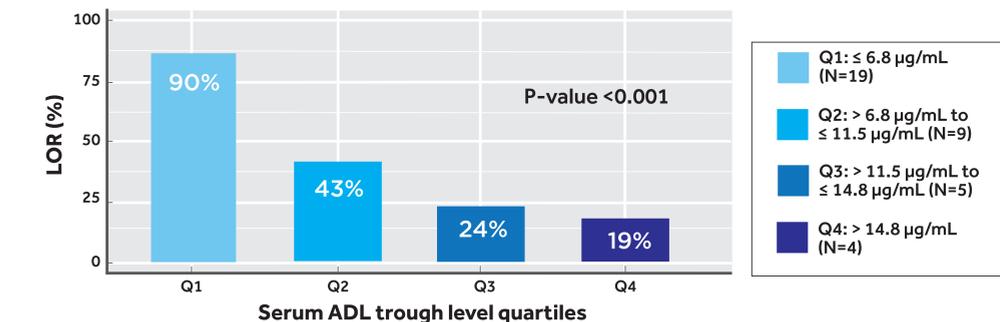


Figure 2-A shows patients losing response to ADL had serum levels significantly lower than those maintaining response. Horizontal lines correspond to medians and boxes to 25th - 75th percentiles. **Figure 2-B** shows significant differences across ADL concentration quartiles in percentages of patients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

CONCLUSION

IBD patients in disease remission on maintenance ADL therapy with ADL levels below 8.0 µg/mL had a 5.34-fold increased risk of loss of response compared to those above 8.0 µg/mL.

Identifying patients at high risk of loss of response with a convenient POC format test enhances the clinical utility of TDM by enabling faster treatment adjustment.