Clinical utility of therapeutic drug monitoring of adalimumab using a point of care test; P561

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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

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 reagent cartridge and read in analyzer device (figure 1), result within 3 minutes. ADL assay measuring range: 1.3 – 51.5 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.

Figure 1: POCT analyzer device and cartridge

Results

A total of 84 IBD patients (LOR=37, No LOR= 47) were included in this study. Area-Under-the-ROC Curve (AUC) value for loss of response was 0.822 (*Figure 2)*. ADL trough cut-off value that optimized sensitivity and specificity was 8 µg/mL (*Table 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 3-A*). Quartile analysis of ADL concentrations shows significant differences in percentage of patients suffering LOR (*P< 0.01 Figure 3-B).*

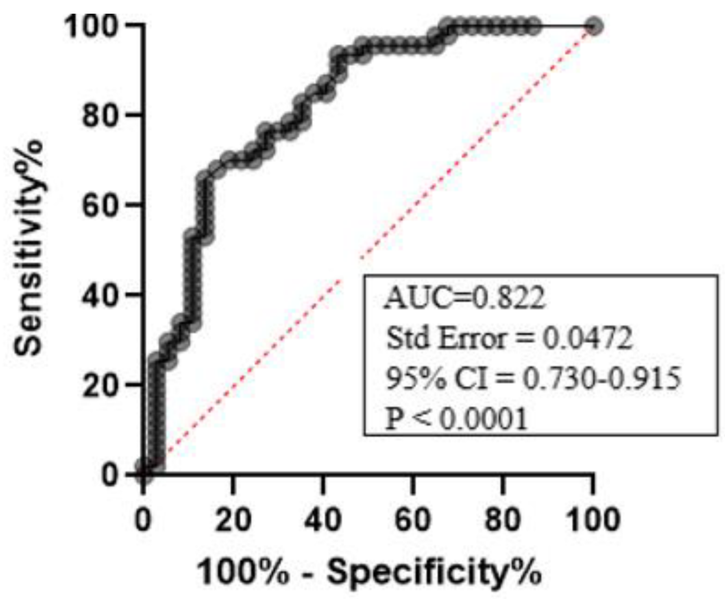

Figure 2. Shows ROC curve analysis of the Procise ADL test for the detection of LOR

Table 1	≤6.0 µg/mL ADL		≤8.0 µg/mL ADL		≤10. µg/mL ADL		≤12. µg/mL ADL	
Statistic	Value	95% CI	Value	95% CI	Value	95% CI	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.

Figure 3-A Patients Suffering LOR vs. No LOR

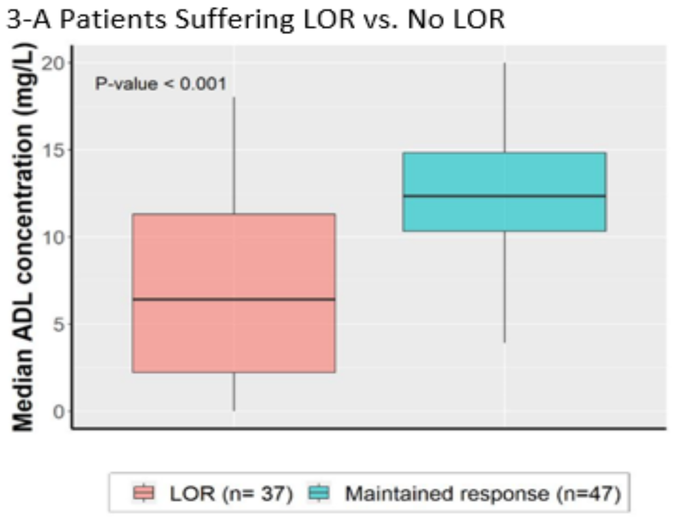

Figure 3-B ADL Concentration Quartiles

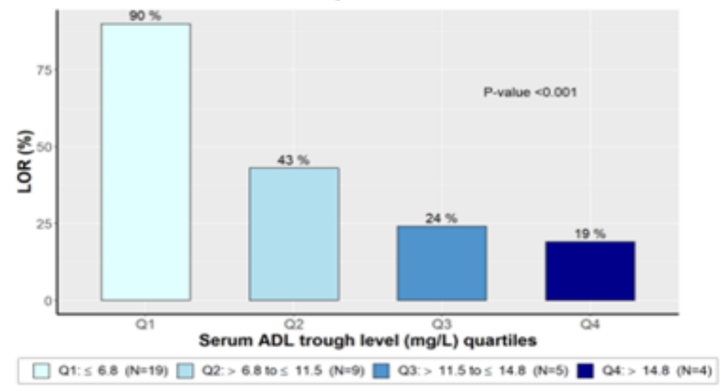

Figure 3-A shows patients losing response to ADL had serum levels significantly lower than those maintaining response. Horizontal lines correspond to medians and boxes to 25th–75th percentile. Figure 3-B shows significant differences across ADL concentration quartiles in percentages of patients with LOR.

Conclusions

- IBD patients in disease remission on maintenance ADL therapy with ADL levels below a cut-off 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 LOR with a convenient POC format test enhances the clinical utility of TDM by enabling faster treatment adjustment.

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Conflicts of interest: this study was funded by ProciseDx. Bayda Bahur and Kurtis Bray are currently employed by ProciseDx.