P283 Quantum Blue® Adalimumab: Development of the first point of care rapid test for therapeutic drug monitoring of serum adalimumab levels

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BACKGROUND

Adalimumab is a human monoclonal antibody directed against tumor necrosis factor alpha (TNFα) used for the treatment of inflammatory diseases like Crohn's Disease (CD) and Ulcerative Colitis (UC). For efficient treatment trough levels of adalimumab need to be adjusted within a therapeutic window, which is 5 to 10 µg/mL (Moss et al., 2015). A rapid test allows a much faster reporting of trough levels, providing a great advantage over test formats that need samples to be send to a central lab. Here we report current results of the completed Quantum Blue® Adalimumab test optimization. The test is now under validation.

METHODS

The sandwich lateral flow immunoassay uses a TNFα coated gold label and a highly specific monoclonal antibody to detect adalimumab in a diluted human serum sample. Sensitivity of the assay was estimated via Limit of Detection (LoD) and Limit of Quantification (LoQ) according to CLSI EP17-A2. Moreover the assay was evaluated regarding cross-reactivity with other therapeutic antibodies targeting TNFα, influence of rheumatoid factors (RFs) and high dose hook effect.

A method comparison was performed using a commercially available ELISA (RIDASCREEN® ADM Monitoring, Art. No. G09043, R-Biopharm, Darmstadt, Germany) to compare the serum level results of 40 adalimumab treated patients.

RESULTS

The current Quantum Blue® Adalimumab test allows analysis of serum samples within 15 minutes. The samples are diluted 1:20 in chase buffer before application on a test cassette (volume 80 µL). The readout is performed with the Quantum Blue® Reader resulting in concentration levels of adalimumab in µg/mL (Tab. 1).

The test exhibits a LoD of 0.2 µg/mL, which was calculated on the basis of the Limit of Blank (LoB). A LoQ of 0.69 µg/mL was determined according to the relevant CLSI-guideline. The obtained data ensure a measuring range of 1 to 35 µg/mL of adalimumab in patient samples. No high dose hook effect was detected for spiked serum samples containing up to 1000 µg/mL adalimumab. Other therapeutic TNFα blockers, like infliximab and golimumab, showed no cross-reactivity with the Quantum Blue® Adalimumab test, furthermore RFs showed no influence on correct measurement of adalimumab at the tested concentrations.

The performed method comparison revealed a slope of 1.12 and a regression coefficient (r^2) of 0.90 (Passing-Bablok, Fig. 1). A Bland-Altman analysis showed a bias of 1.88% confirming the overall excellent correlation of the two methods (Fig. 2). Moreover a comparison of both assays revealed an excellent agreement of 82.5% (Fig. 3).

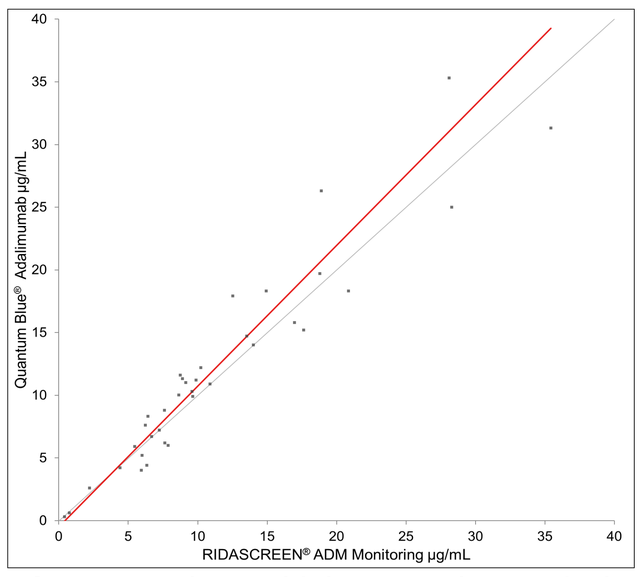

Fig. 1: Passing-Bablok regression analysis of the two assays.

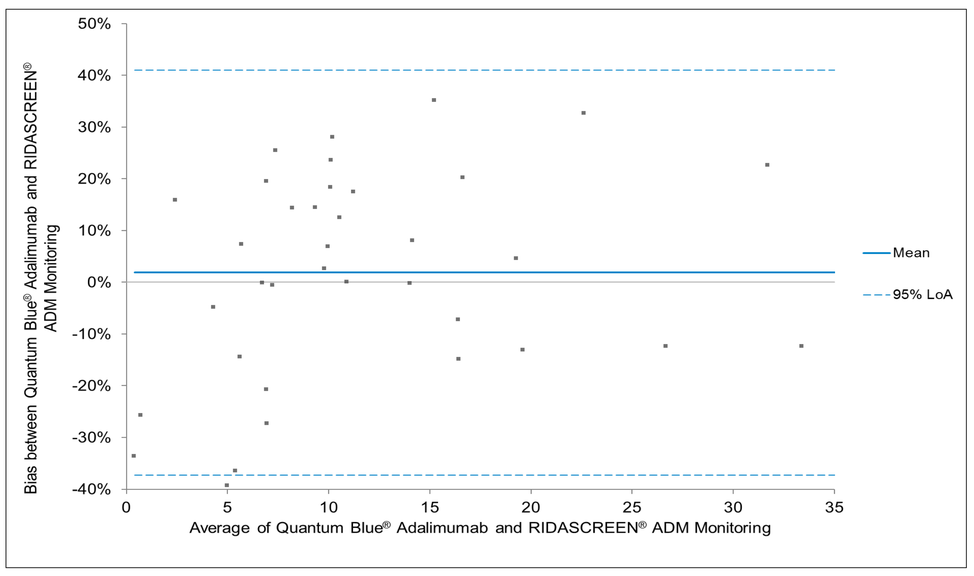

Fig. 2: Bland-Altman analysis revealed a bias of 1.88% in the method comparison.

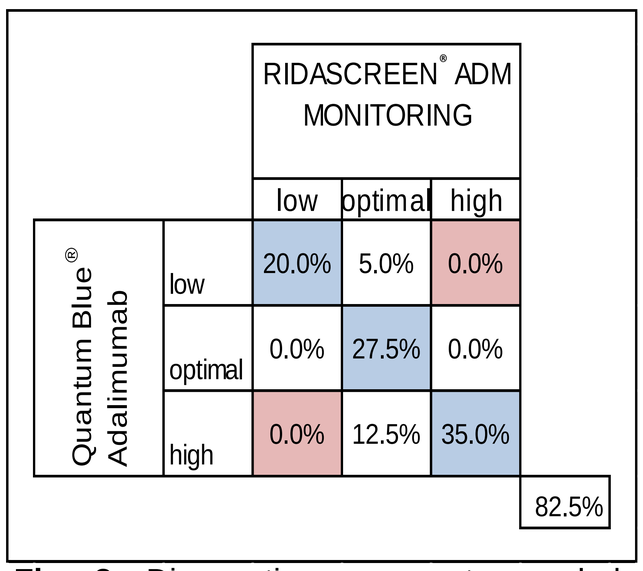

Fig. 3: Diagnostic agreement revealed high comparability between the assays.

Tab. 1: Quantum Blue® Adalimumab test key specifications.

Quantum Blue® Adalimumab	
Measuring Range	1 - 35 µg/mL
Sample Specimen	Serum
Application Volume	80 µL
Sample Dilution	1:20
Time to Result	15 minutes
Assay Read-out	Quantum Blue® Reader

CONCLUSIONS

The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of adalimumab trough level in serum with a time to result of only 15 minutes. The developed assay allows to measure adalimumab over a wide range. Hence, it represents a valuable tool for the clinician to assess the adalimumab trough level.

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