P242 Performance of the BÜHLMANN Quantum Blue® Infliximab point-of-care assay dedicated for therapeutic drug monitoring of serum infliximab trough levels

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BACKGROUND

A successful and cost effective infliximab therapy for patients, suffering *e.g.* from Crohn's Disease and Ulcerative Colitis is jeopardized, if the drug is not adjusted within an ideal therapeutic window (Casteele *et al.*, 2015). Rapid point-of-care (POC) testing allows an immediate determination of the trough level, which cannot be done by other currently used analytical methods. Here, we present the analytical performance characteristics as part of the validation of the first infliximab POC device, *i.e.* the Quantum Blue® Infliximab assay from BÜHLMANN.

METHODS

The sandwich lateral flow immunoassay uses a TNFα coated label and a highly specific monoclonal antibody to detect infliximab in a diluted human serum sample. Quantitative read out of the test cassette (TC) is performed by the BÜHLMANN Quantum Blue® Reader after 15 minutes of incubation. Testing was performed according to CLSI guidelines. The linearity study included multiple levels (12-14) of a serial sample dilution. The inter-lot precision was performed with eight samples within the measuring range (five days - two runs per day in two replicates). Method comparison to LEVEL INFLIXIMAB ELISA kit (M2920, Sanquin, The Netherlands) and to RIDASCREEN® IFX Monitoring (r-biopharm, Germany) is based on 93 serum samples. Cross-reactivity of other TNFα blockers was tested up to 100 µg/mL. Potentially interfering substances were tested *i.e.* other TNFα blockers (10 µg/mL or 1.7 µg/mL), azathioprine (60 µmol/L) / 6-mercaptopurine (37 µmol/L), methotrexate (1363 µmol/L), high level TNFα (2.6 ng/mL) and rheumatoid factors (RF, 497.3 IU/mL).

RESULTS

The BÜHLMANN Quantum Blue® Infliximab assay exhibits a limit of blank of 0.10 µg/mL, a limit of detection of 0.15 µg/mL and a measuring range of 0.4 to 20 µg/mL. The assay is linear beyond the measuring range (Fig. 1, Tab. 1), and exhibits no high dose hook effect (Fig. 2). The total precision of the device was 22.7% with a repeatability of 21.1% (Tab. 2). Beside infliximab, no other TNFα blocker was recognized, nor did they interfere with the determination of infliximab. In addition, no interference was observed with other immunosuppressive drugs, TNFα, RFs nor abnormal serum samples. Method comparisons towards the well-established Sanquin and the RIDASCREEN® IFX Monitoring ELISA revealed a slope of 1.09 and 1.03, a regression coefficient (r) of 0.94 and 0.93 (Passing – Bablok, Fig. 3) as well as a bias (Bland-Altman) of -7.9% and 0.79%, respectively.

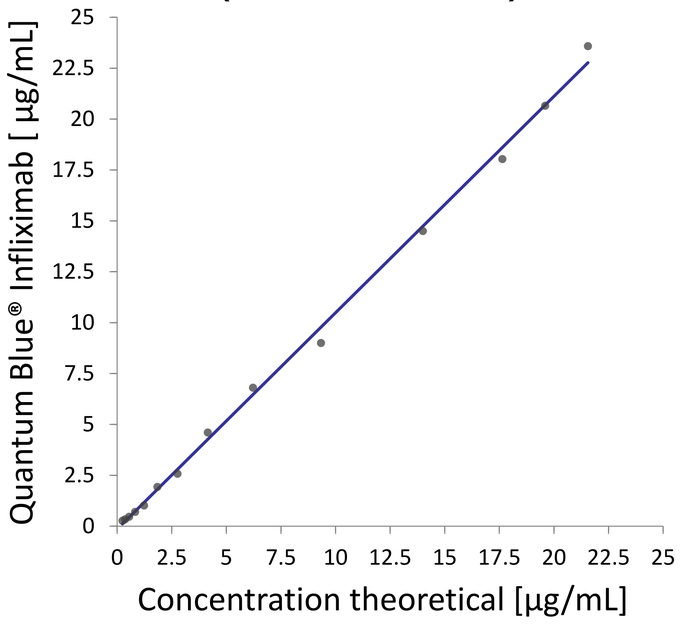

Fig. 1: Dilution- Linearity plot tested with pooled human serum

Lot	1	2
Nr. of Conc.	14	12
Linear range [µg/mL]	0.24 – 21.55	0.26 – 22.27
Total CV [%]	16.5%	23.9%
CV range [%]	10.2% – 21.1%	13.0 – 41.3%
Total Recovery [%]	100%	99.4%
Recovery range [%]	83.5 – 113.3%	85.8 – 108.5%

Tab. 1: Dilution – Linearity of two lots with ≥12 conc. levels. Linear range from 0.26 to 21.55 µg/mL and recovery values between 83.5 and 113.3%.

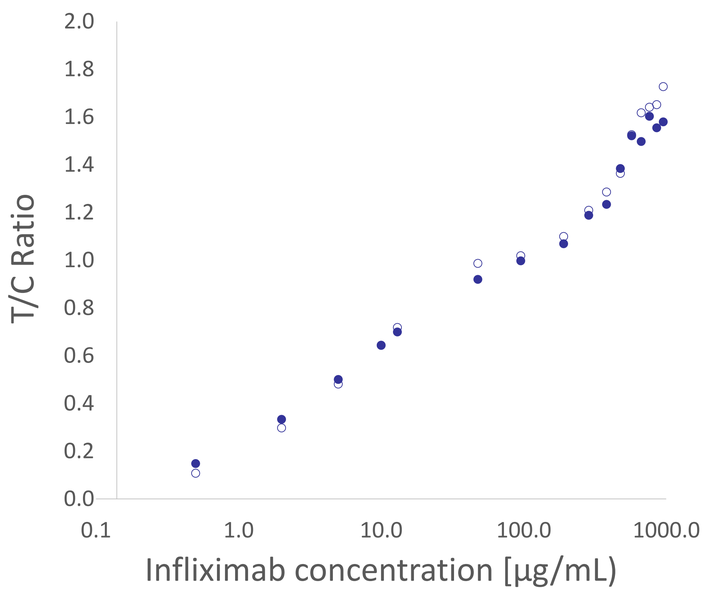

Fig. 2: No signal reduction, *i.e.* no high dose hook effect for serum, spiked with up to 1000 µg/mL infliximab.

[IFX] [µg/mL]	Total Precision CV [%]	Repeatability CV [%]	Inter-Lot Precision CV [%]
18.4	25.7	25.7	0.0
13.3	25.2	24.4	6.2
10.2	23.0	22.0	6.6
7.7	22.8	22.1	5.5
5.1	20.9	17.6	11.3
3.1	23.8	21.8	9.5
1.5	22.2	20.0	9.6
0.5	18.2	15.3	9.9

Tab. 2: Total precision of 22.7%, based on eight concentration levels.

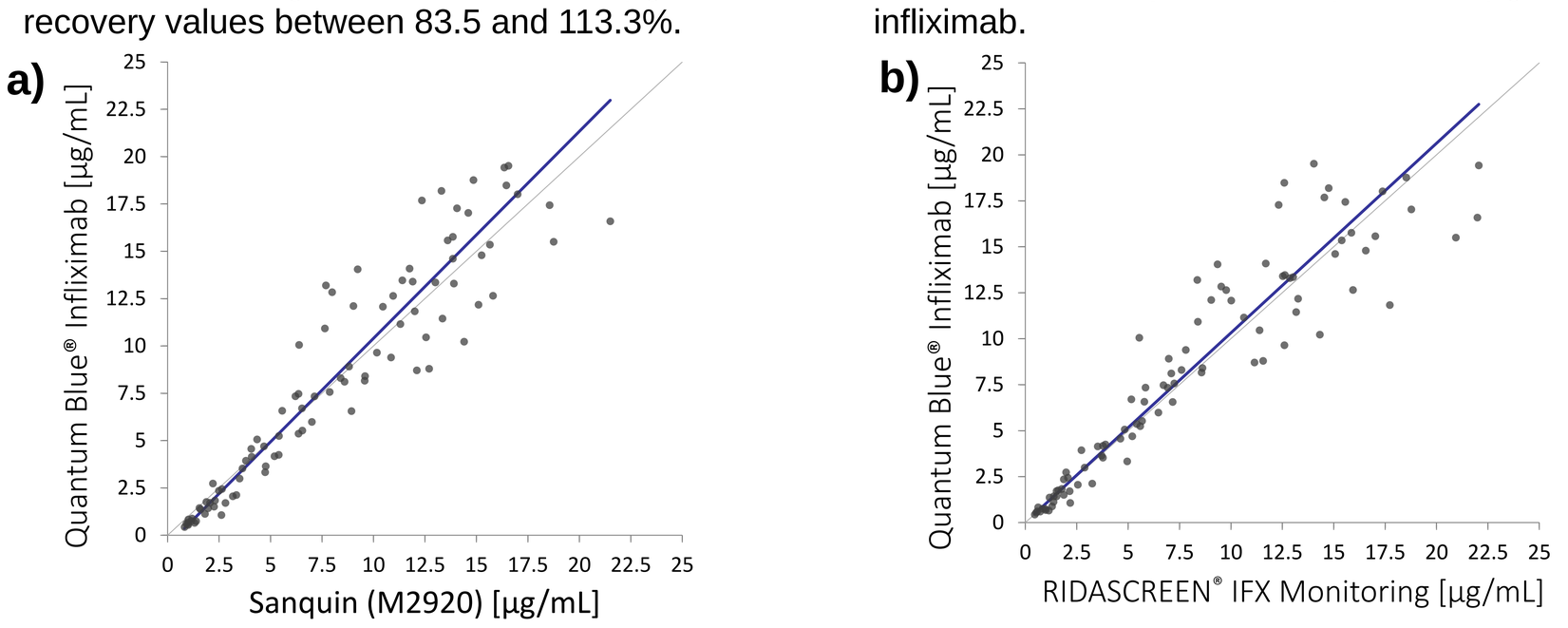

Fig. 3: Passing-Bablok regression analysis (a) vs. Sanquin ELISA (slope 1.09, r 0.94, bias at 3 µg/mL: 8.5%) and (b) vs. RIDASCREEN® IFX Monitoring (slope 1.03, r 0.93, bias at 3 µg/mL: -3.3%).

CONCLUSIONS

The BÜHLMANN Quantum Blue® Infliximab assay enables the quantitative determination of the infliximab trough level in serum with a time to result of only 15 minutes and exhibits an excellent correlation with existing ELISAs. Hence, it represents a valuable tool for the clinician to assess the drug level of the patient right before the next infliximab infusion.

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