Quantum Blue® Anti-Adalimumab: Development and evaluation of a point of care rapid test for measuring anti-adalimumab antibodies in human serum

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BACKGROUND

Patients suffering from inflammatory bowel disease (IBD) treated with adalimumab might not respond to the biologic at all, or might suffer from a secondary loss of response (SLR). A SLR is often caused by an immune response during which neutralizing anti-adalimumab antibodies (ADADs) may develop. The development of ADADs causes a significant decrease of the biologic's trough level. A rapid test for the detection of ADADs is therefore crucial and allows the fast adaptation of the treatment regime.

METHODS

A drug-sensitive sandwich lateral flow assay was developed using adalimumab (Fig 1, green antibodies) coated gold nanoparticles (Fig 1, red spheres) and an adalimumab capture on the membrane, allowing the detection of drug neutralizing anti-adalimumab antibodies (Fig 1, orange antibodies) in human serum samples. Additionally, the membrane comprises a control line, consisting of human ADAD (Fig 1, fuchsia antibodies) ensuring the proper functionality of the rapid test. The calibration is performed with calibrators based on human serum, spiked with monoclonal human ADAD.
The rapid test was compared with the ELISA RIDASCREEN® Anti-ADM Antibodies (R-Biopharm, Darmstadt, Germany) by measuring 102 patient samples.

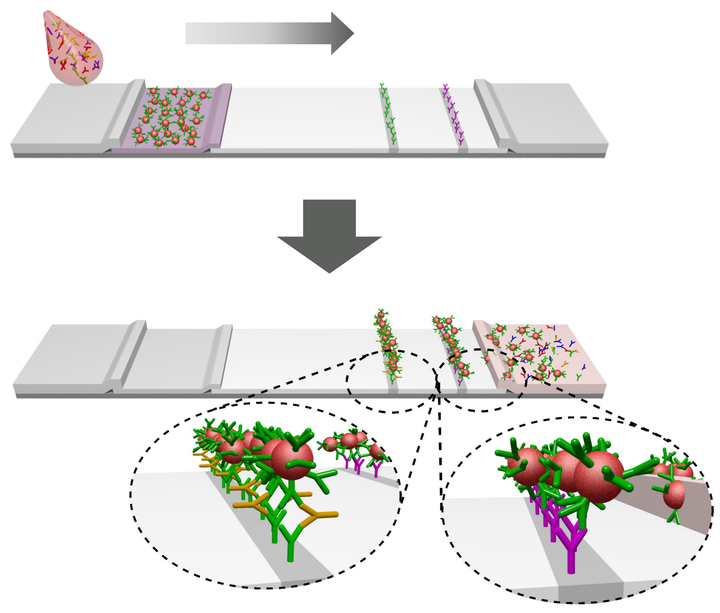

Figure 1: Setup of the ADAD rapid test

RESULTS

The Quantum Blue® Anti-Adalimumab rapid test allows the analysis of diluted human serum samples within 15 minutes. A single 1:10 dilution step of the serum sample is required before sample loading onto the test cassette (volume 80 µL). The readout is performed with a Quantum Blue® Reader resulting in a preliminary measuring range of 0.3 to 12.0 μg_{eq}/mL (Fig 2). A preliminary cut-off of 0.44 μg_{eq}/mL was determined by measuring 119 serum samples from healthy donors (Mean + 3 times SD).
The drug sensitive nature of the assay was demonstrated by spiking experiments with serum samples of healthy donors with ADAD and adalimumab (Fig 3). Due to missing international standard material for ADAD and the polyclonal immune response in patients, the Quantum Blue® Anti-Adalimumab assay was classified as semi-quantitative.

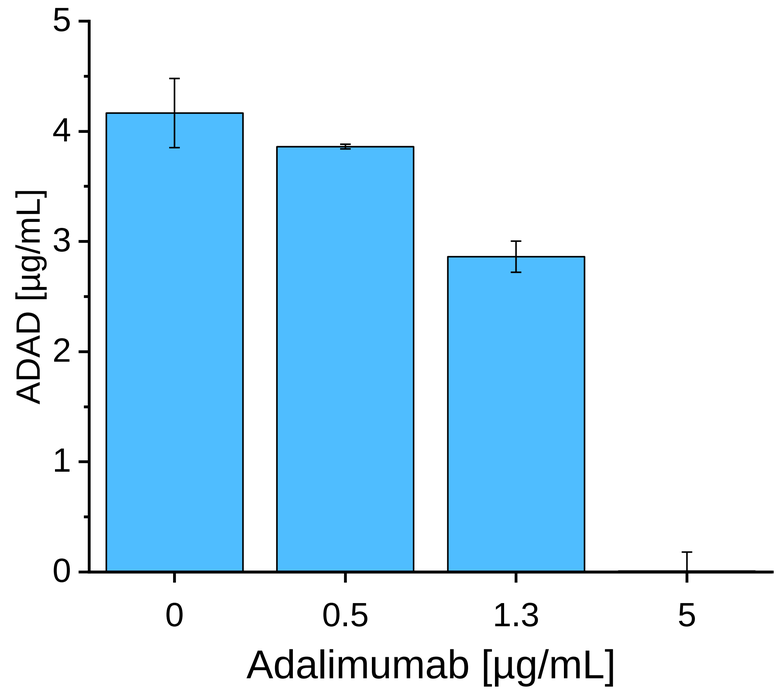

Figure 3: Interference of adalimumab

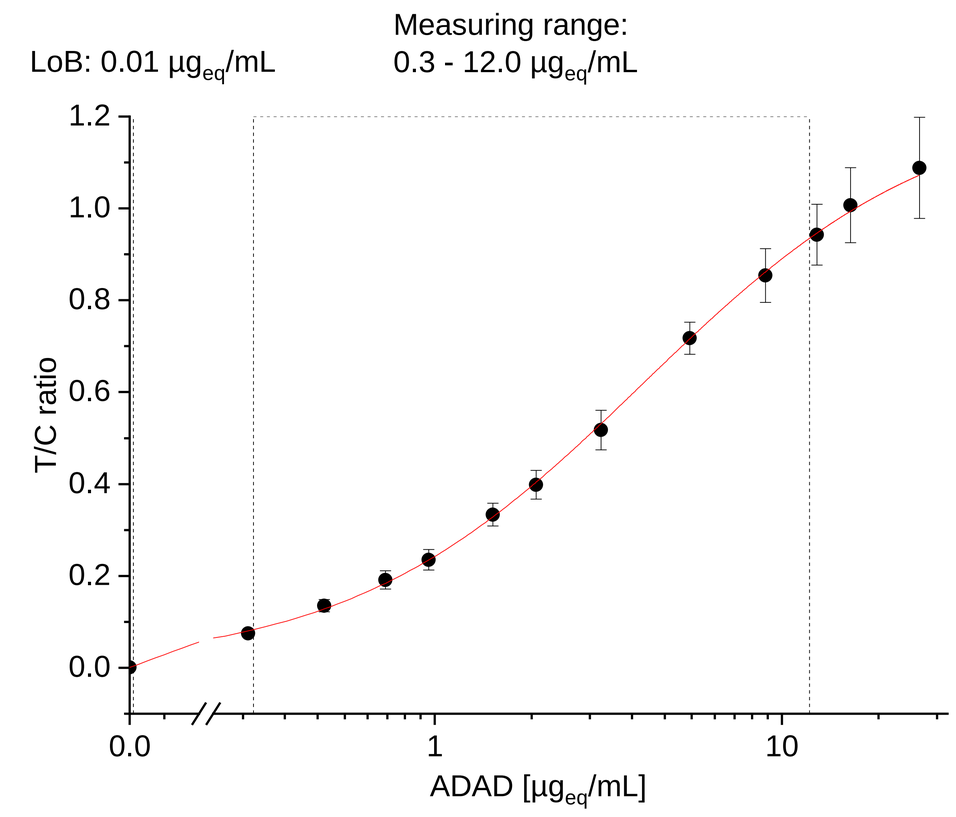

Figure 2: Standard curve with indicated measuring range

The analysis of 102 patient samples with the rapid test and a commercially available ELISA revealed an agreement of 87% (Fig 4). Out of these samples 80 were analysed with the Quantum Blue® Adalimumab and the RIDASCREEN® ADM Monitoring, resulting in an agreement of 100% (data not shown).

RIDASCREEN® Anti-ADM Antibodies	Quantum Blue® Anti-Adalimumab: Positive	Negative	Total
Positive	65	10	75
Negative	3	24	27
Total	68	34	**87%**

Figure 4: Agreement of the rapid test with a commercially available ELISA

CONCLUSIONS

The Quantum Blue® Anti-Adalimumab rapid test allows a fast detection of anti-adalimumab antibodies in human serum samples. The assay can be carried out with a minimum of additional equipment and may therefore support a fast adaption of the treatment regime. The combination of the rapid tests Quantum Blue® Anti-Adalimumab and Quantum Blue® Adalimumab provide a valuable tool for pro-active therapeutic drug monitoring.

14th Congress of ECCO, March 6-9, 2019, Copenhagen/Denmark