Validation of the RIDA®QUICK ADM Monitoring: a rapid test for adalimumab drug concentration monitoring which supports timely dose adjustments in clinical practice

Chris Barthel[1], Sumin Bian[2], Karin Wagenhäuser[1], Daniela Fichtner[1], Steffen Rameil[1], ***Thomas Van Stappen[1,2]***
[1]R-Biopharm AG, Clinical Diagnostics, Darmstadt, Germany; [2]KU Leuven, Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium; contact author: Thomas Van Stappen (*t.vanstappen@r-biopharm.de*)

Introduction

- Adalimumab (ADM; Humira®)
  - Monoclonal antibody against tumour necrosis factor-alpha (TNFα)
  - Treatment of Crohn's disease and ulcerative colitis
- Many patients do not respond to adalimumab induction treatment (up to 40 %) or lose response over time (23 - 46 %)[1]
- Therapeutic drug monitoring of ADM improves treatment efficacy and guides management of patients with loss of response
- Conventional assays for therapeutic drug monitoring (e.g. ELISA):
  - Lack the speed for immediate treatment optimization
  - Require multiple samples to be cost-effective

Aims & methods

- To validate a rapid test for the quantitative measurement of ADM drug concentrations (Fig. 1)
- Limit of quantification and precision as per CLSI guideline EP17-A2 and EP05-A3, respectively
- Method comparison was performed with 212 serum samples of patients with IBD (Fig. 2) versus the RIDASCREEN® ADM Monitoring (ELISA, R-Biopharm AG)

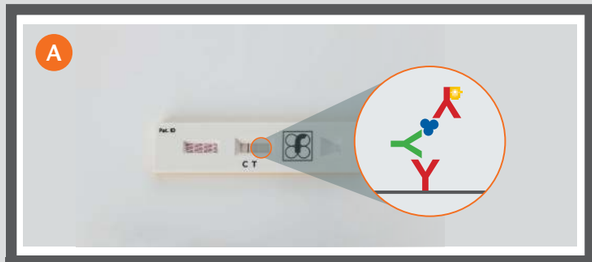

Figure 1: (A) Adalimumab is determined using a sandwich-based approach with the highly specific monoclonal anti-ADM antibody clone 40D8 as detection antibody.[2] (B) The ADM concentration is measured quantitatively using a portable and bench-top size reader, the RIDA®QUICK SCAN II.

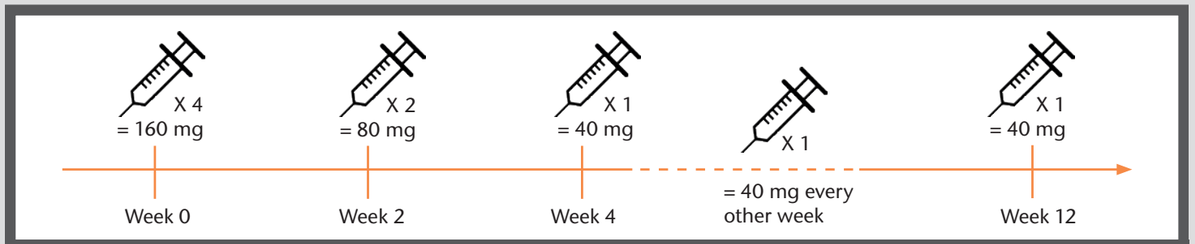

Figure 2: Serum samples were withdrawn just before the next dose administration at week 0 (n = 30), week 4 (n = 100) or week 12 (n = 82) of standard ADM induction therapy.

Results

- Precision (CLSI guideline EP05-A3)
  - Intra-assay precision: CV % 8.5 - 16.8 %
  - Inter-assay precision: CV % 11.8 - 16.6 %
- Recovery: Mean recoveries (observed versus expected concentration) between 90 % - 103 %
- All 30 week 0 samples were below the limit of quantification in both assays
- An excellent agreement with the RIDASCREEN® ADM Monitoring was observed (Fig. 3): Pearson r and intraclass correlation coefficients (ICC) were 0.95; 0.92 (Pearson r; ICC) and 0.98; 0.97, for patient samples collected at week 4 and week 12, respectively[3]

Table 1: Intra-assay precision of the RIDA®QUICK ADM Monitoring, as determined using 5 reference quality control samples (20 replicates per sample).

Reference quality control	1	2	3	4	5
Average (µg/mL)	2.3	5.7	8.9	14.3	25.7
Standard deviation	0.4	0.7	0.8	1.5	3.0
Coefficient of variation (%)	**16.8**	**12.2**	**8.5**	**10.4**	**11.8**

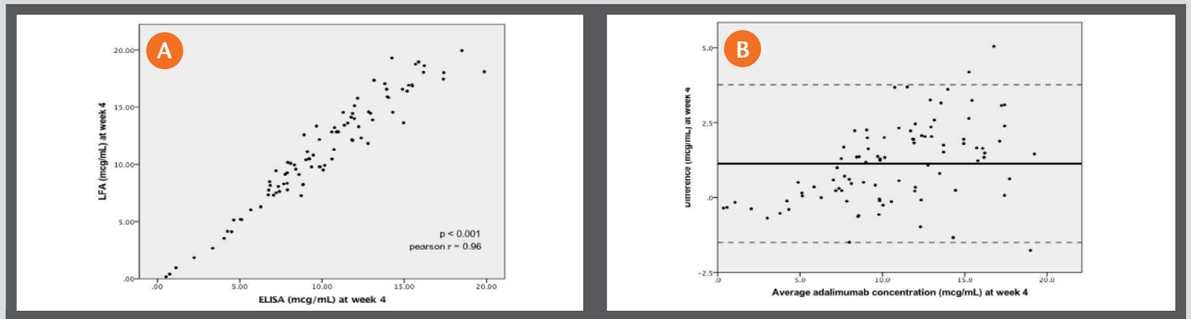

Figure 3: (A) Scatter plot and (B) Bland-Altman plot showing an excellent correlation and agreement of the RIDA®QUICK ADM Monitoring (LFA) with the RIDASCREEN® ADM Monitoring (ELISA) for the quantification of ADM in week 4 samples.[3]

Conclusion

The RIDA®QUICK ADM Monitoring

- allows accurate and precise quantification of adalimumab within the clinically relevant 0.5 - 25 µg/mL concentration range
- shows excellent agreement with the RIDASCREEN® ADM Monitoring (ELISA), which uses the same highly specific antibody clone to improve assay harmonization

Conflicts of interest:
CB, KW, DF, SR, TVS are employees of R-Biopharm. SB declares no conflicts of interest

References:
1. *Ben-Horin S, Kopylov U, Chowers Y.* Optimizing anti-TNF treatments in inflammatory bowel disease. Autoimmun Rev 2014;13:24-30.
2. *Bian S, Van Stappen T, Baert F, Compernolle G, Brouwers E, Tops S, de Vries A, Rispens T, Lammertyn J, Vermeire S, Gils A.* Generation and characterization of a unique panel of anti-adalimumab specific antibodies and their application in therapeutic drug monitoring assays. J Pharm Biomed Anal 2016;125:62-67.;
3. *Verstockt B, Moors G, Bian S, Van Stappen T, Van Assche G, Vermeire S, Gils A, Ferrante M et al.* Influence of early adalimumab serum levels on immunogenicity and long-term outcome of anti-TNF naive Crohn's disease patients: the usefulness of rapid testing. Aliment Pharmacol Ther 2018;48:731-739

10/2018