Validation of two commercial assays for therapeutic drug monitoring of adalimumab biosimilars (P694)

Raf Berghmans[1], Jürgen Naudts[2], Bianca Ferkinghoff[3], Hannah Gören[3], Marie-Luise Henke[3], Andrea Lennerz[4], Thomas Van Stappen[4]
[1]Research & Development, apDia bvba, Turnhout, Belgium; [2]Marketing, apDia bvb, Turnhout, Belgium; [3]QM/RA Technical Validation, R-Biopharm AG, Darmstadt, Germany; [4]Clinical Diagnostics, R-Biopharm AG, Darmstadt, Germany, Contact author: Andrea Lennerz (*a.lennerz@r-biopharm.de*)

Background

- Adalimumab (ADM) revolutionized the treatment of patients with inflammatory bowel disease. However, up to 40 % of patients do not respond to adalimumab induction treatment and 23 - 46 % of patients may lose response over time.[1]
- Therapeutic drug monitoring of adalimumab has shown to be useful to optimize treatment outcomes in patients with inflammatory bowel diseases.[1]
- The recent settlements with Abbvie concerning Humira®, paved the way for biosimilar drugs to enter the European market.
- Available commercial assays for adalimumab quantification were developed and validated using the originator drug, Humira®.
- In this study, we aimed to validate two commercial assays, the RIDASCREEN® ADM Monitoring (ELISA; also known as the apDia Adalimumab ELISA) and the RIDA®QUICK ADM Monitoring (rapid assay), for the quantification of two ADM biosimilars, AMGEVITA® and Imraldi®.

Methods

- To validate the RIDA®QUICK ADM Monitoring (Fig 1A) for the quantification of AMGEVITA® and Imraldi®, the recovery and linearity was determined in two different lots.
- The recovery was determined by spiking three samples containing a low concentration of ADM biosimilar with varying concentrations of ADM biosimilar. The rapid assay complies with the requirements of recovery, if the observed value of ADM biosimilar is within ±20 % of the expected value of ADM biosimilar.
- The linearity was performed on the basis of NCCLS-guideline EP6-A; a sample with high concentration of ADM biosimilar was diluted 1:1 to 1:38.4.
- To validate the RIDASCREEN® ADM Monitoring (Fig 1B), accuracy and recovery were determined by diluting AMGEVITA® and Imraldi® to varying concentrations within the clinical measuring range and in comparison with Humira®.
- The specification of accuracy is met when the deviation of the measured ADM biosimilar value is within ±15 % of the theoretical value. For the recovery, the deviation of the measured ADM biosimilar value has to be within ±15 % of the Humira® value.
- Both assays were performed following manufacturer's instructions.

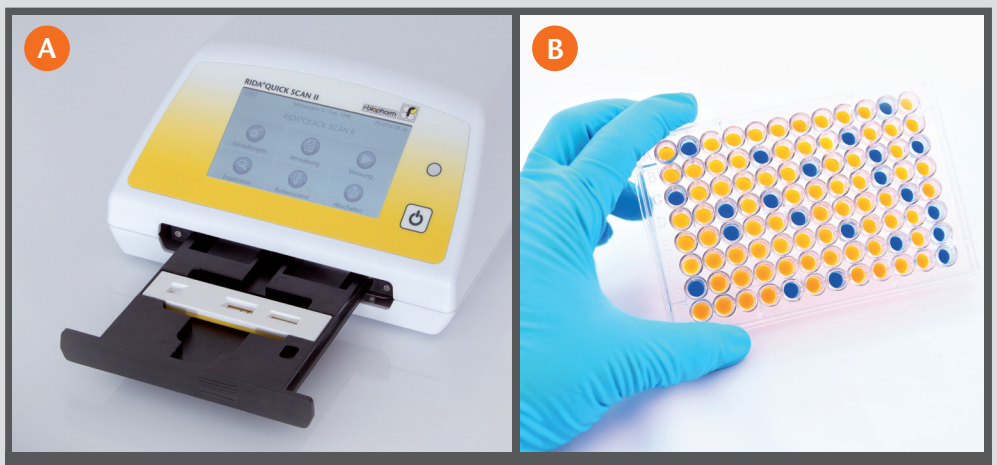

Figure 1: ADM concentrations were measured quantitatively (A) by lateral flow in the RIDA®QUICK ADM Monitoring using a portable and bench-top size reader, the RIDA®QUICK SCAN II and (B) by ELISA in the RIDASCREEN® ADM Monitoring (figure for illustration purposes only).

Results

- In the RIDA®QUICK ADM Monitoring, the mean recovery of three serum samples spiked with varying concentration of AMGEVITA® and Imraldi® ranged from 91 % to 115 %, and 95 % to 101 %, respectively. (acceptance range 80 - 120 %). Data from one lot are shown in Table 1.
- Linearity was shown for both AMGEVITA® and Imraldi®.

Tab. 1: Recovery of AMGEVITA® and Imraldi® in the RIDA®QUICK ADM Monitoring (lot 13249)

Sample	AMGEVITA® Spiked with AMGEVITA® [µg/mL]	Observed concentration [µg/mL]	Expected concentration [µg/mL]	Observed/expected concentration (%)	Sample	Imraldi® Spiked with Imraldi® [µg/mL]	Observed concentration [µg/mL]	Expected concentration [µg/mL]	Observed/expected concentration (%)
1	0	2.1			1	0	1.9		
	13.9	15.9	16	100		13.1	14.5	15	96
	3.5	5.4	5.6	96		3.3	5.4	5.2	103
	12.1	12.9	14.2	90		11.4	14	13.4	105
	8.7	10.8	10.8	100		8.2	10.1	10.1	99
			Average	97				Average	101
2	0	1.8			2	0	1.8		
	12.4	14.2	14.2	100		11.6	14.3	13.3	107
	10.6	14.8	12.4	120		9.9	11.3	11.7	97
	1.8	3.5	3.6	99		1.7	3.4	3.4	101
	8.8	10	10.6	94		8.3	10	10	100
			Average	103				Average	101
3	0	3.1			3	0	2.2		
	14.7	15.3	17.8	86		14.5	17.7	16.7	106
	4.9	6.8	8	85		4.8	5.9	7	84
	8.2	11	11.3	97		8	11.1	10.2	108
	6.5	9.2	9.6	95		6.4	7.8	8.6	91
			Average	91				Average	97

- In the RIDASCREEN® ADM Monitoring, the mean deviation of the measured AMGEVITA® and Imraldi® value vs the theoretical value was -6.6 % and 2.1 %, respectively (Table 2). (acceptance range ±15 %).

Tab. 2: Accuracy of the RIDASCREEN® ADM Monitoring for the quantification of (A) AMGEVITA® and (B) Imraldi® (lot 4813818)

A

Adalimumab measurements in the RIDASCREEN® ADM Monitoring					
Humira® dilutions			AMGEVITA® dilutions		
Theoretical value [µg/mL]	Measured value [µg/mL]	Deviation (%)	Theoretical value [µg/mL]	Measured value [µg/mL]	Deviation (%)
40	41.4	3.5	40	40.2	0.6
20	21.3	6.6	20	18.6	-7.1
10	10.6	6.2	10	9.6	-4.3
7	6.7	-3.6	7	6.4	-9
3	2.7	-8.4	3	2.8	-7
1	1	-3.5	1	0.9	-12.4
Mean deviation (%)		0.1	Mean deviation (%)		- 6.6

B

Adalimumab measurements in the RIDASCREEN® ADM Monitoring					
Humira® dilutions			Imraldi® dilutions		
Theoretical value [µg/mL]	Measured value [µg/mL]	Deviation (%)	Theoretical value [µg/mL]	Measured value [µg/mL]	Deviation (%)
40	43.7	9.2	40	41.3	3.2
20	22.4	12.2	20	20.6	3.1
10	10.1	0.7	10	10.3	3.4
7	7.2	2.7	7	7.2	2.7
3	2.9	-3.2	3	3	1.7
1	1.1	5.3	1.0	1.0	-1.2
Mean deviation (%)		4.5	Mean deviation (%)		2.1

- Recovery of spiked AMGEVITA® and Imraldi® samples in serum revealed a maximum absolute deviation of 12.9 % and 14.8 % vs Humira®. (acceptance range ±15 %).

Conclusion

The RIDASCREEN® ADM Monitoring and RIDA®QUICK ADM Monitoring were successfully validated for the quantification of AMGEVITA® and Imraldi®.
These results encourage therapeutic drug monitoring of ADM biosimilars in routine clinical practice.

Conflicts of interest: RB and JN are employees of apDia bvba; BF, HG, MLH, AL, TVS are employees of R-Biopharm AG.

References: [1] *Ben-Horin S, Kopylov U, Chowers Y.* Optimizing anti-TNF treatments in inflammatory bowel disease. Autoimmun Rev 2014;13:24-30.

01/2020