

A FULLY AUTOMATED ELISA MONOTEST SYSTEM FOR THE DETECTION OF DRUG AND ANTI DRUG ANTIBODIES IN PATIENTS WITH RHEUMATIC DISEASES: A COMPARISON WITH ELISA TEST ROUTINELY USED

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INTRODUCTION

Infliximab (IFX) and Adalimumab (ADL) are biological drugs widely used in rheumatic diseases. Some patients generate anti-drug antibodies associated with reduced drug levels resulting in loss of efficacy, clinical failure and increased risk of adverse effects. We evaluated an automated quantitative method applied to the DIESSE CHORUS TRIO instrument for the determination of IFX and ADL drugs and anti-drug antibody levels, comparing it with enzyme-linked immunosorbent assay (ELISA) LISA-Tracker Duo Adalimumab and LISA-Tracker Duo Infliximab, routinely used in our laboratory.

MATERIALS AND METHODS

The study was performed on 82 patients with rheumatic diseases who did not respond to biological therapy, attending the Rheumatology Unit, San Giovanni di Dio Hospital, Florence.



All sera were analyzed using the fully automated assays CHORUS Promonitor IFX, ADL, anti-IFX and anti-ADL (DIESSE Diagnostica Senese) and LISA-Tracker Duo Adalimumab and Infliximab (Theradiag).

Spearman correlation coefficient was performed to compare the two methods for drugs determination, while Cohen kappa was used to compare the anti-drug antibody results.

RESULTS

Drug levels: the two methods for the detection of drug levels showed an excellent agreement (Spearman coefficient 0,91 and 0,88 for the dosage of IFX and ADL, respectively).

Out of 58 ADL samples, two were discordant, showing borderline results for LISA-Tracker and negative results for CHORUS Promonitor. Out of 24 IFX samples, three were discordant, showing negative results for LISA-Tracker and borderline results for CHORUS Promonitor (Tab. 1-2)

Tab. 1

		LISA-Tracker (Reference method)		LISA-Tracker ADL (µg/ml)	CHORUS ADL (µg/ml)
		Range: 0,3 - 16,0 µg/ml			
Adalimumab	+			#1 0,3	< 0,3
	-			#2 0,8	< 0,3
CHORUS Promonitor (Test method)	+	52	0	anti-ADL (ng/ml)	anti-ADL (AU/ml)
	-	2	4	#2 160	751,3

Range: 0,3 - 50,0 µg/ml

Sample #2 is anti-ADL positive for both anti-drug tests.

Tab. 2

		LISA-Tracker (Reference method)		LISA-Tracker IFX (µg/ml)	CHORUS IFX (µg/ml)
		Range: 0,3 - 16,0 µg/ml			
Infliximab	+			#1 < 0,3	0,37
	-			#2 < 0,3	0,31
CHORUS Promonitor (Test method)	+	19	3	#3 < 0,3	0,38
	-	0	2		

Range: 0,3 - 50,0 µg/ml

Anti-drug levels: the agreement between the methods for the detection of anti-drug antibody levels showed Cohen kappa close to 1,0 for anti-ADL and 0,7 for anti-IFX antibodies.

The analysis of anti-ADL antibodies revealed one discordant result, positive for LISA-Tracker and negative for CHORUS Promonitor; the sample is drug positive in both systems (Tab. 3).

The analysis of anti-IFX antibodies revealed two discordant results, one positive for LISA-Tracker and negative for CHORUS Promonitor and one positive for CHORUS Promonitor and negative for LISA-Tracker; the two samples are drug negative for both systems (Tab. 4).

Tab. 3

		LISA-Tracker (Reference method)		LISA-Tracker anti-ADL (ng/ml)	CHORUS anti-ADL (AU/ml)
		Range: 10 - 160,0 ng/ml			
anti- Adalimumab	+			27,0	< 6,0
	-			ADL (µg/ml)	ADL (µg/ml)
CHORUS Promonitor (Test method)	+	6	0	6,7	6,0
	-	1	51		

Range: 10 - 1650,0 AU/ml

Sample is ADL positive for both drug tests.

Tab. 4

		LISA-Tracker (Reference method)		LISA-Tracker anti-IFX (ng/ml)	CHORUS anti-IFX (AU/ml)
		Range: 10 - 200,0 ng/ml			
anti- Infliximab	+			A 42,0	< 2,0
	-			B < 10,0	625,5
CHORUS Promonitor (Test method)	+	3	1	LISA-Tracker IFX (µg/ml)	CHORUS IFX (µg/ml)
	-	1	20	A < 3,0	< 3,0
				B < 3,0	< 3,0

Range: 5 - 1500,0 AU/ml

CONCLUSIONS

CHORUS Promonitor IFX and ADL and anti-IFX and anti-ADL and LISA-Tracker ELISA assays showed an excellence agreement for drug level detection and Cohen kappa close to 1,0 for anti-drug antibodies.

CHORUS Promonitor assays are a suitable tool in therapeutic drug monitoring thanks to the monotest device and the fully automated system.

