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Article

Comparative Evaluation of Four Commercially Available Immunoassays for Therapeutic Drug Monitoring of Infliximab and Adalimumab

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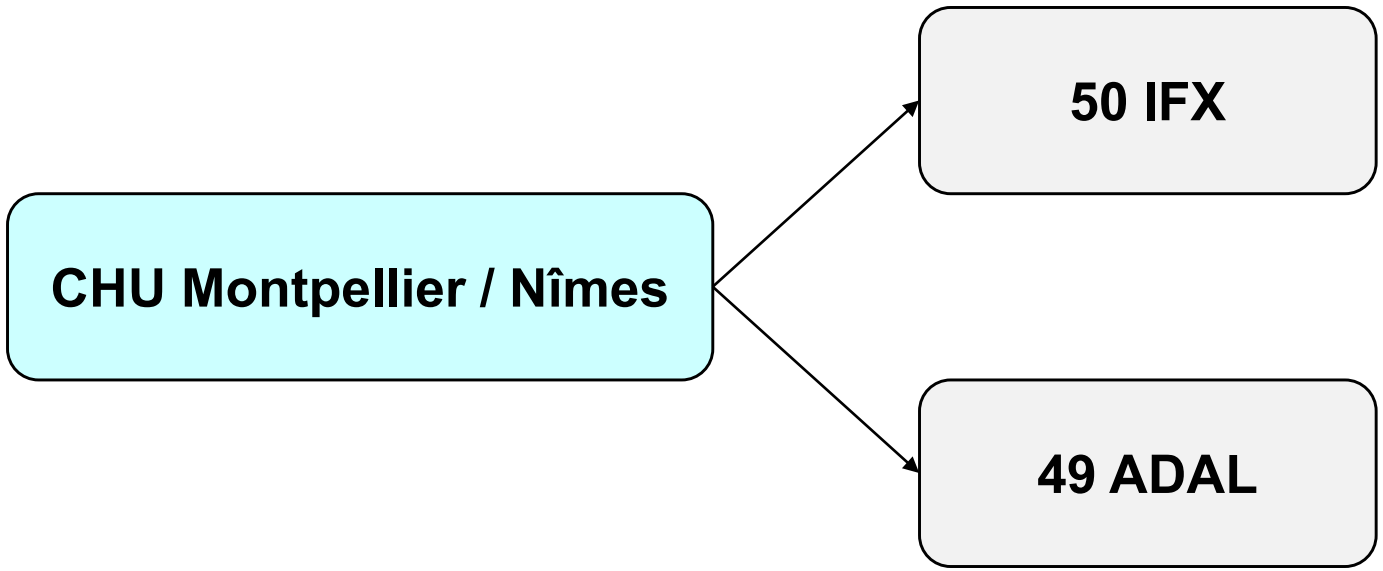
Patients and samples



➔ Stockage +4°C
➔ Dosage dans les 3 semaines

Table 1. Characteristics of assays used for method comparison.

	Company	Method	Measurement Range			
			IFX	Anti-IFX	ADAL	Anti-ADAL
Promonitor	GRIFOLS™	ELISA (Automated)	0.3–14.4 (µg/mL)	2–144 (AU/mL)	0.25–12 (µg/mL)	6–400 (AU/mL)
LisaTracker®	THERADIAG™	ELISA (Automated)	0.3–20 (µg/mL)	10–200 (ng/mL)	0.3–20 (µg/mL)	10–160 (ng/mL)
i-Track10®	THERADIAG™	CLIA	0.3–24 (µg/mL)	10–2000 (ng/mL)	0.5–24 (µg/mL)	10–2000 (ng/mL)
ez-track1	THERADIAG™	TRF	0.2–50 (µg/mL)	4–250 (AU/mL)	0.2–50 (µg/mL)	3–200 (AU/mL)

ELISA: enzyme-linked immunoassay CLIA: chemiluminescence immunoassay; TFF: time-resolved fluorescence; IFX: infliximab; ADAL: adalimumab; AU: arbitrary unit.

Table 2. Imprecision of LT DS2 with the use of low and high IMMUNO-TROL® IFX, ADAL, and ADA.

	IFX		Anti-IFX		ADAL		Anti-ADAL	
	Intrarun (µg/mL) (CV%)	Inter-Run	Intrarun (ng/mL) (CV%)	Inter-Run	Intrarun (µg/mL) (CV%)	Inter-Run	Intrarun (ng/mL) (CV%)	Inter-Run
Low	4 (4.3)	3.3 (12.6)	41 (4.2)	39.9 (10.1)	3.3 (8.6)	3.5 (11.6)	29 (10.2)	37 (11)
High	9.6 (6.4)	ND	129 (2.6)	ND	11.5 (12.2)	ND	111 (4.8)	ND

IFX: infliximab; ADAL: adalimumab; ADA: antidrug antibodies; CV: coefficient of variation; ND: not determined.

Cohen's Kappa

Cohen's Kappa coefficient is used to measure the level of agreement between two raters or judges who each classify items into predefined categories

IFX	LT DS2			
Promonitor DS2				
i-Track10	< 5 µg/mL	5 - 10 µg/mL	> 10 µg/mL	Total
ez-Track1 POC				
	19	1	0	20
< 5 µg/mL	17	1	0	18
	21	7	0	28
	1	14	0	15
5 - 10 µg/mL	4	8	0	12
	0	11	1	12
	0	1	12	13
> 10 µg/mL	0	10	12	22
	0	0	11	11
	20	16	12	48
Total	21	19	12	52
	21	18	12	51
	0.904			
Kappa value	0.565			
	0.752			

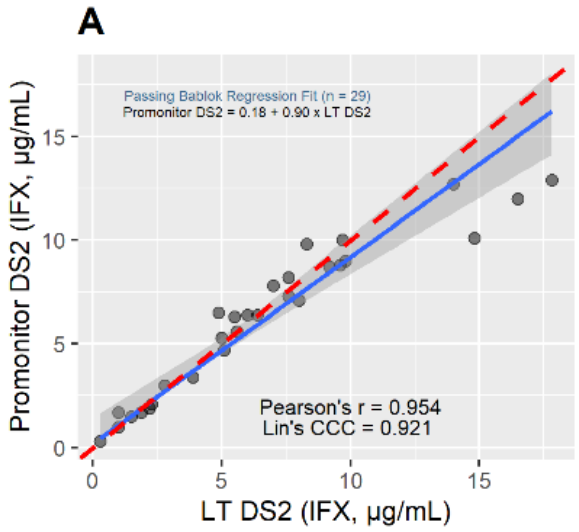
aIFX	LT DS2 (ng/mL)		
Promonitor DS2 (UA/mL)			
i-Track10 (ng/mL)	≥ 10	< 10	Total
ez-Track1 POC (UA/mL)			
	4	0	4
≥ 10	7	13	20
	7	3	10
	1	42	43
< 10	0	31	31
	0	41	41
	5	42	47
Total	7	44	50
	7	44	51
	0.877		
Kappa value	0.345		
	0.788		

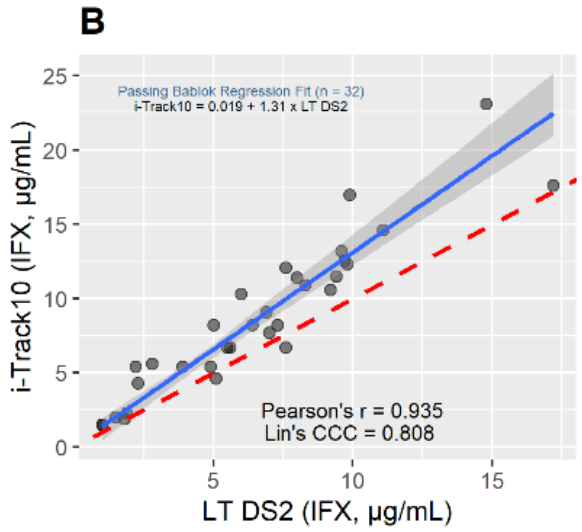
ADAL	LT DS2			
Promonitor DS2				
i-Track10	< 8 µg/mL	8 - 12 µg/mL	> 12 µg/mL	Total
ez-Track1 POC				
	26	0	0	26
< 8 µg/mL	24	0	0	24
	21	1	0	22
	7	9	5	21
8 - 12 µg/mL	11	7	0	18
	11	4	0	15
	0	2	2	4
> 12 µg/mL	0	4	7	11
	0	6	7	13
	33	11	7	51
Total	35	11	7	53
	32	11	7	50
	0.455			
Kappa value	0.517			
	0.401			

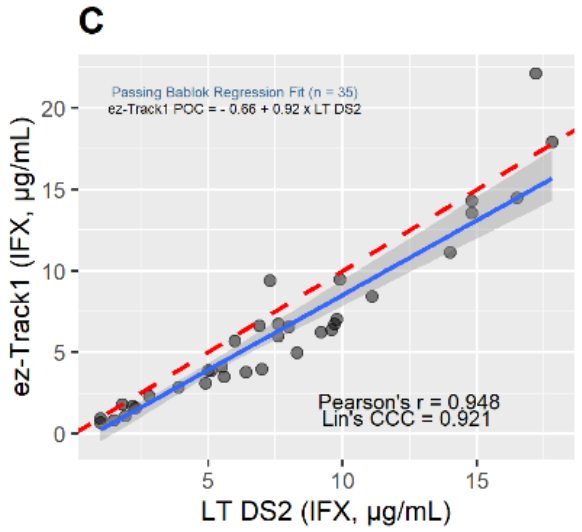
aADAL	LT DS2 (ng/mL)		
Promonitor DS2 (UA/mL)			
i-Track10 (ng/mL)	≥ 10	< 10	Total
ez-Track1 POC (UA/mL)			
	8	0	8
≥ 10	9	1	10
	8	0	8
	0	42	42
< 10	0	43	43
	0	41	41
	8	42	50
Total	9	44	53
	8	41	49
	1.000		
Kappa value	0.936		
	1.000		

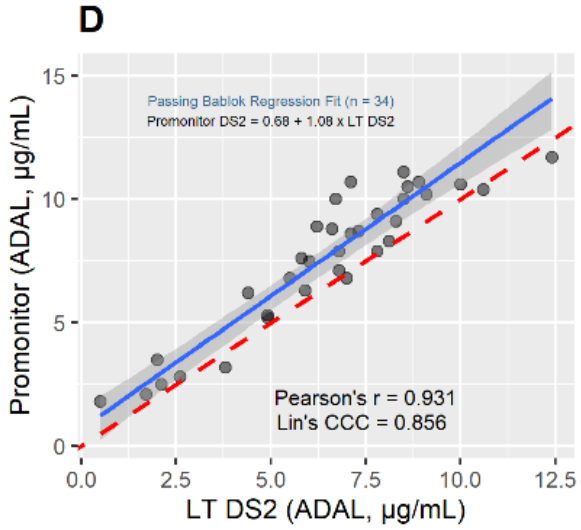
Passing-Bablok regression: IFX - ADAL

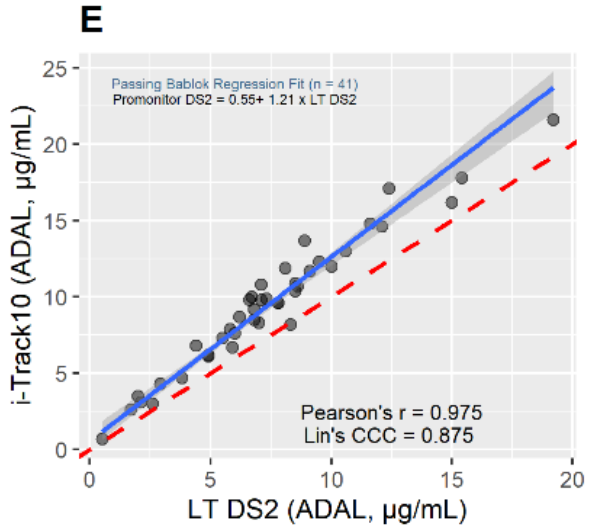
Red dashed lines are identity lines (y=x).
Grey shade areas are the 95% confidence

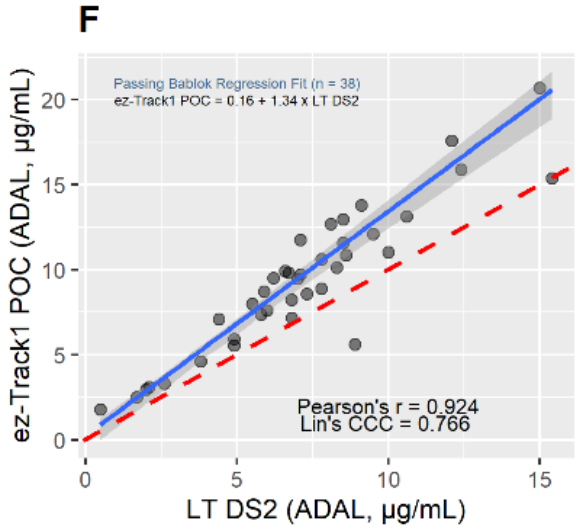






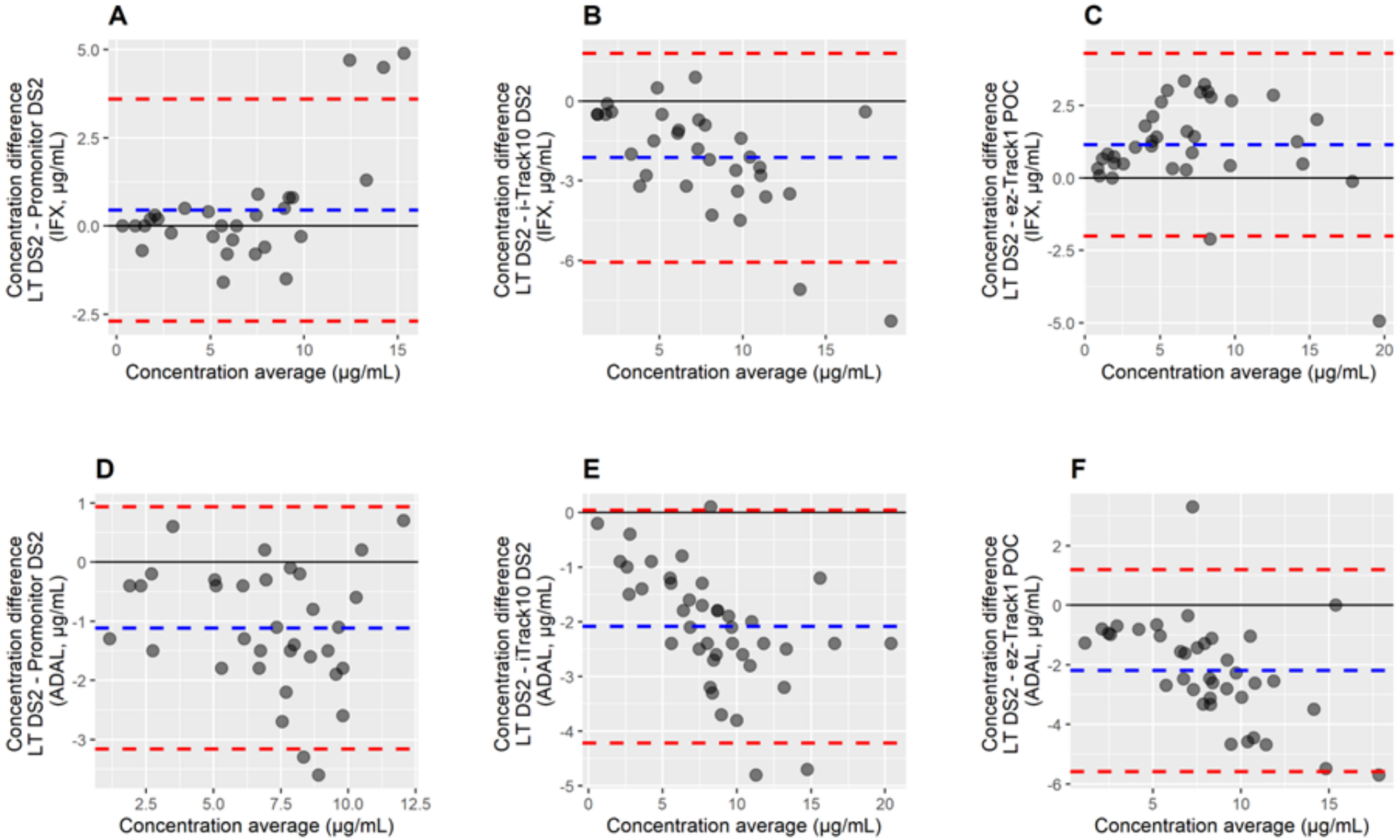






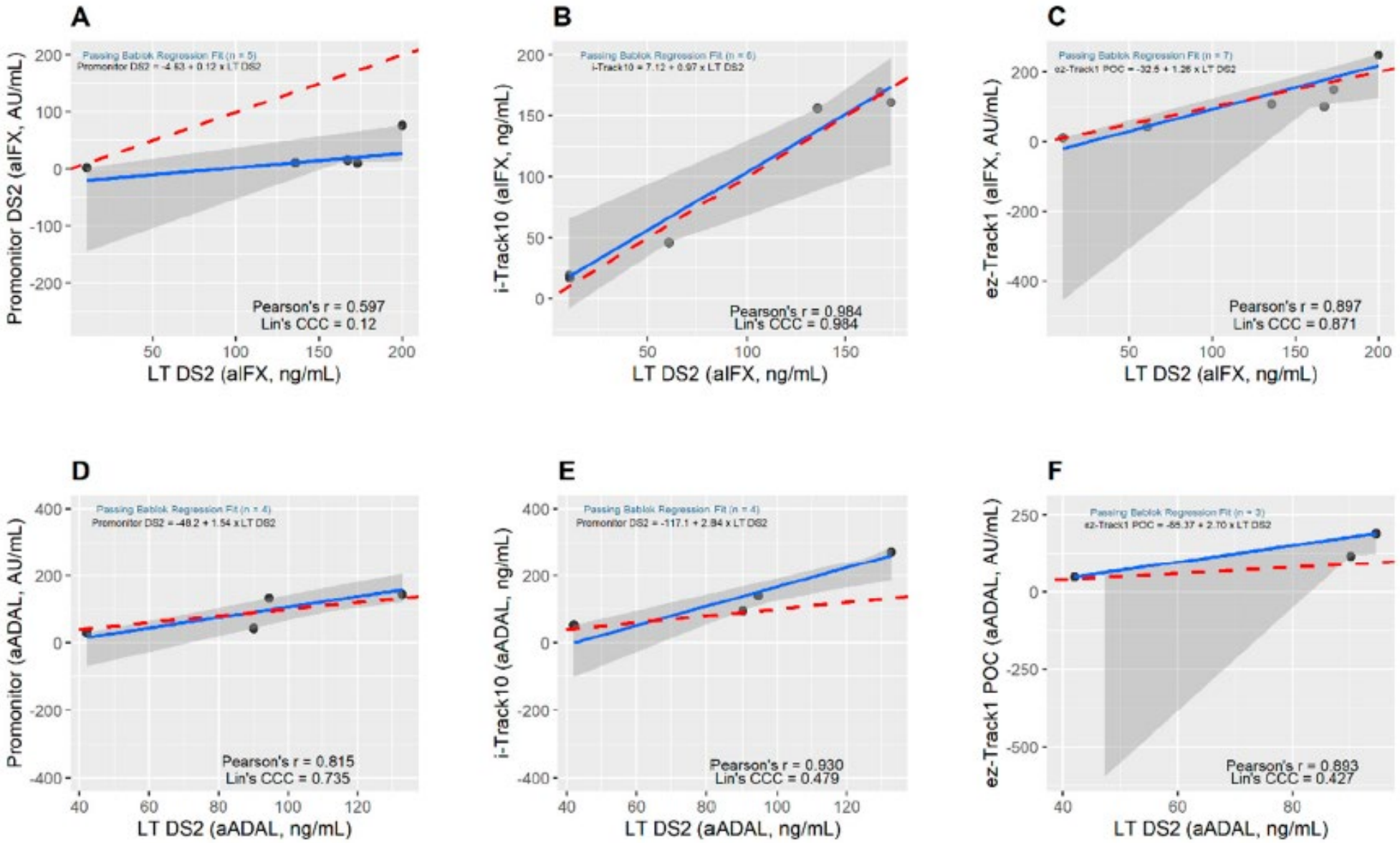
Bland–Altman analysis: IFX - ADAL

The difference between the two measurements is plotted on the y-axis, and the average of the two measurements on the x-axis. Dashed blue lines represent the bias and dashed red lines the 95% limit of agreement (LOA)



Passing-Bablok regression: aIFX - aADAL

The difference between the two measurements is plotted on the y-axis, and the average of the two measurements on the x-axis. Dashed blue lines represent the bias and dashed red lines the 95% limit of agreement (LOA)



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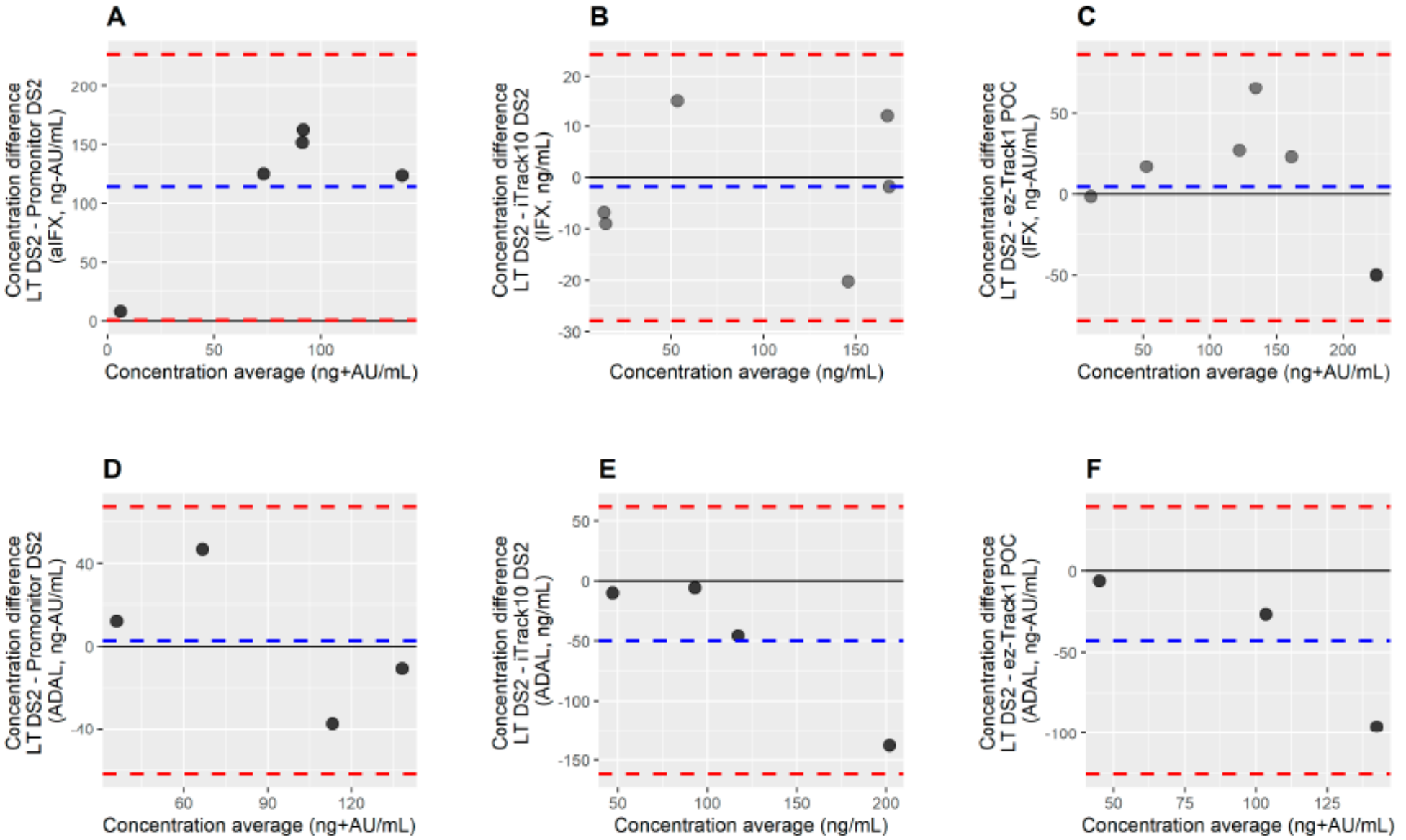


Discordances Lisa tracker / iTrack

IFX LT (ug/ml)	Anti-IFX LT (ng/ml)	date dosage i-Track10	IFX (ug/ml)	Anti-IFX (AU/ml)
2,2	<10	23/09/2022	5,4	19
3,9	<10	28/09/2022	5,4	23
4,9	<10	28/09/2022	8,8	11
1,9	<10	28/09/2022	2,3	11
9,4	<10	28/09/2022	11,5	14
9,2	<10	28/09/2022	11,6	26
7,6	<10	28/09/2022	10,3	14
1	<10	28/09/2022	1,5	19
9,8	<10	28/09/2022	12,6	12
17,2	<10	28/09/2022	24	40

➔ Faux positifs iTrack pour les anti-IFX

➔ Revoir le cut-off ?

Conclusion / discussion

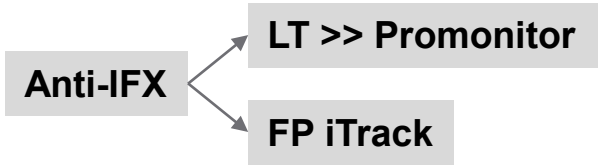
LT DS2 was used as the reference method

50 samples were analyzed

Low number of immunizations

Quantitative analysis indicated a good concordance between the three evaluated assays and our “gold standard”

Use the same assay method for the follow-up of a given patient.



Quelle technique pour quelle utilisation ?

ELISA — Robustesse technique / Manque de souplesse (séries)

→ TDM grosse volumétrie

i-Track — Souplesse random access / Faux positifs ADA ?

→ TDM volumétrie réduite

Ez-Track — Qualité des résultats, Souplesse / Sang total / sérum, 15’ pour l’ensemble des résultats

→ POC

MERCI DE VOTRE ATTENTION

REMERCIEMENTS

Florian Rissel [1], Yoann Cazaubon [2], Syrine Saffar [1], Romain Altwegg [3], Mélanie Artasone [1], Claire Lozano [1], Thierry Vincent [1] and Alexandre Jentzer [1,*]

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