

Rheumatoid factor levels influence serum drug levels and treatment discontinuation in patients with Rheumatoid Arthritis treated with TNF inhibitors

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Acknowledgments: This study was funded by UCB Pharma.

BACKGROUND

In a post hoc analysis from the EXXELERATE study, poorer clinical outcomes were observed in those patients treated with adalimumab (ADL) with baseline rheumatoid factor (RF) above 200 UI/ml. However, patients treated with certolizumab (CZP) had similar responses regardless of RF levels. Currently, real-life data that associates this RF cut-off point with clinical outcomes is lacking

AIM

This study aimed to investigate the impact of RF levels above 200 UI/ml on the TNFi levels and the association with secondary nonresponse in RA patients treated with different TNFi: monoclonal antibodies (MAB) versus pegylated (PEG)

METHODS

This is a retrospective study performed in real-world practice. Patients with RA treated with infliximab (IFX), ADL, or CZP were included. Demographic, clinical, and analytical variables were obtained at the baseline visit (T0). Patients were stratified based on baseline RF levels below or above 200 IU/ml. After 6 months (T6) serum drug levels and anti-drug antibodies (ADA) were measured and reasons for discontinuation were collected

RESULTS

We included **170 patients with RA**:
90 (53%) received IFX, 48 (28%) ADL and 32 (19%) CZP

Table 1. Patient´s characteristis

	Total n=170	MAB n=138	PEG n=32	p
Sociodemographic characteristics				
Female gender, n (%)	141 (83%)	115 (83%)	26 (81%)	0.778
Age (years), Mdn (IQR)	56.0 (45.8-66.1)	55.0 (44.8-65.0)	59.7 (47.7-70.1)	0.070
Smoking status	n=164	n= 136	n= 28	
• Non smoker	97 (59%)	85 (63%)	12 (43%)	0.099
Disease duration, (years)	8.5 (4.3-14.3)	8.5 (4.2-14.4)	8.9 (4.4-11.4)	0.921
Serological characteristics at baseline				
CRP mg/L, Mdn (IQR)	7.5 (3.0-21.4)	7.8 (3.0-22.8)	12.8 (2.4-17.6)	0.734
RF status (n, %))	128 (75%)	103 (75%)	25 (78%)	0.680
RF levels (n, %)				
LL: <200 UI/ml	117 (69%)	95 (69%)	22 (69%)	0.992
HL: ≥200 UI/ml	53 (31%)	43 (31%)	10 (31.3%)	
ACPA status, (n/N, %))	135/168 (80%)	108/136 (79%)	27/32 (84%)	0.525
Clinical characteristics at baseline				
DAS28, mean ±SD	5.06±1.35	5.08±1.36	4.97±1.33	0.480
Treatment characteristics at baseline				
Previous bDMARDs use, n (%)	26(15%)	20 (15%)	6 (19%)	0.547
Monotherapy, n (%)	16 (10%)	16 (12%)	0 (0%)	0.042
MTX use, n (%)	113 (67%)	96 (70%)	17 (53%)	0.067

Table 2: Serum drug levels (ng/ml) at T6 based on RF levels at T0

	Serum drug levels at 6 months of starting TNFi*		p
	Basal RF levels ≤200 UI/ml	Basal RF levels > 200 UI/ml	
Infliximab n=85	376 [0-2076]	0 [0-1057]	0,09
Adalimumab n=44	4570 [1104-7572]	751 [53-2401]	0,01
Certolizumab n=32	3300 [2000-4600]	3200 [1300-3900]	0,6

* In 7 patients serum sample was not available to measure drug levels.

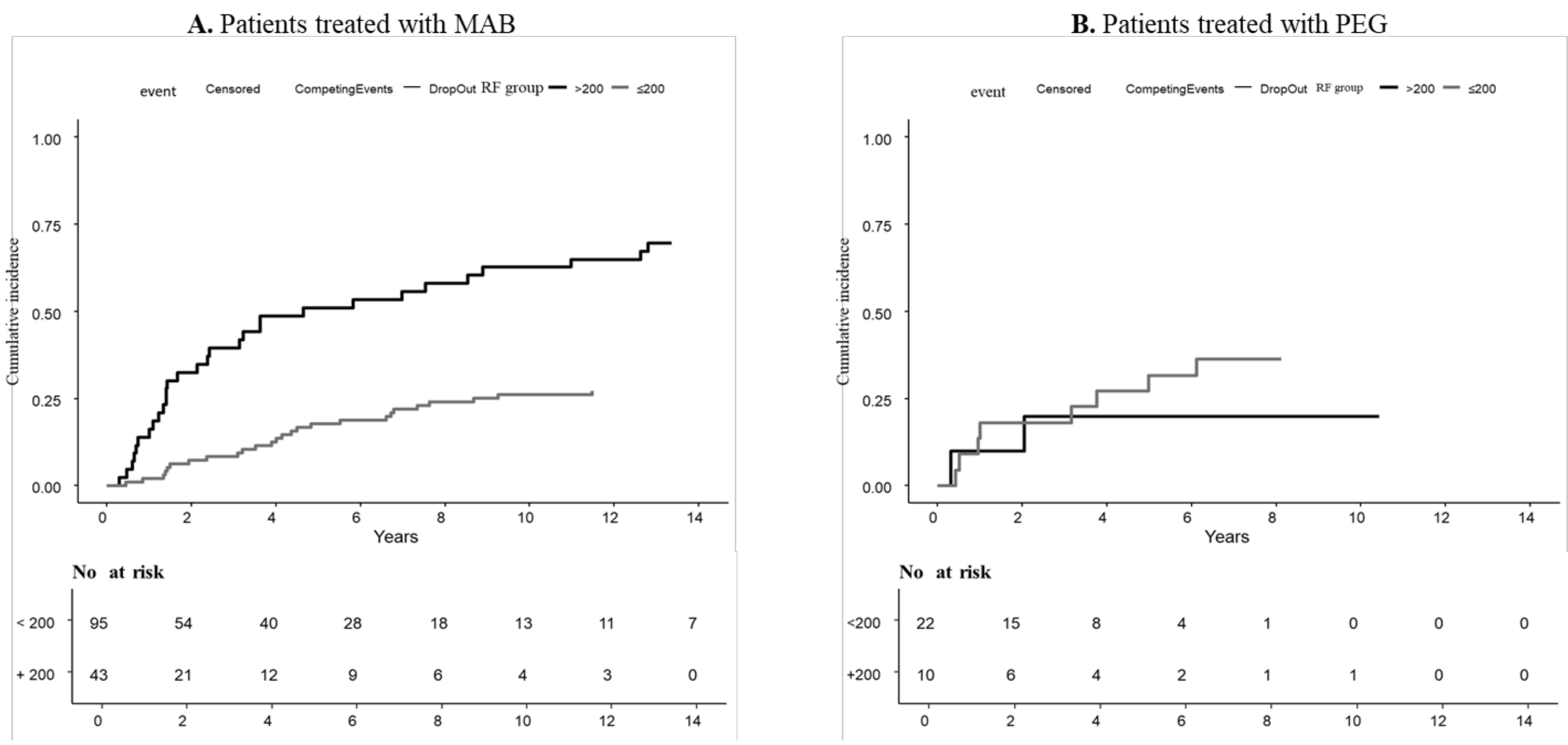
Table 4. Risk factors associated with discontinuation due to secondary ineffectiveness among patients treated with monoclonal antibodies (MAB) and pegylated antibody (PEG)

	HR	95% IC
Monoclonal Antibodies (IFX and ADL) n=138		
Basal RF >200 UI/ml	3.63	2.15-6.14
Non MTX use	0.73	0.42-1.30
Basal DAS28	1.02	0.86-1.20
Age	1.01	0.99-1.02
Female sex	1.41	0.69-2.87
Pegylated Antibody (CZP) n=32		
Basal RF >200 UI/ml	0.46	0.06-3.32
Non MTX use	3.41	0.56-20.78
Basal DAS28	1.35	0.59-3.06
Age	0.94	0.89-1.01
Female sex	3.42	0.72-16.22

Table 3: Reasons to drop out the TNFi treatment according to basal RF levels

	Reasons to drop out				p
	Primary non response	Secondary non response	Adverse Events	Others	
	Monoclonal Antibody (IFX and ADL)				
Basal RF ≤200 UI/ml n=70	19 (27%)	26(37%)	6 (9%)	19 (27%)	0.001
Basal RF >200 UI/ml n=38	3 (8%)	30 (79%)	1 (3%)	4 (10%)	
	Pegylated Antibody (CZP)				
Basal RF ≤200 UI/ml n=15	1 (7%)	8 (83%)	1 (0%)	5 (10%)	0.758
Basal RF >200 UI/ml n=5	1 (20%)	2 (40%)	0 (0%)	2 (40%)	

Figure 1. Cumulative incidence of dropout due to secondary non-response according to baseline RF levels. A. In the MAB group. B. In the PEG group



CONCLUSIONS

Our study supports in clinical settings the relevance of RF levels above 200 IU/ml to predict clinical response and survival of TNFi therapies in patients with RA treated with TNFi. These findings advocate for a more nuanced approach to RA treatment, emphasizing the need for personalized therapeutic strategies based on individual biomarker profiles.

