

SURVIVAL OF TNFi AND ANTI-IL6R b/tsDMARDs IN RHEUMATOID ARTHRITIS AND EVALUATION OF RISK FACTORS ASSOCIATED WITH DISCONTINUATION OF TREATMENT P340

N. López-Juanes, M. Novella-Navarro, C. Plasencia, M. Kafati, I. Monjo, D. Peiteado, A. Villalba, L. Nuño, M. Sanz-Jardón, A. Balsa
Servicio de Reumatología del Hospital Universitario La Paz



Background

As the most used biologic or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARD) in rheumatoid arthritis (RA), the efficacy of **TNF inhibitors (TNFi)** and **anti-IL6R** is widely demonstrated. However, a considerable number of patients do not reach the desirable outcomes and the risk factors for treatment discontinuation are still under study.

Objectives

- To evaluate **TNFi and anti-IL6R survival** in RA.
- To analyze the **reasons for discontinuation** and the risk factors associated with it.

Methods

- Observational retrospective study** with patients with RA initiating TNFi or anti-IL6R between January 2017 and June 2022 with a minimum follow-up of 1 year.
- Sociodemographic and clinical data, comorbidities, disease duration, previous treatments, and disease activity at the start of the first b/tsDMARD and after 6 months of therapy were collected.
- Differences between variables were analyzed with the **χ2 test and the T-test**.
- Drug retention was evaluated as the duration until TNFi or anti-IL6R was discontinued due to inefficacy or adverse event (AE) using **Kaplan-Meier plots** and the **log-rank test**.
- Possible risk factors for discontinuation were assessed by **Cox proportional hazard model** (univariate and multivariate).

Results

- Of the **175 cases** included, **129 received TNFi** and **46 anti-IL6R**. 146 were women, with a mean age at diagnosis of 42.9±14.1 years.
- In the **TNFi cohort**, 38 patients discontinued the drug, 26 due to inefficacy and 12 due to AE.
- The **anti-IL6R** cohort included 16 patients who discontinued therapy, 9 due to inefficacy and 7 due to AE.
- The differences in clinical characteristics, comorbidities, treatments, and disease activity between patients with active TNFi or anti-IL6R and those who discontinued them are summarized in table 1.
- Baseline DAS28** was significantly higher in patients with discontinuation due to inefficacy compared to those with active TNFi or anti-IL6R.
- Patients with **at least 1 previous b/tsDMARD** discontinued therapy more frequently, reaching significant differences in the inefficacy group (p<0.01) and the AE group (<0.01) of the TNFi cohort.
- Analyzing survival, the duration of treatment was **51.5±2.3 months for TNFi** and **48.7±4.2 for anti-IL6R**, with no significance. There were no differences between reasons for discontinuation among both groups.
- In the TNFi inefficacy group, **erosions (p=0.02), ≥2 previous b/tsDMARDs (p<0.01), at least 1 previous b/tsDMARDs (p<0.01) and absence of low disease activity at 6 months (p<0.01)** were associated with worse survival.
- With a multivariate cox regression model, **≥2b/tsDMARD [HR=3.38 CI95%(1.60-7.16)]** and **absence of low disease activity at 6 months [HR=0.39 CI95% (0.19-0.81)]** were independent risk factors for TNFi discontinuation due to inefficacy.
- In the TNFi AE group, **≥2b/tsDMARD** was associated with worse survival (p=0.03).
- In the anti-IL6 cohort, the only significant difference found was the **absence of low disease activity at 6 months (p=0.01)** in the inefficacy group.
- Concomitant treatment with methotrexate did not show significant differences in any of the groups.

Table 1 (n (%)): Comparison of clinical characteristics, comorbidities, treatments and disease activity between patients with active and discontinued TNFi and anti-ILR6

	GENERAL	TNFi: 129 (73.7)						ANTI-IL6: 46 (26.3)					
		ACTIVE	DISCONTINUED: 42 (32.8)				ACTIVE	DISCONTINUED: 19 (45.2)					
			Inefficacy	p	Adverse effects	p		Inefficacy	p	Adverse effects	p		
Total	175 (100)	86 (67.2)	26 (68.4)	0.56	12 (31.6)	0.13	23 (54.8)	9 (56.3)	0.98	7 (43.8)	0.59		
Age at diagnosis (years)	42.9±14.1	44.5±13.3	38.9±15.2	0.09	39.8±10.1	0.39	40.5±14.4	44.8±14.6	0.62	37.9±5.6	0.14		
Rheumatoid factor	142 (81.1)	71 (82.6)	20 (23.1)	0.53	10 (83.3)	0.85	16 (69.6)	9 (100)	0.10	7 (100)	0.15		
Anti-citrullinated protein antibodies	137 (78.3)	74 (86.0)	18 (69.2)	0.06	9 (75.0)	0.51	14 (60.9)	9 (100)	0.03*	5 (71.4)	0.97		
Erosions	64 (36.6)	28 (33.7)	10 (38.5)	0.84	6 (50.0)	0.32	5 (21.7)	7 (77.8)	<0.01*	4 (57.1)	0.28		
Arterial hypertension	37 (21.1)	17 (20.0)	1 (4.0)	0.04*	3 (25.0)	0.47	9 (39.1)	3 (33.3)	0.82	1 (14.3)	0.18		
Diabetes mellitus	10 (5.7)	2 (2.4)	2 (8.0)	0.40	2 (16.7)	0.04*	3 (13.0)	0 (0.0)	0.26	1 (14.3)	0.66		
Fibromyalgia	15 (8.7)	1 (1.2)	5 (20.0)	0.01*	3 (25.0)	0.01*	4 (17.4)	0 (0.0)	0.16	2 (28.6)	0.25		
csDMARDs	166 (94.9)	85 (98.8)	25 (96.2)	0.57	11 (91.7)	0.15	21 (91.3)	7 (77.8)	0.30	5 (71.4)	0.15		
Methotrexate	124 (74.3)	63 (74.1)	20 (80)	0.60	9 (81.8)	0.64	17 (77.3)	5 (71.4)	0.96	2 (40.0)	0.08		
Average number of previous bDMARDs (years)	0.9±1.5	0.4±1.2	0.92±1.2	0.19	1.5±2.2	0.16	1.4±0.9	2.2±1.9	0.41	2.9±2.3	0.05		
Naïve	93 (51.3)	69 (80.2)	12 (46.2)	<0.01*	4 (33.3)	<0.01*	2 (8.7)	1 (11.1)	0.88	1 (14.3)	0.66		
>2 previous b/tsDMARD	19 (10.9)	4 (4.7)	3 (11.5)	0.54	2 (16.7)	0.37	2 (8.7)	3 (33.3)	0.35	3 (42.9)	0.14		
Time from diagnosis to first bDMARD (years)	9.3±8.6	8.7±7.5	10.3±10.8	0.39	6.7±5.4	0.34	11.0±11.8	8.4±6.1	0.17	17.0±9.8	0.12		
Time from diagnosis to initiation of bDMARD under study (years)	12.7±9.9	9.9±8.2	14.0±10.5	0.03*	9.7±6.5	0.66	18.2±10.4	17.5±12.4	0.63	26.2±12.2	0.12		
Baseline DAS28	4.6±1.2	4.5±1.2	5.0±0.9	0.03*	4.4±1.5	0.63	4.1±1.0	5.5±1.3	0.03*	5.4±1.3	0.16		
DAS28 at 6 months	3.0±1.4	2.6±1.2	3.4±1.2	0.03*	3.4±1.8	0.10	2.7±1.2	4.3±1.8	0.09	3.5±2.0	1.0		

Conclusions

- There are no differences in survival between TNFi and IL-6R nor in discontinuation due to inefficacy or AE.
- Previous treatment with ≥2b/tsDMARD and absence of low disease activity at 6 months were independent risk factors associated with discontinuation due to inefficacy in the TNFi group.