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Impact of bDMARDs with different modes of action on fatigue in RA patients

Martin Schaefer*[1], Peter Herzer[2], Cornelia Kühne[3], Herbert Kellner[4], Angela Zink[1], Anja Strangfeld[1]

[1]German Rheumatism Research Centre, Epidemiology Unit, Berlin, Germany, *[2]Scientific Advisory Board, Munich, Germany*, *[3]Rheumatologist, Haldensleben, Germany*, *[4]Rheumatologist, Munich, Germany*

Background:

Fatigue is an important patient-reported outcome. It has been reported to be potentially targetable by DMARDs with specific modes of action, particularly IL-6 inhibition [1].

Objectives:

To assess to which extent patients on DMARDs with different modes of action reach fatigue levels of 2 or less on a 0 (no fatigue) to 10 (high fatigue) scale after 6 months of treatment.

Methods:

The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises bionaive patients who were enrolled with start of a b/tsDMARD between 01/2009 and 04/2019, who had at least 1 follow-up, did not switch during the first 3 months and afterwards only within the same substance, and presented fatigue levels of > 2 at baseline.

Poisson regression models with a robust error variance were used to calculate risk ratios (RRs) for reaching fatigue values ≤ 2, for all DMARD modes of action. Propensity score weighting was used to adjust for confounding by indication. Multiple imputation of missing values was performed.

Results:

Baseline fatigue levels were 5.1 overall and 6.1 among patients with a fatigue level of > 2 points on average. They were comparable among different DMARD modes of action. csDMARD patients had lower values than others regarding disease duration, disease activity, or joint erosions (Table 1).

The RR of IL-6 inhibitors for achieving a fatigue level of ≤ 2 was 1.34 (95% CI: 1.09 – 1.64) compared to csDMARDs. Among other factors, current smoking, prevalent fibromyalgia and depression had a negative impact on achieving a low fatigue level (Table 2).

Table 1: Patient characteristics for different DMARD modes of action

Parameter	csDMARDs	TNFi	RTX	ABA	IL-6	JAKi
N	2376	2772	115	166	357	110
Fatigue at baseline	5.9 (2)	6.1 (2)	5.9 (2)	5.9 (1.9)	6.1 (2)	6.3 (1.9)
Age [years]	58.5 (12.7)	56.3 (12.4)	62.7 (10.9)	59.7 (12.6)	57.9 (12.5)	61.5 (11.5)
Female sex	1809 (76.1)	2060 (74.3)	82 (71.2)	118 (71)	272 (76.3)	79 (70.1)
Disease duration [years]	6.2 (7.2)	8.7 (8.1)	10.8 (9.7)	9.8 (9.2)	7.9 (7.6)	8.5 (10)
Joint erosions	634 (28.4)	1358 (50.5)	62 (56.8)	91 (55.4)	158 (46.4)	45 (41.3)
Prior csDMARD therapies	1.3 (0.6)	2.3 (1)	2.5 (1.1)	2.2 (1)	2.2 (0.9)	1.8 (0.8)
DAS28-ESR	4.6 (1.2)	5 (1.2)	5.3 (1.3)	5.3 (1.2)	5.2 (1.3)	4.9 (1.3)
% of full physical capacity	67.4 (21.6)	64.6 (22)	57 (23.5)	59.5 (21.3)	63.8 (20.9)	61.6 (23)
Glucocorticoid therapy (last 6 months)	1161 (48.9)	1747 (63)	76 (66.4)	93 (56)	198 (55.5)	42 (38.1)
Fibromyalgia	73 (3.1)	111 (4)	6 (5.2)	7 (4.2)	11 (3.1)	1 (0.9)
Depression	180 (7.6)	218 (7.9)	10 (8.7)	14 (8.4)	26 (7.3)	16 (14.6)
Ever smoker	1252 (52.7)	1497 (54)	68 (59)	84 (50.7)	200 (56)	59 (53.5)

Results are presented as mean ± SD or number (percentage). Absolute numbers may be rounded due to multiple imputation.

Table 2: Risk ratios for achieving fatigue levels ≤2

Parameter (at baseline)	RR	95% confidence interval
Fatigue (1 point higher)	**0.83**	**(0.80; 0.86)**
TNF inhibitor (vs. csDMARDs)	1.11	(0.99; 1.24)
Rituximab (vs. csDMARDs)	1.10	(0.71; 1.68)
Abatacept (vs. csDMARDs)	1.13	(0.82; 1.54)
IL-6 inhibitor (vs. csDMARDs)	**1.34**	**(1.09; 1.64)**
JAK inhibitor (vs. csDMARDs)	1.19	(0.81; 1.75)
Age (5 years more)	**0.97**	**(0.95; 0.99)**
Female sex	**0.83**	**(0.74; 0.92)**
Patient global health (1 point higher)	**0.97**	**(0.94; 0.997)**
Joint erosions	**1.19**	**(1.07; 1.32)**
Current smoking	**0.86**	**(0.76; 0.98)**
Former smoking	0.92	(0.82; 1.04)
Fibromyalgia	**0.56**	**(0.35; 0.90)**
Depression	**0.75**	**(0.59; 0.95)**

Conclusion:

Treatment with IL-6 inhibitors significantly increases the chance of reaching low fatigue levels within half a year in RA patients, while current smoking reduces it.

References:

[1] Choy E.H.S. and Calabrese L. H Rheumatology 2018;57:1885-95.

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