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TNF inhibitors are associated with a reduced risk of venous thromboembolism compared to csDMARDs in RA patients

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Background:

While the short-term use of bDMARDs up to 180 days has been associated with an increased risk of venous thromboembolism (VTE) compared to csDMARDs in patients with rheumatoid arthritis (RA), the long term use of more than 730 days has been associated with a decreased risk based on claims data [1]. Among patients with inflammatory bowel disease, observational data indicated that TNF inhibitors may have a protective effect regarding the VTE risk [2].

Objectives:

To assess the effects of TNF inhibitors and newer bDMARDs (including abatacept, rituximab, sarilumab, and tocilizumab) on the VTE risk based on observational data from RA patients.

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 patients who were enrolled with start of a bDMARD between 01/2009 and 04/2019 and had at least one follow-up.

Cox regression models were used to calculate hazard ratios (HRs) for VTEs, for csDMARDs, TNF inhibitors and other bDMARDs. Propensity score weighting was used to adjust for confounding by indication.

Results:

Patients receiving TNF inhibitors or other bDMARDs on average had higher CRP levels and a higher prevalence of cardiovascular diseases at baseline than patients receiving csDMARDs. They also received more often glucocorticoids (Table 1).

The HR of patients receiving TNF inhibitors for a serious VTE event was 0.53 (95% CI: 0.33 – 0.86) compared to csDMARDs, while the HR for patients receiving other bDMARDs was 0.66 (95% CI: 0.40 – 1.09). A CRP level of more than 5 mg/L (HR 2.09, 95% CI: 1.39 – 3.14) and an age above 65 years (HR 2.96, 95% CI: 1.94 – 4.52) increased the risk for a serious VTE event. Better physical function was associated with a decreased risk for VTEs (Table 2).

Table 1: Patient characteristics at baseline for DMARD groups

Parameter	csDMARDs	TNFi	Other bDMARDs
N	3500	5060	2534
VTE event	38 (1.1)	55 (1.1)	23 (0.9)
Age [years]	58.8 (12.6)	56.5 (12.9)	58.1 (12.4)
Female sex	2575 (73.6)	3734 (73.8)	1933 (76.3)
Disease duration [years]	6.2 (7.2)	9.4 (8.6)	11.9 (9.2)
Seropositivity	2189 (62.6)	3739 (73.9)	2048 (80.8)
Joint erosions	1024 (31.0)	2566 (52.4)	1523 (63.3)
Prior bDMARD therapies	0 (0.2)	0.3 (0.6)	1.2 (1.2)
CRP	8.8 (8.1)	11.6 (10.6)	12.4 (11.8)
DAS28-ESR	4.4 (1.3)	4.9 (1.2)	5.1 (1.3)
% of full physical capacity	71.3 (21.8)	66.2 (22.6)	62.1 (23.5)
Current glucocorticoid therapy	2564 (73.3)	3951 (78.1)	2036 (80.4)
Heart failure	36 (1)	113 (2.2)	93 (3.7)
Coronary artery disease	196 (5.6)	326 (6.4)	183 (7.2)
Cerebrovascular disease	60 (1.7)	86 (1.7)	44 (1.7)
Osteoporosis	400 (11.4)	771 (15.2)	530 (20.9)
Ever smoker	1875 (53.6)	2738 (54.1)	1402 (55.3)

Results are presented as mean ± SD or number (percentage).

Table 2: Hazard ratios for VTE events

Parameter (at time of event/end of observation unless specified otherwise)	Hazard ratio	95% confidence interval	
TNF inhibitors (reference: csDMARDs)	**0.53**	**0.33**	**0.86**
Other bDMARDs (reference: csDMARDs)	0.66	0.40	1.09
Age ≥ 65 years (baseline)	**2.96**	**1.94**	**4.52**
CRP ≥ 5 ml	**2.09**	**1.39**	**3.14**
> 5 mg and ≤ 10 mg glucocorticoids/day	1.04	0.55	1.98
> 10 mg and ≤ 15 mg glucocorticoids/day	2.35	0.81	6.79
> 15 mg glucocorticoids/day	2.03	0.76	5.41
% of full physical capacity (per 10 percentage points increase, time of event)	**0.85**	**0.78**	**0.92**
Current smoking (baseline)	0.98	0.61	1.55
Former smoking (baseline)	0.80	0.45	1.43

Conclusion:

Treatment with TNF inhibitors (compared to csDMARDs) and better physical function significantly reduced the risk of serious VTE events, while age above 65 years and high CRP levels increased this risk.

References:

[1] Kim S. C. et al. Am. J. Med. 2015; 128(5): 539.e7–539.e17.

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