Tocilizumab is effective as 1st, 2nd and 3rd-line biologic DMARD in patients with RA

Richter A[1], Strangfeld A[1], Kekow J[2], Bussmann A[3], Krause A[4], Stille C[5], Listing J[1], Zink A[1,6]

[1]German Rheumatism Research Centre, Berlin, [2]Scientific Advisory Board, Magdeburg, [3]Rheumatologist Geilenkirchen, [4]Rheumatologist Berlin, [5]Rheumatologist Hannover, [6]Charité University Medicine Berlin, all Germany

DRFZ BERLIN
Deutsches Rheuma-Forschungszentrum
Ein Institut der Leibniz-Gemeinschaft

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Background & Objectives

In Germany, treatment with Tocilizumab (TCZ) is primarily used in rheumatoid arthritis (RA) patients with previous failures of biologic disease-modifying antirheumatic drugs (bDMARDs). Effectiveness and adherence of TCZ in patients with multiple bDMARD failures has rarely been investigated.

Patients & Methods

We included 765 RA patients enrolled between 2009 and 2015 in the German biologics register RABBIT (**R**heumatoid **a**rthritis: O**b**servation of **bi**ologic **t**herapy) starting with TCZ. Patients were stratified according to the number of bDMARD failures prior to the initiation of TCZ (Table 1). Therapy discontinuation within 12 month after the start of TCZ was investigated using Kaplan-Meier and Cox-proportional hazard regression. Discontinuation was defined as the stop of TCZ therapy. Effectiveness regarding control of disease activity (DAS28-ESR) after 3, 6 and 12 month were examined with linear mixed effects models.

Table 1: Patient characteristics at treatment start.

	Tocilizumab therapy as		
	1st-line	2nd-line	3rd-line
No. of patients	265	255	245
Age in yrs	58.0 (12.9)	56.1 (12.4)	55.2 (13.3)
No. female patients (%)	204 (77)	204 (80)	194 (79.2)
Disease duration in yrs	8.1 (7.3)	11.4 (8.4)	14.1 (9.7)
DAS28	5.2 (1.3)	5.3 (1.3)	5.3 (1.3)
CRP in mg/l	16.0 (20.4)	17.7 (26.1)	21.2 (31.0)
No. prev. csDMARDs	2.1 (0.9)	2.3 (1)	2.6 (1)
Prior non-TNFi failure, n (%)	0	18 (7.3)	61 (25.3)
Concomitant csDMARD, n (%)	114 (43.0)	124 (48.6)	117 (47.8)
Concomitant MTX, n (%)	92 (34.7)	90 (35.3)	93 (38.0)
Hypertension, n (%)	108 (40.8)	109 (42.7)	88 (35.9)
Osteoporosis, n (%)	43 (16.2)	55 (21.6)	50 (20.4)
Chronic renal disease, n (%)	21 (7.9)	11 (4.3)	12 (4.9)

Numbers are mean values (sd) unless otherwise specified. Abbreviations: csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; MTX, methotrexate; TNFi, tumor necrosis factor alpha inhibitors

Results

Patient characteristics

Compared to biologic naive patients, those with prior bDMARD failures at start of TCZ were younger (1 failure: -1.6y (p=0.09); ≥2 failures: -2.8y (p=0.01)), had significantly longer disease duration (8.1 vs. 11.4 vs. 14.1 years; p<0.01) and more csDMARDs failures (p<0.01). Loss of physical function, pain and fatigue were significantly higher in patients with bDMARD failures (p<0.01).

No differences were found regarding the initial composite score DAS28 (5.2 vs 5.3 vs 5.3), its components (TJC and SJC) and the concomitant use of csDMARDs (p=0.3).

Survival

Crude survival on TCZ therapy was significantly lower if patients had bDMARD failures, unadjusted hazard ratios (HR) compared to bDMARD-naive patients were 1.17 (p=0.34) and HR=1.50 (p<0.01) (Figure 1). Adverse events were the most frequent reason for discontinuation, particularly in patients with prior bDMARD failures.

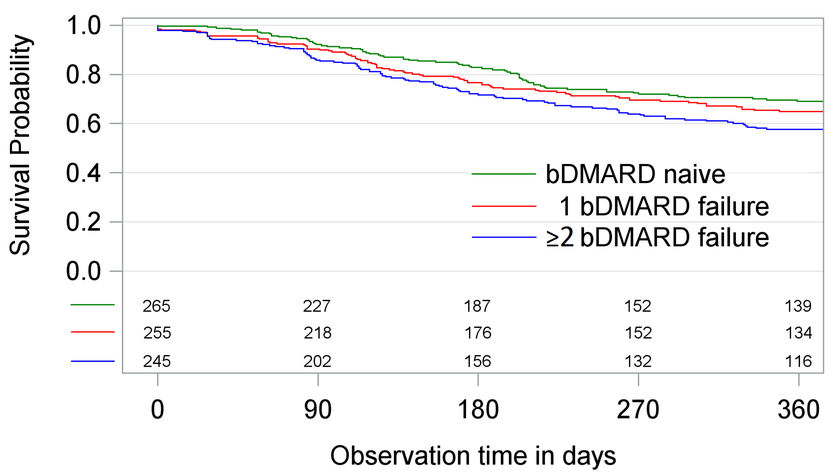

Figure 1: Survival on TCZ therapy stratified by the number of bDMARD failures.

Development of DAS28 during follow-up

During follow-up, disease activity (DAS28) did significantly decrease over time in all TCZ-treatment strata. At month 3, 6 and 12 differences between treatment strata were statistically not significant (Table 2).

Table 2: Means of DAS28 [95% confidence interval] at month 3, 6 and 12 after enrollment with TCZ. Estimates were adjusted for age, disease duration, physical function, comorbidities and concomitant use of biologic disease-modifying antirheumatic drugs (csDMARDs) (yes vs. no).

	DAS28		
	at month 3	at month 6	at month 12
bDMARD naive	3.02 [2.82; 3.22]	2.84 [2.63; 3.04]	2.88 [2.66; 3.10]
1 bDMARD failure	3.19 [3.01; 3.38]	3.04 [2.84; 3.24]	3.07 [2.87; 3.28]
≥2 bDMARD failure	3.37 [3.17; 3.56]	3.21 [3.00; 3.42]	3.06 [2.82; 3.29]

Conclusion

Treatment with TCZ is effective in patients with and without prior bDMARD failures. The majority of patients achieves low disease activity (DAS28<3.2) within 6 months and maintains controlled disease activity throughout month 12.

Despite previous bDMARD failures overall survival rates are comparably high.

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strangfeld@drfz.de