Tocilizumab is similarly effective in RA patients with no or up to two prior bDMARD failures: Results from the German prospective cohort study RABBIT.

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

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

German Rheumatism Research Centre, Epidemiology Unit

EULAR 2016 FRI0226

Background & Objectives

In Germany, tocilizumab (TCZ) is used for the treatment of rheumatoid arthritis (RA) both in biologic-naive patients and those with previous failures of biologic (b)DMARDs.

We aimed to investigate effectiveness and retention rates of TCZ as well as changes in the glucocorticoid dose in patients with multiple bDMARD failures.

Patients & Methods

We included 885 RA patients enrolled with the start of TCZ treatment between 2009 and 2015 in the prospectively observed cohort of the German biologics register RABBIT. Patients were stratified according to the number of bDMARD failures prior to the initiation of TCZ.

We used

- Kaplan-Meier survival methods to examine the retention rates within 12 months after the initiation
- linear mixed models to examine effectiveness (reduction of DAS28-ESR) over 3, 6 and 12 months
- multiple imputations for missing values of DAS28 and LOCF for missing doses of glucocorticoids

Results

Patient Characteristics

Compared to biologic naive patients those with prior bDMARD failures at start of TCZ were younger but had significantly longer disease duration ($p<0.01$). At baseline, patients with ≥3 bDMARD failures had a higher DAS28, impaired physical function and were significantly more often multi-morbid. No differences were found regarding concomitant use of glucocorticoids and csDMARDs.

All patients with ≥3 bDMARD failures had been exposed to TNF-inhibitors (TNFi), 60% had also been exposed to other bDMARD classes. In contrast, only 5.9% (12.9%) of patients with 1 (2) bDMARD failures had been exposed to non-TNFi.

Table 1: Patient characteristics at baseline.

	Tocilizumab therapy as			
	1st-line	2nd-line	3rd-line	4th-line
No. of patients	318	286	186	95
No. female patients (%)	239 (75.2)	227 (79.4)	149 (80.1)	77 (81.1)
Age in yrs	58.0 (12.5)	56.4 (12.4)	**55.7 (12.7)**	**54.6 (14.8)**
Disease duration in yrs	8.0 (7.4)	**11.6 (8.5)**	**13.3 (9.2)**	**15.3 (9.9)**
previous TNFi, n (%)		262 (91.6)	185 (99.5)	95 (100)
prev. other bDMARDs, n (%)		17 (6.3)	24 (15.1)	57 (64.2)
DAS28	5.1 (1.3)	5.2 (1.3)	5.2 (1.3)	**5.5 (1.3)**
Glucocorticoids, mg/d	5.1 (5.7)	4.8 (4.8)	5.9 (8.2)	5.4 (5.1)
Physical function (FFbH)	65.8 (23)	**60.5 (24.5)**	62.1 (23.6)	**56.1 (23.9)**
Fatigue	5.0 (2.9)	**5.5 (2.8)**	**5.6 (2.5)**	**6.3 (2.4)**
1 comorbidity, n (%)	83 (26.1)	65 (22.7)	59 (31.7)	14 (14.7)
2 comorbidities, n (%)	57 (17.9)	50 (17.5)	35 (18.8)	16 (16.8)
≥3 comorbidities, n (%)	96 (30.2)	**111 (38.8)**	51 (27.4)	**45 (47.4)**

Numbers are means (SD), unless otherwise specified.

Drug Survival

Patients with ≥3 bDMARD failures had significantly lower continuation rates than patients with less bDMARD failures. Adverse events were the most frequent reason for discontinuation in all strata.

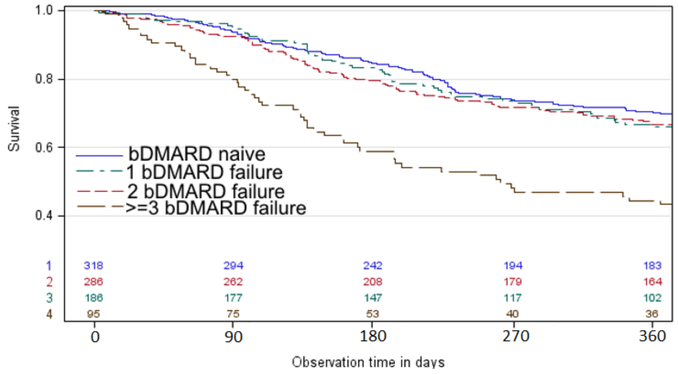

Figure 1: Survival on TCZ therapy stratified by the number of bDMARD failures.

Effectiveness

Low disease activity (DAS28 <3.2) was reached by all patients with ≤2 bDMARD failures while those with ≥3 bDMARD failures remained in moderate disease activity (3.2 ≤ DAS28 < 5.1).

Table 2: Least-Square mean of baseline DAS28 value and estimated means of DAS28 adjusted for age, disease duration, physical function, DAS28 and number of comorbidities.

	DAS28 at			
	Baseline	month 3	month 6	month 12
1st-line	5.2	3.0	2.8	2.8
2nd-line	5.2	3.2	3.0	3.0
3rd-line	5.2	3.2	3.1	3.0
4th-line	5.2	3.6	3.4	3.4

Glucocorticoids

Doses of glucocorticoids were decreased during follow-up. This resulted in an average reduction of more than 1.5 mg/d in patients with 0 or 2 bDMARD failure and of about 1 mg/d in the other strata.

Table 3: Mean dose of glucocorticoids at baseline and during follow-up (unadjusted).

	Baseline	month 3	month 6	month 12
1st-line	5.1	4.0	3.4	3.1
2nd-line	4.8	4.4	3.7	3.4
3rd-line	5.9	4.9	4.1	4.1
4th-line	5.4	4.6	4.7	4.2

Conclusions

TCZ was similarly effective in biologic naive patients and in patients with up to 2 prior bDMARD failures. The majority of those patients achieved low disease activity (DAS28<3.2). However, in patients with ≥3 bDMARD failures disease activity remained on a higher level and treatment continuity was significantly lower. It seems that despite all progress in the treatment of RA during the last decades a small patient group remains in which the disease is difficult to be controlled.

We thank all participating rheumatologists, especially those who have enrolled 40 and more patients for the register: Kaufmann J, Klopsch T, Krause A, Liebhaber A, Rockwitz K, Eisterhues C, Bergerhausen H, Tony H, Bussmann A, Gräßler A, von Hinüber U, Demary W, Kapelle A, Wassenberg S, Kekow J, Burmester G, Wilden E, Ochs W, Zinke S, Richter C, Dockhorn R, Krummel-Lorenz B, Remstedt S, Edelmann E, Bohl-Bühler M, Meier L, Balzer S, Berger S, Stille C, Aringer M, Kellner H, Schwarze I, Tremel H, Pick D, Bruckner A, Richter C, Röser M, Ständer E, Lebender S, Krüger K, Körber H, Kühne C, Fricke-Wagner H, Wiesmüller G, Weiß K, Thiele A, Karberg K, Müller L, Harmuth W, Herzer P, Schulze-Koops H, Grünke M, Zänker M, Burmester G, Backhaus M, Haas F, Braun J, Sörensen H, Späthling-Mestekemper S, Dexel T, Alliger K, Schneider M, Iking-Konert C, Moosig F, Krause D, Hamann F, Manger K, Schmitt-Haendle M, Schuch F, Wendler J, Kleinert S, Möbius C, Grebe T, Menne H, Walter J, Reck A, Karger T, Fliedner G, Gauler G, Seifert A, Gause A, Häntsch J, Prothmann U, Rech J, Biewer W, Leumann K, Eidner T, Feuchtenberger M, Gause A, Euler H, Möbius E, Zeh G, Fischer K, Riechers E

Funding: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Hospira, MSD Sharp & Dohme, Pfizer, Roche, and UCB.

baganz@drfz.de