

Effectiveness of treatment with rituximab depends on autoantibody status – results from 2 years of experience in the German biologics register RABBIT

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Background

Rituximab (RTX) has been available in Germany since July 2006. It is approved in combination with methotrexate after failure of (at least) one TNF- α blocker.

The German biologics register has observed patients with rheumatoid arthritis (RA) treated with any of the approved biologic agents since 2001.

Objective

To investigate the effectiveness of treatment with rituximab over the first six to twelve months in daily rheumatologic care.

Patients and Methods

RABBIT is a long-term observational prospective cohort study observing all biologic agents licensed for the treatment of RA in Germany. More than 300 German rheumatologists participate in the register.

Since the approval of RTX, patients with RA can be enrolled with a first or repeat treatment cycle of RTX. They will be followed-up for at least 5 years irrespectively of any new treatment starts, stops and changes. Regular assessments (at 3 months and thereafter every 6 months) include clinical status as well as therapy.

Results

A total of 797 patients have been enrolled so far with a new cycle of RTX. At inclusion 624 patients were naive to RTX. In 446 of them follow-up data for at least 6 months were available. The patients had long-standing, active disease with a poor functional status. 84.6% were rheumatoid factor positive. The patients were refractory to a high number of conventional DMARDs and a mean of 1.8 prior biologic agents, mostly TNF blockers.

	Total (n = 797)	RF + (n = 674)	RF - (n = 123)
Female	78.6%	78.0%	81.3%
Age	57.3 (12.0)	58.1 (11.8)	52.9 (12.3)
Disease duration, years, median (IQR)	12 (7-19)	12 (7-20)	9 (4-16)
RF positive	84.6%	100%	0%
Anti-CCP positive	65.7%	77.1%	14.1%
DAS28	5.5 (1.2)	5.6 (1.3)	5.3 (1.1)
CRP mg/l, median (IQR)	10 (3-26)	10 (4-26)	9 (3-33)
FFbH, % of full function	51.8 (22.7)	51.4 (23.1)	53.7 (20.8)
Morning stiffness, minutes	106 (92)	109 (90)	91 (100)
No. of previous biologic failures	1.8 (1.1)	1.9 (1.2)	1.7 (1.1)

Table 1: Baseline characteristics of patients receiving RTX, values represent means (standard deviations) if not otherwise indicated.

Response in autoantibody positive vs. autoantibody negative patients

Of the 624 patients with no prior exposure to RTX at baseline, 15.2% achieved a good and 46.4% a moderate EULAR response after 6 months of treatment.

Rheumatoid factor (RF) positive patients had a significantly better response than seronegative ones (Figure 1, $p=0.005$). While 65.3% of the seropositive patients were good or moderate responders, this was only the case with 45.3% of the seronegative ones. Taking the baseline status into account the difference corresponds to an adjusted odds ratio (OR) of 1.9 (95% CI: 1.2 - 3.3).

A similar, albeit smaller, difference was seen with regard to anti-CCP status: 67.4% of seropositive and 55.7% of seronegative patients achieved a good or moderate response (OR 1.4 (95% CI: 0.8 - 2.5)).

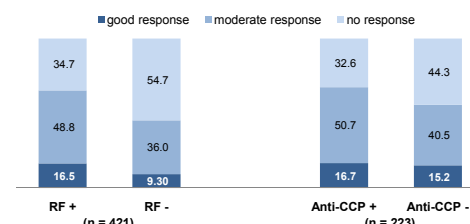


Fig. 1: EULAR response after 6 months by autoantibody status in RTX naive patients.

322 patients observed for at least 12 months received a second cycle of RTX after a mean duration of 9.1 months (SD 3.68).

The percentage of patients that received a second cycle was significantly different between RF+ and RF- patients. Whereas only 9% of the RF+ patients were considered to be not eligible for a second cycle of RTX, this was the case in 26% of the RF- patients.

The course of disease activity according to RF status in patients receiving a second cycle of RTX between month 6 to 9 is shown in Figure 2.

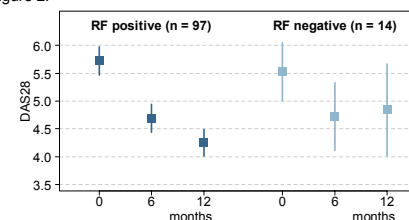


Fig. 2: Mean DAS28 (95% CI) after 6 and 12 months in patients receiving a second cycle of RTX.

There seems to be no real difference in response between RTX monotherapy and the combination with methotrexate (MTX). However, the patients might not be fully comparable.

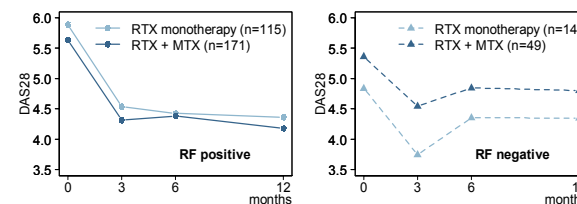


Fig. 3: Change in DAS28 for RTX in combination with MTX versus monotherapy.

Conclusion

The data show effectiveness of rituximab in a majority of unselected real-life RA patients. The higher improvement in rheumatoid factor positive patients supports the idea that B-cell depletion is more effective in autoantibody positive patients.

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