

## **Efficacy of rituximab retreatment in clinical practice: data from the CERERRA collaboration.**

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**Background:** Rituximab (RTX) is used in the treatment of rheumatoid arthritis (RA), more often after the failure of one or more TNF inhibitors. Cohort studies provide useful information and answer some of the questions regarding the use of RTX in clinical practice.

**Objectives:** To analyse the efficacy of retreatment with RTX within 12 months of the first course and to identify predictors of response.

**Methods:** Ten European registries submitted anonymized datasets with baseline, 3, 6, 9 and 12 month data for patients who had started RTX. These datasets were pooled and analysed. Heterogeneity between countries was analyzed by ANOVA. Predictors of response were analysed by logistic regression. Patients who received retreatment during the first 12 months after the first course were analyzed separately.

**Results:** Baseline data were available for 2048 patients with RA who had been treated with RTX. The mean (SD) age of patients was 53.8 (13.3) years and the mean (SD) disease duration was 12.1 (8.9) years. 80.4% of them were female, 85.6% were RF positive and 76.6% (448 out of 585 patients) were anti-CCP positive. The numbers of confirmed double seropositive and seronegative patients were 367 and 59 respectively. The mean (SD) numbers of previous DMARDs and biologics were 2.7 (1.6) and 1.1 (1.1) respectively. Significant

heterogeneity was noted between countries for all baseline characteristics. Significant reduction of DAS28 was observed at 6 months [ $\Delta$ DAS28 0-6m=1.95 (SD=1.5)]. At 6 months RF-positive patients achieved significantly better results compared to RF-negative ones, as did ACPA-positive patients compared to ACPA-negative ones and double-positive compared to double-negative ones (table).

Data were available for 350 patients who were retreated with RTX during the first 12 months. At 12 months the retreated patients had a significantly greater mean reduction in DAS28 compared to at 6 months ( $p < 0.005$ ). Double positive patients who had received retreatment achieved significantly higher reductions in DAS28 at 12 months compared to double seronegative retreated patients (table).

Prognostic factors of EULAR Good Response at 6 months were found to be positive ACPA ( $p = 0.02$ , coef=1.02), lower number of previous DMARDs ( $p = 0.0003$ , coef=-0.29) and biologics ( $p = 0.001$ , coef=-0.33), and at 12 months lower number of prior biologics ( $p = 0.02$ , coef=-1.8) and lower HAQ at baseline ( $p = 0.01$ , coef=-0.6).

**Conclusions:** In patients who were retreated with rituximab during the first 12 months DAS28 improvements at 12 months were significantly better than those at 6 months in the same patients. Seropositivity was associated with greater DAS28 improvements at 6 and 12 months. Lower number of prior biologics and lower HAQ at baseline predicted 12-month EULAR Good Response.

	DAS28 improvement at 6 months (n=810)			DAS28 improvement at 12 months (retreated patients only) (n=124)		
	Positive	Negative	p	Positive	Negative	p
RF	2.0 ± 1.5	1.7 ± 1.5	0.02	2.3 ± 1.4	1.8 ± 1.2	NS
ACPA	2.1 ± 1.4	1.5 ± 1.5	0.006	2.6 ± 1.3	2.1 ± 1.3	NS
DOUBLE	2.1 ± 1.4	1.4 ± 1.5	0.009	2.8 ± 1.2	1.3 ± 0.7	0.004

Table 1. Mean ± SD reductions in DAS28 at 6 and 12 months by serology.