

Background

Tocilizumab, a biologic agent approved for the treatment of rheumatoid arthritis (RA), is a human anti-interleukin (IL)-6 receptor antibody. Clinical studies reported high response and remission rates in patients treated with this agent. Blocking the IL-6 receptor directly inhibits the production of acute-phase reactant proteins (including CRP) in hepatocytes. CRP or ESR are important components of the disease activity score (DAS) used to measure the effectiveness of a treatment.

Objectives

To investigate the contribution of the single components of the DAS28 regarding treatment response in tocilizumab treated patients in daily rheumatologic care.

Patients and Methods

RABBIT is a nationwide long-term observational prospective cohort study observing all biologic agents licensed for the treatment of RA in Germany.

RA patients can be enrolled with a start of a biologic treatment or, as controls, with the start of a new DMARD treatment after failure of at least one other DMARD. Since the approval of tocilizumab (TOC) in January 2009 also patients starting this treatment could be enrolled in RABBIT. After inclusion all patients 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. Disease activity is measured with the DAS28 using the ESR.

Conclusion

Treatment with tocilizumab improves RA in a substantial proportion of patients, response and remission rates are high. However, when considering EULAR response rates, changes in DAS28 scores or DAS28 remission rates the high impact of ESR changes on these measures has to be taken into account.

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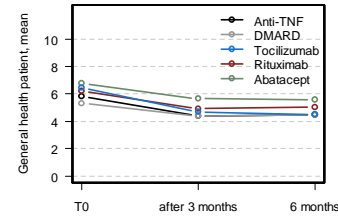
Baseline characteristics

	Anti-TNF	DMARD	Tocilizumab	Rituximab	Abatacept
Age	56 ± 13	59 ± 13	57 ± 12	58 ± 12	55 ± 13
Female	77%	77%	84%	79%	79%
Disease duration, years	8 (4-15)	3 (2-8)	10 (5-18)	12 (6-20)	12 (6-18)
No. of previous therapy failures	3 (2-4)	1 (1-2)	4 (3-5)	5 (4-6)	5 (4-7)
Rheumatoid factor positive	74%	56%	75%	84%	72%
DAS28	5.1 ± 1.3	4.6 ± 1.3	5.5 ± 1.4	5.5 ± 1.3	5.5 ± 1.2
BSG	28 (14-45)	22 (11-36)	26 (12-47)	28 (14-47)	28 (14-45)
CRP	8.0 (3-19)	4.6 (3-12)	7.2 (3-21)	9.6 (3-25)	8.4 (3-22)
No. of swollen joints	6.0 ± 4.7	4.3 ± 3.5	7.8 ± 6.0	7.9 ± 5.8	6.6 ± 5.9
No. of tender joints	8.7 ± 6.9	6.7 ± 5.8	10.9 ± 7.5	10.4 ± 7.4	10.0 ± 7.6

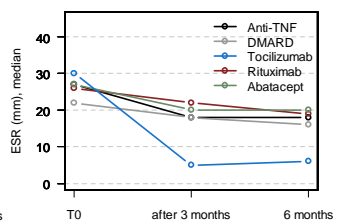
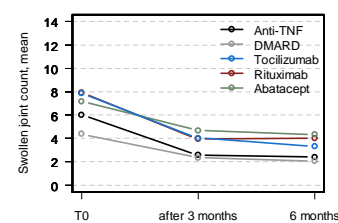
(Values represent mean ± standard deviation or median (IQR))

EULAR response

Of 152 patients treated with tocilizumab and three months of follow-up, 48% achieved a good and 30% a moderate EULAR response. 34% of the patients were in remission (DAS28 < 2.6). After 6 months (n = 114) the proportion of patients reaching a good EULAR response was 45%, a moderate response was reached by 32%, and 36% of the patients were in remission.



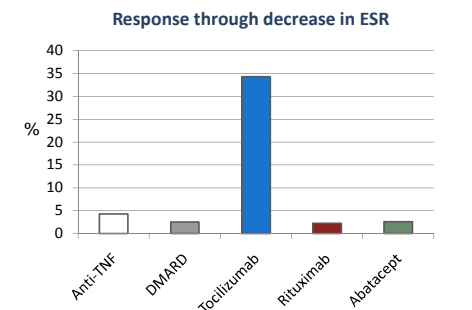
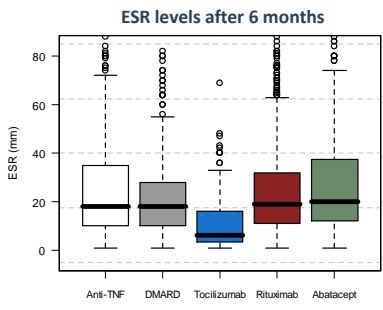
Separating the DAS28 into its components, significant changes in swollen and tender joint counts and patient global assessment were observed in patients treated with tocilizumab. Compared to patients receiving other biologics the decrease in ESR levels was significantly higher.



Decrease of ESR

The ESR levels reached after 6 months of therapy were very low in tocilizumab treated patients. From all DAS28 components the percentage change of the ESR after 6 months was highest with 80% under treatment with tocilizumab compared to 33% under anti-TNF treatment.

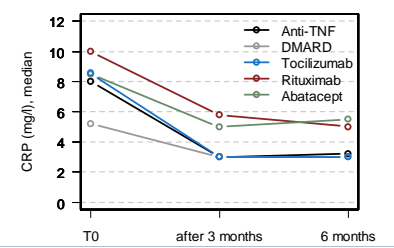
In a high number of patients treated with tocilizumab the decrease in ESR was sufficient to reach EULAR response.



Decrease of CRP

The change in CRP was more comparable to changes observed under other treatments (65% under tocilizumab, 60% under anti-TNF treatment).

We therefore suggest to use the DAS28(CRP) modified according to Hensor et al. (*Rheumatology (Oxford)*, 2010; 49(8): 1521- 9) to evaluate the effectiveness of tocilizumab. The EULAR response rates then decrease to 32% good response and 34% moderate response after 6 months of treatment with tocilizumab.



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