Comparative effectiveness of biological therapies in rheumatoid arthritis is influenced by response measures and disease activity state

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Introduction

Several biological therapies have become available in the last years, widening the therapeutic arsenal in the management of rheumatoid arthritis (RA). Two of the most common drug classes include anti-tumor necrosis factor (TNF) and anti-interleukin-6 (IL-6) agents, which target central cytokines in the disease pathway. We have previously shown that the proportion of patients achieving remission was higher in the tocilizumab group, an anti-IL-6 agent compared to anti-TNF therapies, but the magnitude of the effect was associated with the disease activity measure used, namely DAS28, CDAI or SDAI.

The aim of this study is to assess whether this difference remains significant in other RA disease activity states.

Methods

We included biologic-naïve RA patients registered in the Rheumatic Diseases Portuguese Register, Reuma.pt, who have started therapy with anti-TNF (adalimumab, infliximab, golimumab) and anti-IL-6 (tocilizumab) monoclonal antibodies after 1st January 2008. Our primary outcome was the proportion of patients in each disease activity state (remission, low, moderate, high) at 6 months, applying DAS28, CDAI and SDAI. Univariate and multivariate logistic regressions were performed to compare the groups.

Results

Two hundred and twenty RA first biological therapy users were enrolled, 180 treated with anti-TNF monoclonal antibodies and 40 with tocilizumab. Both groups had similar baseline characteristics, except for disease duration, which was shorter in tocilizumab-treated patients, as well as SJC, DAS28, SDAI and CDAI, all higher in the tocilizumab group.

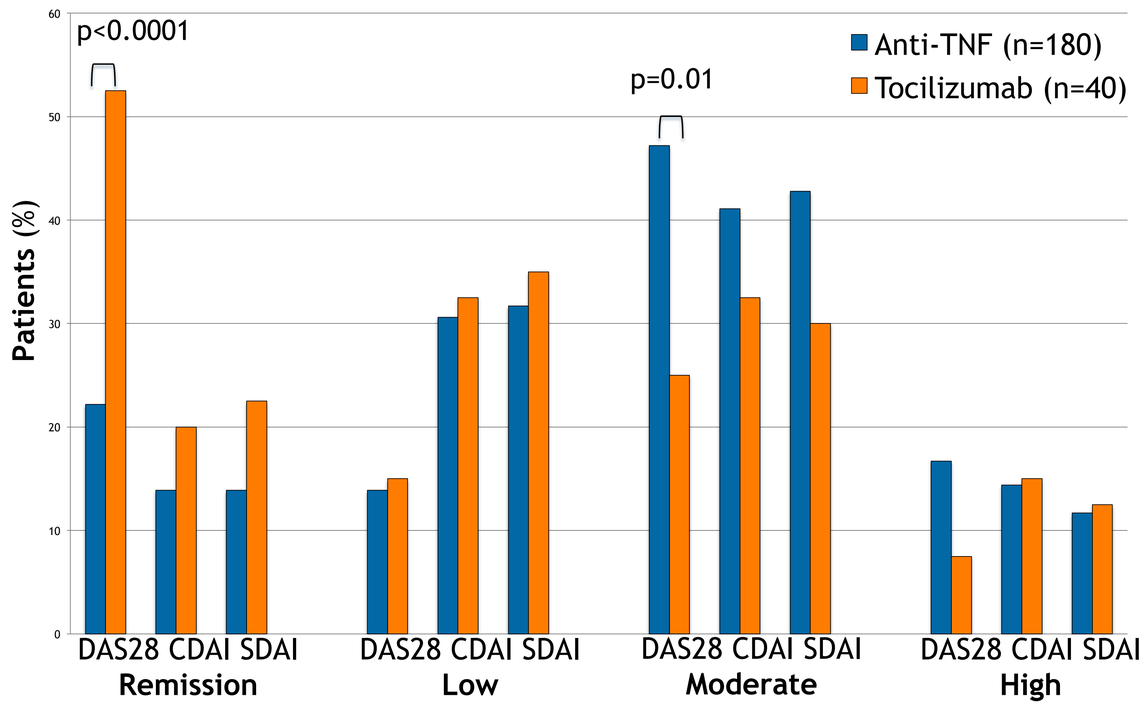
Table 1 – Baseline characteristics of 220 patients registered in Reuma.pt treated with anti-TNF antibodies or tocilizumab

	anti-TNF (n=180)	Tocilizumab (n=40)	p
Age (y)	53.02 ± 12.52	53.76 ± 11.73	0.74
Female (%)	80.0	90.6	0.06
Smokers (%) (n=196)	22.5	16.0	0.34
Education (y) (n=174)	6.99 ± 4.50	6.41 ± 3.61	0.64
Disease duration (y) (n=204)	12.23 ± 13.42	8.25 ± 7.61	0.043*
RF-positive (%) (n=187)	81.1	76	0.51
Steroids (%)	70.0	77.2	0.33
Methotrexate (%)	85.0	80.6	0.51
TJC (n=181)	9.95 ± 7.52	12.23 ± 8.24	0.13
SJC (n=182)	6.69 ± 5.05	10.03 ± 5.46	0.001*
HAQ (n=152)	1.45 ± 0.63	1.55 ± 0.59	0.40
DAS28 (n= 185)	5.39 ± 1.30	5.93 ± 1.26	0.027*
SDAI (n=150)	29.77 ± 14.51	36.37 ± 14.54	0.046*
CDAI (n=158)	27.21 ± 13.58	34.11 ± 14.18	0.029*

*p<0.05

At 6 months, a significantly higher proportion of patients treated with tocilizumab reached the DAS28 remission threshold, but no difference was seen with CDAI or SDAI. The anti-TNF group had a higher proportion of patients with moderately active disease only when DAS28 was considered. No differences were seen for high and low disease activity.

Figure 1 – Proportion of patients in each disease activity state at 6 months, according to different disease activity measures



Multivariate logistic regression reinforced the differences seen in the unadjusted analysis and demonstrated significant differences for SDAI in the remission state and for DAS28 in high disease activity. No differences were detected in the low disease activity state.

Table 2 – Comparison of anti-TNF and tocilizumab groups by disease activity measure and state, through univariate and multivariate logistic regression

	OR univariate (95% CI)	p	OR multivariate⌘ (95% CI)	p
DAS28$_{remission}$	0.26 (0.13-0.53)	<0.0001*	0.16 (0.06-0.38)	<0.0001*
CDAI$_{remission}$	0.65 (0.27-1.56)	0.33	0.41 (0.13-1.25)	0.12
SDAI$_{remission}$	0.56 (0.24-1.31)	0.18	0.29 (0.09-0.91)	0.033*
DAS28$_{low}$	0.91 (0.35-2.4)	0.86	0.63 (0.22-1.78)	0.38
CDAI$_{low}$	0.91 (0.44-1.90)	0.81	0.56 (0.23-1.38)	0.21
SDAI$_{low}$	0.86 (0.42-1.77)	0.68	0.68 (0.28-1.64)	0.39
DAS28$_{moderate}$	2.68 (1.24-5.82)	0.012*	3.49 (1.44-8.43)	0.006*
CDAI$_{moderate}$	1.45 (0.70-2.99)	0.32	2.20 (0.89-5.44)	0.09
SDAI$_{moderate}$	1.74 (0.83-3.65)	0.14	2.48 (0.94-6.53)	0.07
DAS28$_{high}$	2.47 (0.71-8.53)	0.15	6.13 (1.32-30.89)	0.028*
CDAI$_{high}$	0.96 (0.37-2.50)	0.93	1.71 (0.45-6.49)	0.43
SDAI$_{high}$	0.86 (0.33-2.62)	0.68	2.01 (0.42-9.60)	0.39

*p<0.05; ⌘adjusted for disease duration and baseline DAS28/CDAI/SDAI

Conclusions

Globally, tocilizumab-treated patients had better disease activity outcomes, but the magnitude of the effect was dependent on the disease activity measure used, being higher for DAS28. This is in accordance with our previous results and underlines the pronounced reduction of inflammatory markers (i.e., ESR and CRP) seen with tocilizumab that ultimately translates into lower DAS28 and SDAI, respectively. Furthermore, this effect was also related to the disease activity state considered, being more pronounced for patients in remission. This may be explained by the fact that these activity indexes distinctly weigh the several disease components and seem to classify some patients into different disease activity states.

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