

TOCILIZUMAB IS ASSOCIATED WITH HIGHER CDAI/SDAI REMISSION IN BIOLOGIC-NAÏVE RHEUMATOID ARTHRITIS PATIENTS – DATA FROM REUMA.PT

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EULAR 2014, Paris, 12th June 2014

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eular

Paris
11-14 June 2014



DISCLOSURES

- The authors are fully responsible for the presentation content.
- Reuma.pt is supported by unrestricted grants from Abbvie, MSD, Pfizer, Roche and UCB.

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Background

- **Tocilizumab** (IL-6 receptor blocker) and **anti-TNF biologics**: key therapies in the management of **rheumatoid arthritis**
- **Equally effective** in combination therapy and few head-to-head comparisons available (e.g., ADACTA trial)
- **Tocilizumab:**
 - ↑ effect on acute phase reactants
 - ↑ response rates using **composite scores** that include ESR or CRP (e.g., DAS28)

Aims

- **Compare remission rates according to different criteria in RA patients treated with:**
 - Tocilizumab
 - anti-TNF agents
- Assess the impact of previous biologic therapies on treatment response

Material and Methods

- **Inclusion criteria:**

- RA patients, fulfilling ACR 1987
- Registered in Reuma.pt
- Starting tocilizumab or anti-TNF (infliximab, etanercept, adalimumab, golimumab) between January 1st 2008 and July 26th 2013
- Treated for at least 6 months
- Available DAS28 scores at baseline and 6 months

Material and Methods

- **Primary Outcome**
 - Proportion of patients who achieved remission by DAS28, CDAI, SDAI or Boolean criteria at 6 months
- **Statistical analysis**
 - Student's t-test / χ^2 test to compare groups
 - Stratification on previous biologic therapy status
 - Multivariate logistic regression models best predicting remission according to each criteria
 - P-value significant at <0.05

Results

- **524** patients included
 - **95 Tocilizumab**
 - **429 anti-TNF**: 106 adalimumab, 202 etanercept, 43 golimumab, 78 infliximab

Results

- Baseline characteristics (n = 524)

	Tocilizumab (95)	anti-TNF (429)	p
Age	53.8 ± 10.9	53.5 ± 12.3	0.791
Female (%)	82 (86.3)	375 (87.4)	0.772
Dis. duration (n=489)	10.7 ± 9.0	11.7 ± 9.5	0.372
Education (n=387)	7.4 ± 4.6	7.1 ± 4.5	0.611
Smokers (%), n=450	12 (14.3)	43 (11.8)	0.522
RF+/ACPA+ (%), n=463	73 (81.1)	312 (83.7)	0.564
Erosions (%), n=380	16 (22.5)	75 (24.3)	0.757
Nº previous biologics	0.81 ± 1.13	0.17 ± 0.44	<0.001*
Biologic-naïve (%)	52 (54.7)	365 (85.1)	<0.001*
MTX (%)	75 (79.0)	353 (82.3)	0.447
Corticosteroids (%)	77 (81.1)	334 (77.9)	0.493

Results

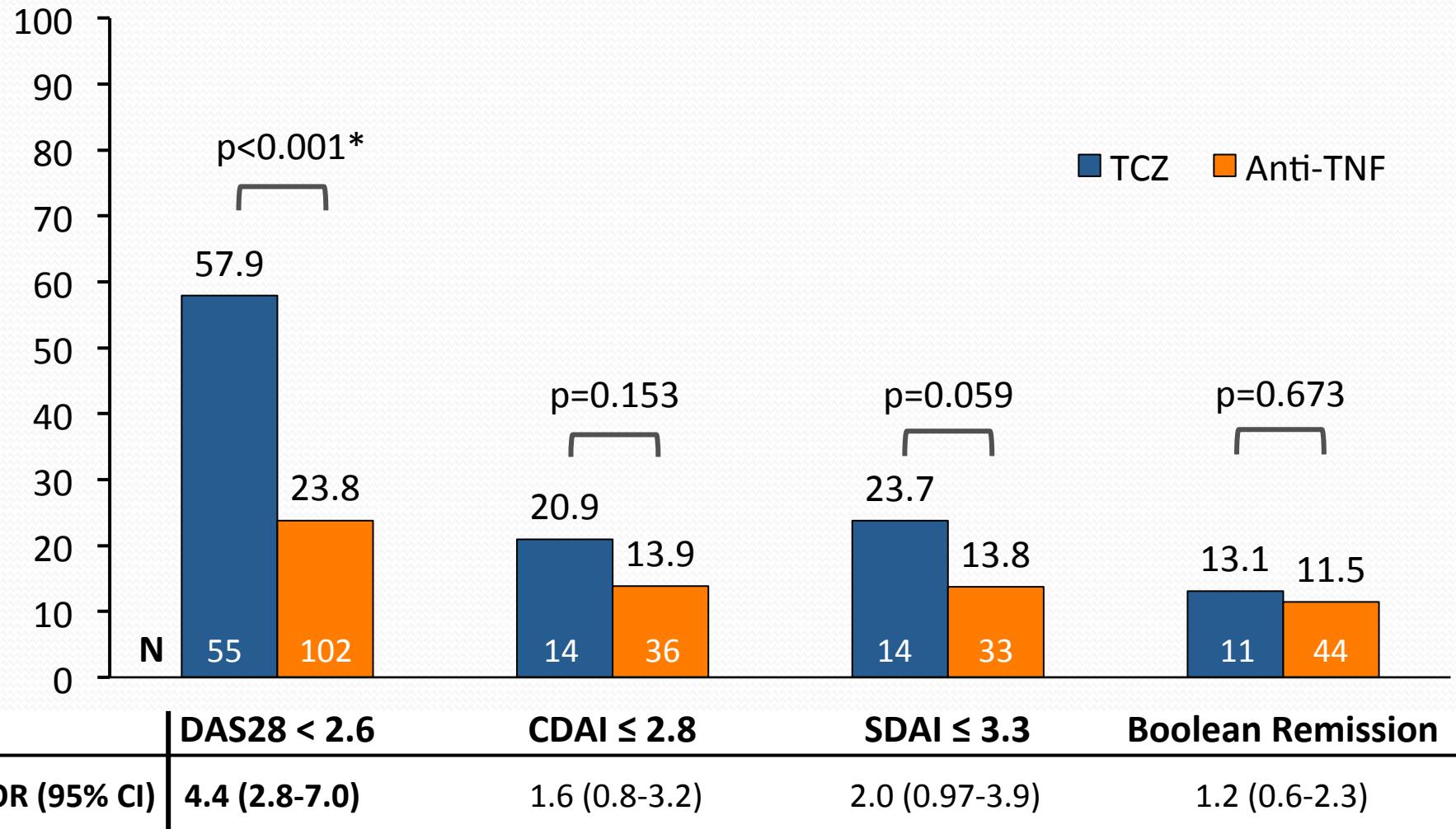
- Baseline characteristics (n = 524)

	Tocilizumab (95)	anti-TNF (429)	p
TJC28	12.4 ± 7.5	10.5 ± 7.6	0.028*
SJC28	10.4 ± 6.4	6.8 ± 5.1	<0.001*
ESR (n=522)	45.6 ± 27.1	37.1 ± 25.6	0.004*
CRP (mg/dL, n=491)	2.8 ± 3.2	2.1 ± 2.7	0.035*
Patient VAS (n=496)	59.8 ± 24.3	58.0 ± 23.2	0.496
Physician VAS (n=376)	60.0 ± 17.9	51.0 ± 19.8	0.001*
DAS28	6.1 ± 1.1	5.4 ± 1.3	<0.001*
CDAI (n=376)	33.3 ± 13.2	28.1 ± 13.6	0.003*
SDAI (n=361)	35.6 ± 13.1	30.4 ± 14.4	0.006*
HAQ (n=415)	1.6 ± 0.6	1.5 ± 0.6	0.150

*p<0.05

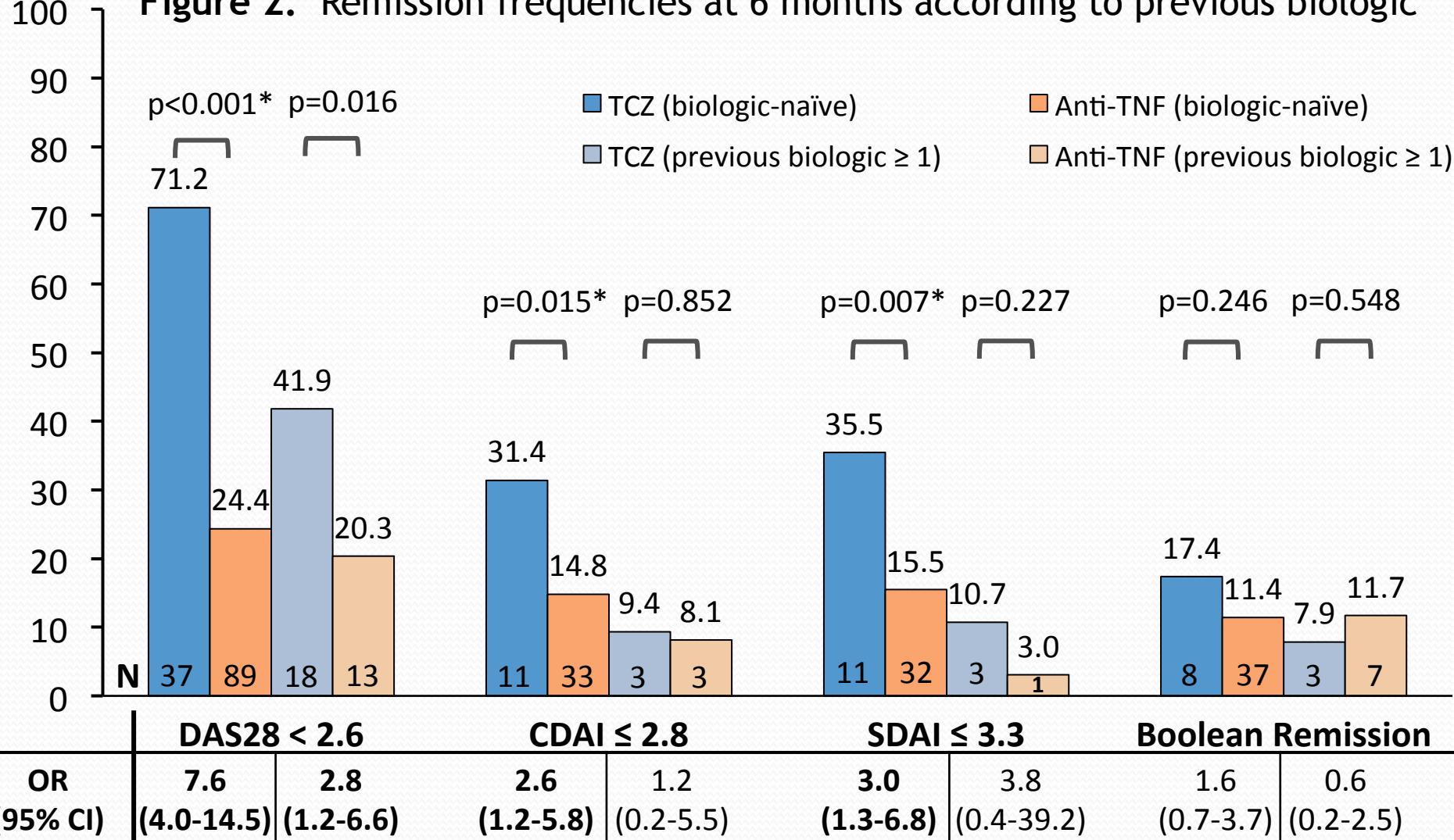
Results

Figure 1. Remission frequencies at 6 months according to different criteria



Results

Figure 2. Remission frequencies at 6 months according to previous biologic



Results

- Multivariate logistic regression models best predicting 6-months remission

	Odds Ratio	95% CI	P-value
DAS28<2.6 (n=489)	13.3	6.9-25.4	<0.001*
CDAI≤2.8 (n=308)	2.9	1.3-6.6	0.009*
SDAI≤3.3 (n=282)	4.1	1.7-9.5	0.001*
Boolean (n=442)	2.1	0.91-4.78	0.083

Adjusting for age, number of previous biologics, disease duration and baseline disease activity

*p<0.05

Discussion

- **Tocilizumab** users: higher baseline disease activity, lower N
- **Inflammatory markers** impact response assessment:
 - Response DAS28 > SDAI > CDAI
- **Missing values** → logistic regression models excluded several patients for CDAI and (N=308) and SDAI (N=282) remission

Discussion

- **Tocilizumab remission rate (57.9% DAS28<2.6):**
 - Higher than observed in RCTs: 27% OPTION, 39.9% ADACTA, 30.1% RADIATE, 59% SAMURAI^(52 weeks)
Smolen, Lancet 2008; Gabay, Lancet 2013; Emery, Ann Rheum Dis 2008; Nishimoto, Ann Rheum Dis 2007
 - Similar to other observational registry-based studies: 39-58% DANBIO, 53.3-57.5% Michinoku, 47.8% CABUKI, 54.9% FRAB
Leffers, Ann Rheum Dis 2011; Hirabayashi, Clin Rheumatol 2013; Yoshida, Rheumatol 2011;
Nakashima, Mod Rheumatol 2014
- **Anti-TNF:** small differences between analysis population and 1st users (23.8 vs. 24.4% DAS28<2.6)
 - 85.1% anti-TNF group naïve to biologics
 - Biologic-naïve vs. ≥1 previous biologic: ↑ disease activity (DAS28 5.5 vs. 5.1, p=0.041) and ↑ SJC (7.1 vs. 4.8, p<0.001)

Conclusions

- At 6 months, treatment with **tocilizumab** was associated with **higher rate of DAS28 remission**
- Previous biologic therapy significantly affected CDAI and SDAI remission
- No differences in Boolean remission rates between tocilizumab or anti-TNF groups

Acknowledgments

- Fernando Martins IT (SPR)
- All patients, physicians and health professionals contributing to Reuma.pt