FRI0224 RITUXIMAB SELECTIVELY REDUCES IGG4 LEVELS IN RHEUMATOID ARTHRITIS PATIENTS

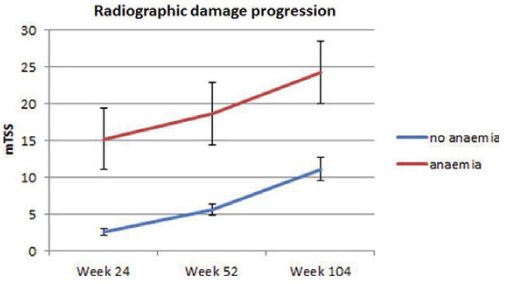
A. Sarantopoulos, I. Gkougkourelas, M. Mytilinaiou, P. Klonizakis, A. Georgiadou, P. Boura. *Clinical Immunology Unit, 2nd Dpt of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Rituximab has been applied as a therapeutic strategy in a variety of diseases, including Rheumatoid Arthritis (RA) and IgG4-Related Disease (IgG4-RD)[1]. On IgG4-RD, it has been shown that apart from B-cell depletion, rituximab induces remission by reducing IgG4 levels[2].
Objectives: On this regard, we investigated weather B-cell depletion in RA is also associated with a selective reduction of any IgG subclass, especially IgG4.
Methods: 31 RA patients, 25/6 female/male, median age 59 years (34–73), duration of disease 9,5 years (1–30) on standard of care DMARD treatment and rituximab administration every 6 months for 2 years were investigated for alterations on disease activity along with Igs' and IgG subclasses levels. All parameters were assessed at enrollment (T0), and after 6, 12 and 24 months. On this 2-year period all patients had been periodically receiving rituximab every 6 months.
Results: After 2 years of rituximab administration, patients achieved a good response to treatment (EULAR criteria). Igs' levels were not statistically altered, though all of them declined (data for IgM and IgA not shown). Furthermore, from IgG subclasses, only IgG4 levels statistically declined.
Conclusions: This is the first time that IgG4 variations are investigated in a non-IgG4RD after rituximab administration. Our results imply that IgG4 may be actively implicated in RA pathophysiology, since disease remission is accompanied by only IgG4 level reduction among all classes and subclasses of Igs'. Furthermore, in RA patients, rituximab may exert its therapeutic results not only via B-cell depletion, but also via IgG4 levels reduction.
References:
[1] Carruthers MN, Topazian MD, Khosroshahi A, et al. Rituximab for IgG4-related disease: a prospective, open-label trial. Ann Rheum Dis. 2015 Jun;74(6):1171–7.
[2] Khosroshahi A, Bloch DB, Deshpande V, Stone JH. Rituximab Therapy Leads to Rapid Decline of Serum IgG4 Levels and Prompt Clinical Improvement in IgG4-Related Systemic Disease. Arthritis Rheum. 2010 Jun; 62(6): 1755–62.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6690

FRI0225 ANEMIA IS A BETTER PREDICTOR FOR RADIOGRAPHIC DAMAGE IN RHEUMATOID ARTHRITIS THAN DAS28 WHEN DETERMINED BEFORE START OF TOCILIZUMAB-TREATMENT – A SECONDARY ANALYSIS FROM THE ACT-RAY TRIAL

B. Möller[1], G. Scholz[1], M. Dougados[2], T. Huizinga[3], P.M. Villiger[1], A. Finckh[4]. *[1]Rheumatology, Immunology & Allergology, Inselspital - Bern University Hospital, Bern, Switzerland; [2]Rheumatology, Hôpital Cochin, Paris, France; [3]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [4]Rheumatology, University Hospital Geneva, Geneva, Switzerland*

Background: Clinical remission, or at least low disease activity, as measured by DAS28 or alternative compound indices is currently the goal of RA treatment. Anemia in the context of RA is mainly driven by tumor necrosis factor alpha (TNF-α) and interleukin-six (IL-6), and may serve as a simple biological marker of inflammation. Anemia was recently discovered as a largely DAS28-independent parameter to predict radiographic damage progression in RA, both with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or with anti-TNF agents.
Objectives: To study the predictive value of anemia in relation to DAS28 for radiographically detectable joint damage progression in patients treated with IL-6R inhibitor tocilizumab (TCZ) plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) when used in a treat to target concept.
Methods: In the ACT-RAY trial, all patients were methotrexate (MTX) inadequate responders and randomized to receive either TCZ plus MTX (add-on) or TCZ plus placebo (switch strategy) for at least one year. After week 24, open-label csDMARDs other than MTX could be added according to a treat-to-target approach in patients with moderate or high disease activity (DAS28≥3.2). After week 52, patients in sustained clinical remission (DAS28<2.6) could discontinue TCZ before stopping csDMARDs, and finally MTX/Placebo. The exposure of interest was anemia, defined using the WHO definition or the more liberal NHANES definition, both at baseline and over time. The primary outcome was the rate of joint damage progression measured by the change in the modified total Sharp score (ΔmTSS). We used longitudinal multivariate mixed effects models to test the impact of anemia on ΔmTSS. To examine the association of anemia to ΔmTSS independently from RA disease activity, the models were run with and without DAS28 at baseline and DAS28 over time.
Results: Of 556 randomised patients, complete datasets for fully adjusted models were available from 285 patients. Overall radiographic progression was regarded to be minimal, with insignificant differences in favor of the add-on strategy. Median annual ΔmTSS before inclusion was 2.9 (IQR 1.5 to 6.4) in patients without and 5.5 (IQR 2.7 to 11.1) in patients with baseline anemia, but evolved subsequently similar when being on TCZ. Anemia at baseline was a strong predictor of mTSS (per WHO definition: coefficient 14.8, 95% CI 7.6–21.9, p<0.001; per NHANES definition: coefficient 14.6 95% CI 7.6–21.5 p<0.001), as well as baseline DAS28 (coefficient 3.9, 95% CI 0.7–7.0, p=0.016). Mean DAS28 over time (p<0.001), in contrast to anemia data over time when obtained in patients already on TCZ, was significantly associated with subsequent ΔmTSS. Baseline anemia in contrast to baseline DAS28 remained a significant predictor of mTSS for up to two years on TCZ in fully adjusted multivariate analyses (p<0.05), including time-variant DAS28.



Conclusions: Anemia may be a strong and DAS28-independent long-term predictor of radiographic joint damage progression. Present data from patients on IL-6R blockade, a potent target-specific RA treatment with major impact also on erythropoiesis, add importantly to the growing body of evidence for the studied association.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6685

FRI0226 RITUXIMAB IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE: A MULTICENTER STUDY

C. Fernández-Díaz[1], M. Martin-Lopez[2], M. Carrasco-Cubero[3], D. Reina-Sanz[4], P. Rubio-Muñoz[5], A. Urruticoechea-Arana[6], J. Miranda-Filloy[7], N. Vegas-Revenga[1], L. Dominguez-Casas[1], M. Gonzalez-Gay[1], R. Blanco[1]. *[1]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander; [2]Rheumatology, Hospital Universitario 12 de Octubre, Madrid; [3]Rheumatology, Hospital Infanta Cristina, Badajoz; [4]Rheumatology, Hospital Sant Joan Despi Moises Boggi; [5]Rheumatology, Hospital Universitario Germans Trias i Pujol, Barcelona; [6]Rheumatology, Hospital Can Misses, Ibiza; [7]Rheumatology, Hospital Universitario Lucus Augusti, Lugo, Spain*

Background: Anti-TNFα drugs and several conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of Interstitial Lung Disease (ILD).
Objectives: Our aim was to assess the efficacy and safety of Rituximab (RTX) in RA patients with ILD.
Methods: Multicenter study of RA patients with ILD treated with RTX. ILD was diagnosed by high-resolution computed tomography (HRCT). RTX was used at standard dose (1 gx2 and premedication with iv Methylprednisolone for a six month interval. We assess the the following variables: a) 1-point change in the degree of dyspnea according to the Modified Medical Research Council (MMRC); b) FVC improvement ≥10%; and improvement ≥10% in DLCO; c) radiological changes in HRCT scan, and d) changes in the joint assessment measured by DAS28 score.
Results: We studied 18 patients (13 women /5 men) with ILD associated to RA. The mean age±SD was 62.8±11.0 years. The median [IQR] to progression of RA was 5.25 [2–12.8] years. They had received the following DMARDs previously; MTX (n=11), Leflunomide (LFN) (n=9) mycophenolate (MMF) (n=1) sulfasalazine (SSZ) (n=5), hydroxichloroquine (HCQ) (n=4), azathioprine (AZA) (n=1), gold salts (n=1), D-penicillamine (n=1), cyclophosphamide (n=1). 7 patients had previously received biological drugs. RA was seropositive in 16 cases (89%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 4 patients. In 2 patients ILD was drug-related: MTX (n=2). RTX was prescribed as monotherapy (n=7) and combined with DMARDs (11. The DMARDs prescribed were: LFD (4), SSZ (2),

Abstract FRI0224 – Table 1. DAS28 and IgG class and subclasses variations. Because of non-normal distribution of our sample, the results were expressed as median and range and statistical analysis was performed by using the Kruskal Wallis tests

	DAS28	IgG	IgG1	IgG2	IgG3	IgG4
T0	4,46 (2,06–6) *	12,2 (5,1–23,1)	7,7 (3,59–12,4)	2,7 (0,844–5,21)	0,573 (0,079–1,85)	0,451 (0,032–2,1)*
T6	3,8 (2,2–6,44)	11,1 (5,78–15)	7,28 (3,38–11,2)	2,7 (1,23–5,36)	0,445 (0,086–1,58)	0,35 (0,044–1,06)
T12	4,01 (1,68–5,77)	11,1 (5,36–19,2)	6,81 (3,35–12,2)	2,53 (0,876–4,67)	0,423 (0,07–1,88)	0,279 (0,036–1,24)
T24	3,27 (1,5–5,07) *	11,2 (4,92–14,5)	6,59 (3,34–10,3)	2,42 (0,92–4,7)	0,405 (0,08–0,823)	0,248 (0,025–1,08)*
	*p<0.05					*p<0.05