REFERENCES

[1] Chatzidionysiou, et al. J Rheumatol. 2017 Feb;44(2):162-169.

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AB0409

B CELLS PROFILE AS A BIOMARKER FOR EARLY IDENTIFICATION OF OPTIMAL RESPONDERS TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: The most common biological agents used as disease-modifying treatment in rheumatoid arthritis (RA) are TNF inhibitors (TNFi). Although these new strategies to treat RA have improved the course of the disease, approximately 30-50% of patients do not respond to this therapy. Early identification of optimal responders is crucial in the clinical setting.

Objectives: The aim of this study was to investigate if baseline percentages of different leukocyte subsets in peripheral blood (PBMCs) can contribute to identify RA patients who will respond to TNFi.

Methods: This was a prospective bi-center pilot study including 100 RA patients under TNFi therapy. Clinical activity was assessed at baseline and 6 months of treatment by disease activity score 28 (DAS28), considering optimal responders if they reached remission at 6 months (DAS28≤2.6). PBMCs were obtained before treatment and different leukocyte subsets were evaluated by flow cytometry (FACSCantoII instrument). The association between the percentage of PBMCs at baseline and clinical response at 6 months was evaluated through logistic regression models (odds ratio; 95% CI). All the analyses were adjusted by sex, age, disease duration, concomitant methotrexate, baseline DAS28 and seropositivity (ACPA and/or RF).

Results: Demographic characteristics are shown in Table 1. After 6m of TNFi treatment, 40% of the patients achieved clinical remission. A significant association between higher percentage of total B cells (OR=1.19; 95% CI:1.05-1.35; p=0.007) and naïve B cells (Bn; OR=1.32; 95% CI:1.08-1.61; p=0.007) at baseline and clinical response was found. The other PBMC subsets (monocytes, NK cells, CD4+ and CD8+ T cells subtypes) did not show statistical differences (Figure 1).

Conclusion: Our results suggest that basal B cells profile may contribute to identify optimal responders to TNFi in RA. (Funding: ISCIII (PI16/01092, PI16/00474).

Figure 1. legend: Association between the percentage of PBMC subset before TNFi and the clinical remission. Multivariate logistic regression analysis was performed for each PBMC subset. The percentage of total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets. The analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity and baseline-DAS28.

Baseline patients' characteristics	Total patients (n=100)
Age (years); mean±SD	53±13
Female; n (%)	84 (84)
Disease duration (years); median (IQR)	8 (4-12)
Rheumatoid factor positive; n (%)	77 (77)
ACPA positive; n (%)	83 (83)
Smoking habit; n (%)	
no	46 (46)
smoker	20 (20)
ex-smoker	34 (34)
Body mass index (kg/m ²); median (IQR)	24.8 (22.9-29.6)
DAS28; mean±SD	4.8±1.2
CRP (mg/L); median (IQR)	5.7 (2.2-12.4)
Previous TNFi treatment; n (%)	13 (13)
TNFi type; n (%)	
Monoclonal antibodies	55 (55)
Etanercept	45 (45)
TNFi monotherapy	4 (4)
Concomitant csDMARD; n (%)	96 (96)
OnlyMethotrexate (MTX)	51 (51)
OnlyothercsDMARDs (OD)*	18 (18)
MTX + OD	27 (27)
Prednisone; n (%)	57 (57)

Table1

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AB0410

DISCONTINUATION OF ORAL GLUCOCORTICOID AFTER INITIATION OF BIOLOGICAL DMARD DUE TO A HIGHER DOSE OF METHOTREXATE; A RETROSPECTIVE OBSERVATIONAL STUDY BASED ON DATA FROM A JAPANESE MULTICENTER REGISTRY STUDY

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Background: In the treatment of rheumatoid arthritis, glucocorticoid that provide anti-inflammatory effects in the early stage of treatment is an important drug. We recommend discontinuing of glucocorticoid as much

as possible within 6 months[1], but many patients have taken oral glucocorticoid for the long term in daily clinical practice. The frequency of use of glucocorticoid has gradually declined, and there are several reports on discontinuation of glucocorticoid due to the initiation of bDMARD[2, 3]. However, there is no report showing the relation between discontinuation of glucocorticoid and MTX dose.

Objectives: The aim of this study is to examine association of methotrexate (MTX) dose with discontinuation of glucocorticoid after one year since initiation of biological DMARD (bDMARD) as 1st bDMARD.

Methods: We established the large observational cohort, the Nagoya University orthopedic facility multicenter study (TBCR), and a total of 3119 patients used biological DMARD. 564 patients who used glucocorticoid and MTX when bDMARD was initiated as 1st bDMARD were enrolled. In the first study, we examined predictive factors of discontinuation of glucocorticoid after one year since initiation of bDMARD by using multivariate analysis in the two groups, which patients continued to use glucocorticoid and discontinued to use glucocorticoid. In the second study, we adjusted the background at the time of initiation of bDMARD by using propensity score matching (PS) in the two groups, MTX≤8mg (L group) and MTX>8mg (H group).

Results: 400 patients continued to use glucocorticoid and 164 patients discontinued to use glucocorticoid. In the multivariate analysis, age (Odds ratio (OR)0.98), MTX dose (OR1.09) and glucocorticoid dose (OR0.88) were independently predictive factors of discontinuation of glucocorticoid. When we adjusted age, disease duration, sex, disease activity, RF/ACPA, glucocorticoid dose by using PS matching, 105 pairs were extracted. There were obvious significant differences between 24 patients (22.9%) in the L group and 43 cases (41.0%) in the H group ($P = 0.007$), where glucocorticoid was discontinued at one year after the initiation of bDMARD.

Conclusion: This cohort study investigated the association with discontinuation of oral glucocorticoid and MTX dose in the patients treated with bDMARD. TBCR revealed that, in the clinical practice, glucocorticoid use was decreasing in the patients treated with bDMARD. MTX dose at the time of initiation of bDMARD was predictive factor of discontinuation of glucocorticoid. A higher dose of MTX associated with discontinuation of glucocorticoid in the patients treated with bDMARD.

REFERENCES

- [1] Smolen JS, Landewe R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017 Jun; 76(6):960-977.
- [2] Shimizu Y, Tanaka E, Inoue E, Shidara K, Sugimoto N, Seto Y, et al. Reduction of methotrexate and glucocorticoids use after the introduction of biological disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis in daily practice based on the IORRA cohort. *Mod Rheumatol*. 2018 May; 28(3):461-467.
- [3] Seror R, Dougados M, Gossec L. Glucocorticoid sparing effect of tumour necrosis factor alpha inhibitors in rheumatoid arthritis in real life practice. *Clin Exp Rheumatol*. 2009 Sep-Oct; 27(5):807-813.

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AB0411

TNF ALPHA INHIBITORS INFLUENCE THE CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients die because of cardiovascular diseases more often than the general population. Nowadays RA is considered as an independent risk factor for cardiovascular disease (CVD). A long-lasting inflammatory process, immunological dysregulation and endothelial dysfunction play an important role in the pathogenesis of progressive atherosclerosis in RA [1,2].

Objectives: The aim of the study was to assess the influence of biological treatment on cardiovascular risk factors in RA population

Methods: 38 RA patients with active disease (DAS28>5.1) and 22 age and sex matched healthy controls were enrolled in the study. All the patients were treated with TNF alpha inhibitors (n=20 etanercept, n=18 adalimumab), with the background methotrexate (10-25mg weekly). The clinical state was assessed at the beginning of the study and 6, 12 and 18 months after. All the patients underwent the following tests: DAS 28 assessment, basic laboratory measurements (including homocysteine levels, fibrinogen, lipid profile), electrocardiogram (ECG), flow-mediated dilation (FMD) and carotid intima-media thickness (cIMT) assessment and echocardiography. The local bioethics committee approved the study (KB-753).

Results: 27 woman and 11 man (71% and 29% respectively) with high disease activity despite long-term treatment with synthetic disease modifying antirheumatic drugs were enrolled in the study. Mean age was 52 years (SD ± 9.6), 95% of the patients were RF-positive, 63% anti-CCP-positive. Of them 24% were current smokers, 58% had arterial hypertension and 66% had concomitant hypercholesterolaemia. In comparison to the control group, there were statistically significantly higher values of cIMT in RA patients. Moreover there was a positive correlation between cIMT thickness and duration of RA. A reduction of cIMT (mainly during first 12 months) and an increase in FMD values were observed in the course of the treatment ($p<0.05$). The increase in FMD value (0.03 vs 0.37) correlated with decrease of the inflammatory markers, which may be a result of an improvement in endothelial dysfunction due to anti-TNF-alpha treatment. The decrease in total cholesterol ($p<0.05$), LDL cholesterol ($p=0.03$) and Castelli risk index ($p<0.05$) were also noted, no changes of the doses of cholesterol-lowering therapy were done during the follow up. There was a positive correlation between homocysteine and uric acid levels and there was a statistically significant decrease in both parameters in the course of the treatment (11.31 vs 8.91 [mol/l] and 5.92 vs 4.77 [mg/dl], respectively). Normal left ventricular geometry was observed after 12 months of biological therapy in patients with concentric remodeling of the left ventricle. Furthermore echocardiography revealed a significant decrease in LVEDD, IVSD, LA, FS, RVEDD after 18 months of the biologic treatment.

Conclusion: Our results confirm earlier data that TNF alpha inhibitors may favorably influence on endothelial dysfunction. Besides TNF inhibitors can protect against increase in relative wall thickness of left ventricle. The anti-TNF alpha therapy not only reduces the activity of the disease in affected joints but also has a positive impact on selected cardiovascular risk factors in RA population.

REFERENCES

- [1] Solomon DH., Goodson NJ., Katz JN., i wsp. Patterns of cardiovascular risk in rheumatoid arthritis. *Ann Rheum Dis*. 2006; 65: 1608-1612
- [2] Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Metabolic syndrome in rheumatoid arthritis. *Maedica (Buchar)*. 2012 Jun;7(2):148-52.

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