Background: Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology, which is characterized by erosive arthritis (synovitis) and systemic inflammation. Tofacitinib (TFCN) is a small molecule Janus kinase (JAK) inhibitor that targets JAK1/JAK3. Identification of patients sensitive to TFCN before treatment could significantly improve therapy outcome. Presently it is not possible to predict TFCN efficacy in every patient while some patients are non-responsive to the drug that may produce adverse effects. TFCN function in RA patients has been recently associated with alterations in bioenergetics, mitochondrial function, and ATP production [1]. Therefore, we hypothesized that baseline metabolic status of RA patients prior to drug administration can predict the therapeutic outcome.

Objectives: To investigate the importance of baseline expression of genes involved in energy generation in RA patients, which could serve prognostic biomarkers for treatment response to tofacitinib.

Methods: Peripheral blood of 28 RA patients aged 52.2±15.6 years old, average disease duration 3.5 years (range 0.6-19) treated with TFCN (5-10 mg twice a day) during three months and 26 healthy age-matched control subjects were examined. Clinical response was assessed by disease activity score (DAS28-ESR), serum levels of ACPA antibodies, rheumatoid factor (RF), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Clinical remission was assessed according to ACR criteria and DAS28 (DAS28 <2.6). Protein concentrations were measured using ELISA. Total RNA was isolated and used in gene expression studies performed with quantitative real-time RT-PCR.

Results: All of the patients were Steinbrocker's radiographic stage II-III at baseline. The majority of patients demonstrated erosive arthritis (23 out of 28), they were ACPA- (25 out of 28) and RF- (24 out of 28) positive. TFCN treatment significantly decreased the disease activity according to DAS28. At the end of the study the majority of patients demonstrated moderate disease activity (3.2< DAS28 <5.1), four patients retained high disease activity while 8, attained remission (DAS28 <2.6). This was accompanied by significant decrease in CRP and the number of swollen and tender joints. ESR values were not changed significantly. Gene and protein expression analysis revealed that RA patients, which attained clinical remission after TFCN treatment demonstrated significantly lower baseline expression of genes associated with glycolysis (pyruvate kinase), oxidative phosphorylation (succinate dehydrogenase and uncoupling protein (UCP) 2) compared to other examined RA patients and control subjects. Moreover, these gene expressions increased in RA patients who attained clinical remission in the course of follow-up while in refractory for TFCN treatment patients these gene expressions were tending to downregulate.

Conclusion: Clinical remission attainment in RA patients treated with tofacitinib is associated with lower baseline expression of genes associated with energy generation pathways (pyruvate kinase, succinate dehydrogenase, and UCP2) compared to other examined subjects. Non-responsiveness to tofacitinib is accompanied by high baseline expression of genes related to glycolysis and oxidative phosphorylation compared to controls.

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POS0100

VITAMIN D LEVEL IN RHEUMATOID ARTHRITIS PATIENTS STARTING A BIOLOGIC DISEASE-MODIFYING DRUG AND ITS CORRELATION WITH DISEASE ACTIVITY AND RESPONSE TO TREATMENT

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Background: Vitamin D, a fat soluble vitamin that is mainly involved in the regulation of calcium/phosphate metabolism, has a increasingly understood role in immunomodulatory activity, both in innate and adaptive immune system. In rheumatoid arthritis (RA), vitamin D showed to suppress the proliferation of synovial cells and to reduce the production of proinflammatory cytokines, in vitro. (1) Recently the hypothesis has been raised that vitamin D has a negative association with RA activity. (2)

Objectives: This study aimed to evaluate the relationship between the 25-hydroxyvitamin D (25(OH) vitD) level, RA activity and response to a first biologic disease-modifying drug (bDMARD).

Methods: This is a longitudinal, retrospective study including consecutive patients with the diagnosis of RA followed at our rheumatology department. Demographic, clinical, and laboratorial data were collected from our national database at baseline, 6 and 12 months after initiation of a first bDMARD. Statistical analysis was performed using SPSS 23.0. Correlations between variables were studied using Spearman correlation analysis and comparison between groups was performed using Wilcoxon and Kruskal-Wallis tests; p<0.05 was considered statistically significant.

Results: Mean age of patients (n=236) was 51.5± 11.2 years old, 192 (81.4%) were females with a median disease duration of 10.1 [4.7, 16.7] years. Seropositivity for anti-citrullinated protein antibodies was present in 192 (81.4%) patients and for rheumatoid factor in 175 (74.2%). The majority exhibited a very high or high disease activity at baseline (median DAS28 5.75 [4.99 – 6.63]) and 90% (n=212) of them were concomitantly using corticosteroids and/or other disease-modifying anti-rheumatic drugs (117 with methotrexate (MTX), 62 with leflunomide and 32 with sulfasalazine). Regarding bDMARD, 56.8% (n=134) initiated an TNF alpha inhibitor.

After 6 and 12 months from a bDMARD initiation there was a significant reduction of ESR, CRP levels, TJC, SJC and DAS28 (all p-values < 0.001), as expected. Median baseline serum 25(OH) vitD concentrations was 25.5 [16.5, 30.0] ng/mL; notably, 34.2% of our sample was affected by hypovitaminosis D at baseline 25(OH) vitD < 20 ng/mL).

Among our study population 42.5% patients were responders to first bDMARD (23.8% good and 18.7% moderate responders) according to the EULAR response criteria. Disease remission (DAS28 <2.6) was achieved by 17.6% of patients.

The percentage of good responders was significantly lower in the subgroup of patients with hypovitaminosis D compared to subjects with normal 25(OH) vitamin D levels at baseline (p=0.002), as it was for the percentage of disease remission (p=0.015).

The bivariate correlation analyses showed that 25(OH) vit D levels at baseline correlated with CRP levels and good response to RA treatment after 12 months (Spearman's coefficient -0.201, p=0.028; Spearman's coefficient 0.255, p<0.019, respectively). 25(OH) vit D levels at baseline, 6 and 12 months after bDMARD initiation did not correlate with age, BMI, ESR, number of tender or swollen joints, DAS28, HAQ or with SDAI or CDAI at 6 or 12 months of treatment.

Conclusion: In patients with RA, basal 25(OH) vit D levels correlated with response to a bDMARD. These results suggest a role of basal vitamin D status in the prediction of disease evolution and support the hypothesis that vitamin D has an immunomodulatory potential.

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SLE, Sjögren's and APS - clinical

POS0101

ADVERSE HEALTH-RELATED QUALITY OF LIFE OUTCOME DESPITE ADEQUATE CLINICAL RESPONSE TO TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Despite improvements in medical care that have contributed to prolonged life expectancy for people living with systemic lupus erythematosus (SLE) over the past decades, they still suffer from substantial diminutions of health-related quality of life (HRQoL) compared with the general population and with other chronic diseases.

Some studies have demonstrated that conventional synthetic and biological disease-modifying agents contribute to improvements in SLE patients' HRQoL, and responders to treatment have been shown to report greater improvements than non-responders. Although these observations are clinically relevant,