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

S. Garcia¹, B. M. Fernandes¹, F. Oliveira Pinheiro¹, M. Rato¹, D. Fonseca², A. Martins¹, D. Santos Oliveira^{1,3}, F. R. Martins⁴, G. Terroso¹, M. Bernardes^{1,5}, L. Costa¹. ¹São João University Hospital Center, Rheumatology, Porto, Portugal; ²Centro Hospitalar Vila Nova de Gaia / Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal; ³Faculdade de Medicina da Universidade do Porto - FMUP, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal; ⁴University Hospital Center of Algarve, Faro, Rheumatology, Faro, Portugal; ⁵Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal

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

A. Gomez^{1,2}, J. Lindblom^{1,2}, V. Qiu^{1,2}, A. Cederlund^{1,2}, A. Borg^{1,2}, S. Emamikia^{1,2}, Y. Enman^{1,2}, J. Lampa^{1,2}, I. Parodis^{1,2}. ¹Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden; ²Karolinska University Hospital, Department of Gastroenterology, Dermatology and Rheumatology, Stockholm, Sweden

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,

improvement following a therapeutic intervention does not necessarily signify that the individual has achieved a satisfactory health state perception. In rheumatoid arthritis, significant pain and severe fatigue persist in a substantial proportion of patients who achieve a good clinical response to treatment or remission. This paradoxical observation has not been thoroughly explored in SLE.

Objectives: To determine the prevalence of adverse HRQoL outcomes in patients with SLE who achieved an adequate clinical response after a 52-week long period on standard therapy plus belimumab or placebo, within the frame of two phase III clinical trials. We further aimed to compare frequencies of adverse HRQoL outcomes across different age categories and ethnic groups, and sought to identify contributing factors.

Methods: We included patients who met the primary endpoint of the BLISS-52 (NCT00424476) and BLISS-76 (NCT00410384) trials (N=760/1684), i.e. attainment of the SLE Responder Index 4 at week 52. Accordingly, evaluation of adverse HRQoL outcomes was based on patient reports at week 52 from treatment initiation, using the Medical Outcomes Study Short Form 36 (SF-36) health survey and the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue) scale. Adverse HRQoL outcomes were defined as (i) SF-36 scale scores $\leq$ the 5th percentile derived from age- and sex-matched US population-based norms from the SF-36 health survey user manual; and (ii) FACIT-Fatigue scores <30 .

Pearson's chi-square or Fisher's exact tests were used to investigate associations between dichotomous variables. Comparisons of continuous data between SLE patients and age- and sex-matched norms were performed using the Wilcoxon signed-rank test. Multivariable logistic regression models were created in order to assess independence and priority of potential factors associated with adverse HRQoL outcomes.

Results: We found clinically important diminutions of HRQoL in SLE patients compared with matched norms and high frequencies of adverse HRQoL outcomes, the highest in SF-36 general health (29.1%), followed by FACIT-Fatigue (25.8%) and SF-36 physical functioning (25.4%). Overall, frequencies were higher with increasing age. Black/African American and White/Caucasian patients reported higher frequencies than Asians and Indigenous Americans, while Hispanics experienced adverse HRQoL less frequently than non-Hispanics. Increasing organ damage was associated with adverse physical but not mental HRQoL outcomes; disease activity showed no impact. In multivariable logistic regression analysis, addition of belimumab to standard therapy was associated with lower frequencies of adverse SF-36 physical functioning (OR: 0.59; 95% CI: 0.39–0.91; P=0.016) and FACIT-F (OR: 0.53; 95% CI: 0.34–0.81; P=0.004).

Conclusion: Substantial proportions of SLE patients reported adverse HRQoL outcomes despite adequate clinical response to treatment, especially in physical aspects. Particularly high proportions were seen within Black/African American and White/Caucasian patients. Add-on belimumab may be protective against adverse physical functioning and severe fatigue. Our results corroborate that HRQoL diminutions constitute a substantial burden in patients with SLE, and highlight the limitations of current therapeutic strategies.

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POS0102

GO ASK YOUR PATIENTS! PSS-QoL REPORTED PERCEPTION OF DRYNESS CORRELATES WITH LACRIMAL AND SALIVARY FLOW IN PRIMARY SJÖGREN'S SYNDROME

A. Lackner¹, P. Bosch¹, S. Zenz¹, J. Hermann¹, J. Horwath-Winter², D. Rabensteiner², M. Stradner¹. ¹Medical University of Graz, Department of Rheumatology, Graz, Austria; ²Medical University of Graz, Department of Ophthalmology, Graz, Austria

Background: The patient perspective is an essential outcome parameter in the quest for effective therapy in primary Sjögren's Syndrome (PSS). The EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) is recommended by EULAR to quantify patient's symptom burden and has been used in several clinical trials. Surprisingly, the patient's perception of dryness quantified with ESSPRI does not correlate with objective measures of salivary or lacrimal flow.

Objectives: Thus, we evaluated a newly developed assessment tool-the Primary Sjögren's Syndrome Quality of Life Questionnaire (PSS-QoL) - for quantifying symptoms of dryness in comparison with the ESSPRI and objective measurements of salivary and lacrimal flow.

Methods: Data of patients from the PSS registry of the Medical University of Graz fulfilling the 2016 ACR/EULAR classification criteria for PSS were analysed. The patient perspective was analyzed by PSS-QoL, ESSPRI, Xerostomia Inventory (XI) and Ocular Surface Disease Index (OSDI). Sicca signs were measured with Schirmer's test, unstimulated salivary flow test (USF) and stimulated salivary flow test (SSF). Patients were categorized into groups based on the presence of subjective and/or objective dryness: 1) objective dryness only, 2) subjective dryness only, and 3) both, subjective and objective dryness. ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index) and EGA (Evaluator Global Assessment, numeric rating scale from 0 to 10) were obtained. In addition, free light chains (FLC) κ and λ , rheumatoid factor (RF) IgM and IgA were determined.

Results: Data from 123 PSS patients were analyzed; 91.9% (n=113) were female, with a mean disease duration of 6.2 ($\pm$ 5.3) years and mean age of 60.1 ($\pm$ 12.4) years. PSS-QoL-dryness revealed significant negative correlations with Schirmer's test ($r=-0.31$, $p<0.05$) and SSF-test ($r=-0.39$, $p<0.01$). In contrast, we found no significant correlation between ESSPRI-dryness and any objective dryness test. Lower perceived dryness was associated with higher immunological activity determined by increased levels of IgG, FLC and RF-IgA. Patients with objective signs and subjective symptoms of dryness had higher clinical and immunological disease activity compared to patients with subjective symptoms only (table 1).

Conclusion: Patients' perception of dryness assessed by PSS-QoL correlates with objective measurements of salivary gland function while ESSPRI-dryness did not. Based on the PSS-QoL and objective measures of dryness two distinct groups of PSS patients could be distinguished, which may have implications in daily practice and future clinical studies.

Table 1. Comparison of perceived dryness-groups with clinical parameters

	PSS-QoL Mouth		p	PSS-QoL Eyes		p
	subj	obj/subj		subj	obj/subj	
EGA	1.0 [0-5]	2.0 [0-7]	<0.05	1.0 [0-3]	2.0 [0-7]	<0.05
ESSDAI	1.0 [0-14]	4.0 [0-15]	<0.05	3.0 [0-7]	4.0 [0-15]	ns
ESSPRI-pain	3.0 [0-9]	3.0 [0-10]	ns	4.0 [1-8]	3.0 [0-10]	<0.05
RF-IgM	19.0 [5-524]	31.0 [7-417]	ns	10.0 [5-33]	26.0 [7-524]	<0.01
FLC- λ	15.1 [70-68.3]	20.1 [2.6-124.0]	<0.01	13.4 [70-54.5]	18.7 [2.6-124.0]	<0.01
IgG	11.9 [6.5-372]	16.1 [7.4-33.8]	ns	12.8 [6.5-20.6]	14.8 [7.4-372]	ns
C4	0.2 [0.01-0.41]	0.17 [0.00-0.43]	<0.01	0.2 [0.09-0.41]	0.18 [0.00-0.43]	ns
RF-IgA	11.0 [1-500]	103 [0-500]	<0.01	4.5 [1-465]	63 [0-500]	<0.01

C4=Complementfactor 4; EGA=Evaluators Global Assessment; ESSDAI=EULAR Sjögren Syndrome Disease Activity Index; ESSPRI=EULAR Sjögren Syndrome Patient Reported Index; FLC- λ =Free light chain Lambda; IgG=Immunoglobulin G; obj/subj=objective and subjective dryness-group; PSS-QoL=Primary Sjögren Syndrome Quality of Life Questionnaire; RF-IgA=rheumatoid factor Immunoglobulin A; RF-IgM=rheumatoid factor Immunoglobulin M; subj=subjective dryness-group.

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POS0103

C3 AND C4 VARIATIONS IN SLE PREGNANCIES: PRELIMINARY RESULTS FROM THE GR2 STUDY

M. Larosa^{1,2}, V. Le Guern¹, G. Guettrot Imbert¹, E. Diot³, C. Morati-Hafsaoui⁴, N. Abisror Jeannin⁵, N. Morel¹, O. Souchaud-Debouvierie⁶, F. Sarrot-Reynauld⁷, P. Orquevaux⁸, V. Queyrel⁹, T. Goulenok¹⁰, N. Limal¹¹, A. Doria², A. Moltó¹², E. Lazaro¹³, N. Costedoat-Chalumeau¹ on behalf of GR2 Group. ¹AP-HP, Hôpital Cochin; Centre Référence Maladies Rares, Service de médecine interne, Paris, France; ²University of Padova, Rheumatology Unit, Department of Medicine-DIMED, Padova, Italy; ³CHRU de Tours - Hôpital Bretonneau, Service de médecine interne, Tours, France; ⁴CH Annecy Genevois, Service Infectiologie et médecine interne, Annecy, France; ⁵AP-HP, Hôpital Saint-Antoine, Service de Médecine interne, Paris, France; ⁶CHU de Poitiers - Milétrie, Service de Médecine interne, Poitiers, France; ⁷CHU Grenoble, Service de médecine interne, Grenoble, France; ⁸CHU de Reims-Robert Debré, Service de Médecine interne, Reims, France; ⁹Hôpital de l'Archet, CHU de Nice, Service de Médecine interne, Nice, France; ¹⁰AP-HP, Hôpital Bichat, Service de Médecine interne, Paris, France; ¹¹Hôpital Henri Mondor, Service de Médecine interne, Creteil, France; ¹²AP-HP, Hôpital Cochin, Service de Rhumatologie B, Paris, France; ¹³CHU-Hôpital Haut-Lévêque, Service de Médecine interne et maladies infectieuses, Bordeaux, France