also increased from 28.7 to 38.2 per 100 000 adults ($p<0.001$). The mean duration of hospitalisation was 12.5 ± 2.7 days (13 days; 2–26 days) and increased from 11.6 to 12.7 ($p=0.03$).

Abstract FRI0253 – Table 1

	2011	2012	2013	2014	2015
Population size in Minsk, adults	1537880	1555210	1568320	1585480	1598120
Incidence per 100 000	25.0	26.2	35.3	38.0	35.5
Prevalence per 100 000	179	228	248	255	290
Hospitalisation rate per 100 000	28.7	36.8	33.5	33.9	38.2
Hospitalisation duration, days	11.6	12.5	13.1	12.7	12.7

Conclusions: We revealed significant increase in incidence, prevalence as well as hospitalisation rates for gout in adults in Minsk (the Republic of Belarus) for the 5 year period (2011–2015) in 1.4, 1.6 and 1.3 times, correspondingly.

REFERENCES:

- [1] Kuo CF, Grainger MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheum* 2015;11(11):649–62.
- [2] Roddy E, Choi H. Epidemiology of Gout. *Rheum Dis Clin North Am*. 2014;40(2):155–175.
- [3] Dehlin M, et al. Incidence and prevalence of gout in Western Sweden. *Arthritis Res Ther* 2016;18:164.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5549

FRI0254

CLINICAL FEATURES AND RISK FACTORS FOR DEVELOPING GOUT ATTACKS DURING ANTI-TUBERCULOSIS MEDICATION: A CASE-CONTROL STUDY IN SOUTH KOREA

¹Y.-J. Ha, S.W. Chung², J. Lee³, E.H. Kang¹, Y.J. Lee¹, Y.W. Song³. ¹Division Of Rheumatology, Department Of Internal Medicine, Seoul National University Bundang Hospital, Seongnam; ²Division Of Rheumatology, Department Of Internal Medicine, Incheon Sarang Hospital, Incheon; ³Division Of Rheumatology, Department Of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of

Background: Gout is a form of inflammatory arthritis that develops in some people with hyperuricemia. Several drugs may induce hyperuricemia and gout attack. Some anti-tuberculosis (TB) medications are also known to increase uric acid level and trigger acute gout attack. However, there have been no well-described studies for gout during anti-TB therapy.

Objectives: To investigate the clinical features and risk factors of gout attacks following anti-TB treatment in South Korea.

Methods: We conducted the case-control study including 49 patients who developed gout attack following anti-TB medications and 147 age- and sex- matched TB controls without gout attack. Demographic, clinical features and laboratory findings of patients with gout attacks following anti-TB medication were analysed and compared to those of controls in order to establish risk factors associated with gout attack during anti-TB treatment.

Results: The mean age was 67.7 ± 13.2 years and 39 patients (79.6%) were male. Twenty-four patients (49.0%) had a previous history of gout. The mean time interval to develop gout attack from the initiation of anti-TB therapy was 4.13 ± 4.49 months. The attacks tended to involve lower extremity joints (43/49, 87.8%), especially the ankle and the first metatarsophalangeal joint. Factors associated with experiencing gout attack during anti-TB medication were higher body mass index (BMI, 23.7 ± 3.6 vs 21.8 ± 3.6 , $p=0.003$), higher pre-treatment uric acid level (7.2 ± 2.5 vs 6.2 ± 1.7 mg/dL, $p<0.001$), previous history of gout (49.0% vs 1.4%, $p<0.001$), absence of dyslipidemia (4.1% vs 16.3%, $p=0.008$), and decreased renal function (eGFR 63.6 ± 27.5 vs 82.6 ± 29.9 , $p=0.003$). In multivariate model, higher BMI, chronic kidney disease (CKD, eGFR <60 ml/min/1.73m²), previous history of gout, and pre-treatment hyperuricemia (uric acid ≥ 6.8 mg/dL) were

found to be independent risk factors for gout attack following anti-TB medication (table 1).

Abstract FRI0254 – Table 1. Multivariate analysis of risk factors for post-TB medication gout

	Odds ratio	95% CI	p-value
Body mass index (BMI)	1.202	1.029–1.403	0.020
Previous history of gout	71.39	12.790–398.467	<0.001
Chronic kidney disease (eGFR<60 ml/min/1.73m ²)	2.794	1.012–7.719	0.047
Pre-treatment hyperuricemia (Serum uric acid ≥ 6.8 mg/dL)	4.866	1.770–13.378	0.002

Conclusions: TB patients with obesity, history of gout, pre-treatment hyperuricemia, and CKD have higher risk for having gout attack following anti-TB medication. When starting anti-TB therapy in TB patients with these risk factors, physicians should pay attention to the development of gout attack and educate the patients.

REFERENCES:

- [1] Gerdan G, Nurullah A, Ucan ES, et al. Paradoxical increase in uric acid level with allopurinol use in pyrazinamide-induced hyperuricemia. *Singapore Med J*. 2013;54(6):e125–128.
- [2] Postlethwaite AE, Bartel AG, Kelley WN. Hyperuricemia due to ethambutol. *N Engl J Med*. 1972;286(14):761–762.
- [3] Ben Salem C, Slim R, Fathallah N, Hmouda H. Drug-induced hyperuricemia and gout. *Rheumatology (Oxford)* 2017;56(5):679–688.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6590

FRIDAY, 15 JUNE 2018

SLE, Sjögren's and APS – etiology.3, pathogenesis and animal models

FRI0255

INJECTION OF CD40 DNA VACCINE AMELIORATES THE AUTOIMMUNE PATHOLOGY OF NON-OBESE DIABETIC MICE WITH SJÖGREN'S SYNDROME

Y.-B. Zhou¹, X. Yuan¹, Q.-K. Wang¹, H. Zhang¹, G.-S. Wang¹, X.-P. Li¹, Y.-P. Wang², X.-M. Li¹. ¹Rheumatology and Immunology, The First Affiliated Hospital of University of Science and Technology of China, Hefei, Anhui, China; ²Westmead Institute for Medical Research, the University of Sydney, Westmead 2145 NSW, Australia

Background: In the patients with primary Sjögren's syndrome (pSS), overexpression of CD40 was reported. The increased CD40 expression contributes to enhance CD40-CD40L interaction and promotes the inflammatory response in various ways.

Objectives: To investigate whether CD40 DNA vaccine could inhibit the immune response and slow the disease progression of SS in non-obese diabetic (NOD) mice.

Methods: Female 8-week-old NOD mice were randomly divided into 3 groups. CD40 DNA vaccine group received pTaget CD40 DNA vaccine at a weekly dose of 50 ug for 4 weeks. Vector and NS group were administered an equivalent amount of empty vector or NS. Serum anti-CD40 antibody was measured by ELISA. Lymphocytes infiltration in the salivary glands was monitored by focus score (FS) calculation. Salivary CD40 was stained by immunohistochemistry. Splenic lymphocyte phenotypes were analysed by flow cytometry. CD40, TNF- α and IL-6 levels in the salivary glands were detected by PCR. Serum ANA was monitored by immunofluorescence.

Results: 1) CD40 DNA vaccination induced anti-CD40 antibody response. We found the positive rate on anti-CD40 antibody in vaccine group was 80% at week 6 and 100% at week 10, which was significantly increased compared with that in nonvaccinated ones ($p<0.05$ and $p<0.01$, respectively)

2) Expression of CD40 decreased in salivary glands in vaccine group

At week 10, CD40 expression on ductal epithelial and endothelial cells in NOD mice of vaccine group was significantly decreased positive staining. CD40 mRNA expression level showed a significantly reduction compared to vector group (0.51 ± 0.31 vs. 1.56 ± 0.53 , $p < 0.05$).

3) Down-regulation of lymphocytes infiltration in the salivary glands of mice in vaccine group

At week 10, infiltration of lymphocytes was inhibited in treated group while increased in control group ($F = 5.275$, $P < 0.05$). FS was significantly decreased in vaccine group as compared to NS group (2.00 ± 1.73 vs. 11.33 ± 5.51 , $P < 0.05$). Average weight of wet salivary gland and the ratio of average salivary gland weight to body weight of NOD mice in vaccine group were significantly lower than that in control groups ($p < 0.05$ and $p < 0.05$, respectively).

4) CD40 DNA vaccine reduced the expression of TNF- α and IL-6 in the salivary glands

In vaccine group, the expression level of TNF- α mRNA in salivary glands were declined significantly as compared to baseline (0.41 ± 0.25 vs. 0.98 ± 0.16 , $p < 0.05$) and IL-6 mRNA expression was down-regulated compared with control groups at week 10 ($p < 0.05$; $p < 0.01$, respectively).

5) Disturbances in spleen DC and plasma cell subpopulations

At week 6, the total numbers of CD11c⁺DC decreased as compared with two control groups ($p < 0.05$ and $p < 0.05$, respectively). CD11c⁺DC and CD19⁺CD138⁺plasma cells were significantly reduced compared to basal level ($p < 0.01$ and $p < 0.05$, respectively).

6) Level of ANA reduced in the vaccine group

At week 10, the expression of ANA in HEp-2 cells is strong positive (++++ in both control groups, but only positive (+) in vaccine group.

Conclusions: These findings indicate that CD40 DNA vaccine can downregulate the expression of proinflammatory cytokines of TNF- α and IL-6, decrease the percentage of DCs and plasma cells, ameliorate the pathologic change in NOD mice with SS, and thus inhibit the autoimmune inflammation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3939

FRI0256 EFFECTS OF ANIFROLUMAB ON OXIDATIVE STRESS AND MACROPHAGE ACTIVATION: NOVEL BIOMARKERS AND IMPACT OF TYPE I INTERFERON BLOCKADE IN SYSTEMIC LUPUS ERYTHEMATOSUS

X. Guo¹, S. Wang¹, L. Wang², L.K. Roskos¹, W.I. White¹. ¹Medimmune; ²AstraZeneca, Gaithersburg, USA

Background: Type I interferons (IFNs) drive several aspects of systemic lupus erythematosus (SLE) etiology and pathophysiology. Anifrolumab, a fully human anti-IFN- α receptor monoclonal antibody, substantially reduced disease activity compared with placebo in a Phase IIb study of SLE patients.¹ Previous results indicated beneficial effects of anifrolumab on dysregulated lymphocyte, neutrophil, and complement systems in SLE.² However, the impact of type I IFN blockade remains to be fully elucidated.

Objectives: We characterised biomarkers for oxidative stress and macrophage activation in SLE and assessed downstream effects of anifrolumab on those two key disease pathways.

Methods: In the MUSE study,¹ 305 patients with moderate to severe SLE were randomised in a 1:1:1 ratio to receive placebo or anifrolumab (300 or 1,000 mg) every 4 weeks for 48 weeks. A four-gene expression assay was used to define type I IFN gene signature (IFNGS) test status. In our study, four protein biomarkers were measured in sera of healthy controls (HCs) and SLE patients with samples available at baseline, and 85, 169, and 365 days after administration, using a multiplex luminex immunoassay. Wilcoxon rank-sum test was used to evaluate baseline protein concentrations and posttreatment changes between different groups.

Results: Two oxidative stress biomarkers, peroxiredoxin 4 (PRDX4) and aldose reductase (AKR1B1), were found in greater serum concentrations in 195 SLE patients than in 20 HCs ($p < 0.01$). Their increased concentrations were associated with greater SLEDAI scores and abnormal anti-dsDNA concentrations ($p < 0.05$). PRDX4 concentrations were greater for IFNGS test-high ($n = 144$) vs IFNGS test-low ($n = 51$) patients ($p < 0.01$), whereas AKR1B1 was not associated with type I IFNGS-test status. Anifrolumab suppressed PRDX4 in IFNGS test-high patients compared with placebo ($p < 0.05$). In contrast, no significant changes were observed for AKR1B1 after anifrolumab treatment. Folate receptor 3 (FOLR3) and CD163 are markers of activated macrophages, the former of which has not been characterised in SLE. Our results demonstrated greater concentrations of both FOLR3 and CD163 in IFNGS test-high than in IFNGS test-low patients and HCs, along with significant associations with SLEDAI score and anti-dsDNA concentrations. Anifrolumab reduced serum concentrations of both FOLR3 and CD163 in IFNGS test-high but not IFNGS test-low patients vs. placebo ($p < 0.05$). Moreover, cellular enumeration data demonstrated anifrolumab-induced upregulation of

monocyte count in IFNGS test-high patients, which may result from reduced activation, apoptosis, and/or tissue infiltration of monocytes/macrophages.

Conclusions: Our results identified PRDX4 as an oxidative stress marker and FOLR3 as a macrophage activation marker associated with disease activities and type I IFNGS test status in SLE. Anifrolumab administration elicits reduced oxidative stress and decreased monocyte/macrophage activation, which may contribute to the clinical efficacy of anifrolumab in SLE patients.

REFERENCES:

- [1] Furie R, et al. Arthritis Rheumatol. 2017;69:376–86.
- [2] Guo X, et al. Ann. Rheum. Dis. 2016;75:118.

Disclosure of Interest: X. Guo Shareholder of: AstraZeneca, Employee of: MedImmune, S. Wang Shareholder of: AstraZeneca, Employee of: MedImmune, L. Wang Shareholder of: AstraZeneca, Employee of: AstraZeneca, L. Roskos Shareholder of: AstraZeneca, Employee of: AstraZeneca, W. White Shareholder of: AstraZeneca, Employee of: MedImmune
DOI: 10.1136/annrheumdis-2018-eular.3842

FRI0257 THE STAT4 SLE RISK ALLELE RS7574865[T] IS ASSOCIATED WITH INCREASED IL-12-INDUCED IFN-GAMMA PRODUCTION IN T CELLS FROM SLE PATIENTS

N. Hagberg¹, M. Joelsson¹, D. Leonard¹, S. Reid¹, M.-L. Eloranta¹, J. Mo², M. Nilsson², A.-C. Syvänen³, Y.T. Bryceson^{4,5}, L. Rönnblom¹. ¹Department of Medical Sciences, Rheumatology and Science for Life Laboratories, Uppsala University, Uppsala; ²Respiratory, Inflammation and Autoimmunity, IMED Biotech Unit, AstraZeneca, Gothenburg; ³Department of Medical Sciences, Molecular Medicine and Science for Life Laboratories, Uppsala University, Uppsala; ⁴Department of Medicine, Center for Hematology and Regenerative Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden; ⁵Department of Clinical Sciences, Broegelmann Research Laboratory, University of Bergen, Bergen, Norway

Background: Genetic variants in the transcription factor *STAT4* are associated with increased susceptibility to systemic lupus erythematosus (SLE) and a more severe disease phenotype.

Objectives: This study aimed to clarify how the SLE-associated intronic *STAT4* risk variant rs7574865[T] affects the function of immune cells in SLE.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from 52 SLE patients in remission (SLEDAI-2K≤4). *STAT4* and *STAT1* protein levels and phosphorylation status in response to interferon (IFN)- α , IFN- γ , or interleukin (IL)-12 were determined, before and after pre-activation of cells with phytohemagglutinin (PHA) and IL-2, in CD56^{dim} NK cells, CD56^{bright} NK cells, B cells, CD4⁺ T cells, CD8⁺ T cells and monocytes by flow cytometry. The frequency of IFN- γ ⁺ cells upon IL-12 or PMA (phorbol 12-myristate-13-acetate) stimulation and the frequency of T-bet⁺ cells was determined in PHA/IL-2 pre-activated cells. Cellular responses and phenotypes were correlated with *STAT4* risk allele carriage (rs7574865[T], 21 homozygous protective, 22 heterozygous and 9 homozygous risk) using an additive linear regression model. Janus kinase inhibitors (JAKi) selective for TYK2 (TYK2i, Compound 35) or JAK2 (JAK2i, BMS-911543) were evaluated for inhibition of IL-12 or IFN- γ -induced activation of SLE PBMCs.

Results: In resting PBMCs, the *STAT4* risk allele was neither associated with protein levels of *STAT4* or *STAT1*, nor cytokine-induced phosphorylation of *STAT4* (pSTAT4) or *STAT1* (pSTAT1). However, following PHA/IL-2-activation, CD8⁺ T cells from *STAT4* risk allele carriers displayed increased levels of *STAT4* ($p = 0.04$), resulting in increased pSTAT4 in response to IL-12 ($p = 0.003$) and IFN- α ($p = 0.04$). Analysis of T cell subsets revealed that the effect was seen in CD45RA⁺CD57⁻ naïve and CD45RA⁺CD57⁺ memory CD8⁺ T cells, but not in CD45RA⁺CD57⁺ memory or CD45RA⁺CD57⁺ effector CD8⁺ T cells. A slight increase in *STAT4* protein levels and IL-12-induced pSTAT4 was also observed in CD4⁺ T cells from *STAT4* risk allele carriers ($p = 0.08$ and $p = 0.09$, respectively). *STAT4* risk allele carriers displayed an augmented IL-12-induced IFN- γ production in CD8⁺ and CD4⁺ T cells ($p = 0.03$ for both), whereas PMA-induced IL-12 production was normal ($p = 0.31$ and $p = 0.10$, respectively). T-bet expression was not correlated to the *STAT4* genotype. The TYK2i and the JAK2i efficiently blocked IL-12 and IFN- γ -induced activation of PBMCs from *STAT4* risk patients, respectively.

Conclusions: T cells from SLE patients carrying the *STAT4* risk allele rs7574865 [T] display an augmented response to IL-12 and IFN- α . This subset of patients may benefit from JAKi treatment.

Disclosure of Interest: N. Hagberg: None declared, M. Joelsson: None declared, D. Leonard: None declared, S. Reid: None declared, M.-L. Eloranta: None declared, J. Mo Employee of: AstraZeneca, M. Nilsson Employee of: AstraZeneca, A.-C. Syvänen: None declared, Y. Bryceson: None declared, L. Rönnblom: None declared