pharmaceutical companies, Antonis Fanouriakis Paid instructor for: Paid instructor for Enorasis, Amgen, Speakers bureau: Paid speaker for Roche, Genesis Pharma, Mylan

DOI: 10.1136/annrheumdis-2020-eular.6255

FRI0171

THE CHANGES OF IMMUNE FUNCTION AND CLINICAL INDEXES WITH SYSTEMIC LUPUS ERYTHEMATOSUS AFTER IMMUNOREGULATORY COMBINATION THERAPIES

X. Liu¹, X. Liu², H. Hou³, X. Li¹ on behalf of Li Xiaofeng Team. ¹The Second Hospital of Shanxi Medical University, Taiyuan, China; ²Taiyuan University of Technology, Taiyuan, China; ³Inner Mongolia Normal University, Huhehaote, China

Background: Recent studies have reported that some drugs such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10 could promote the proliferation and functional recovery of regulatory T cells (Treg) in patients with autoimmune diseases. However, the effects on the balance of Treg cells and pro-inflammatory lymphocytes and long-term efficacy have rarely been reported.

Objectives: To evaluate the changes of peripheral lymphocyte subsets, conventional drugs and remission rate in patients with systemic lupus erythematosus (SLE) after immunomodulatory combination therapies.

Methods: A total of 189 patients with SLE from the Second Affiliated Hospital of Shanxi Medical University from January 2016 to October 2019 were enrolled, who were divided into well-controlled group and untargeted control group taking a full consideration of the patient's symptoms, signs and related laboratory findings. We measured the absolute counts of B, NK, CD8+T and helper T 1 (Th1), helper T 2 (Th2), helper T 17 (Th17) and Treg cells in peripheral blood of patients before immunomodulatory combination therapies and during the 3 months and 6 months of follow-up and 190 sex- and age- matched control individuals using flow cytometry. Moreover, the ratios of various cells to Treg cells were calculated.

Results: Compared with healthy controls, Treg cells in SLE patients were significantly lower before the treatment with immunomodulator, while the ratios of various pro-inflammatory lymphocytes to Treg cells (such as Th2/Treg, Th17/Treg, CD8+T/Treg, etc.) were higher. After 3 months and 6 months with immunomodulatory therapy, the absolute number of Treg cells in peripheral blood of SLE patients increased obviously reaching to normal level. Accordingly, the ratios of various pro-inflammatory lymphocytes to Treg cells recovered. At the same time, the dose of glucocorticoid and disease-modifying antirheumatic drugs (DMARDs) decreased distinctly. Additionally, the well-controlled group was able to maintain a high remission rate, and the untargeted control group could achieve a higher response rate after immunomodulatory treatment.

Conclusion: The imbalance between pro-inflammatory lymphocytes and Treg cells caused by the significant decrease of Treg cells may be the main cause of SLE. And immunomodulatory combination therapies we came up with may reverse the imbalance of proinflammatory lymphocytes and Treg cells, which is an potential and effective treatment for SLE.

References:

- Noack M, Miossec P. Th17 and regulatory T cell balance in autoimmune and inflammatory disease[J]. *Autoimmun Rev*, 2014, 13(6): 668-677.
- Yu A, Snowwhite I, Vendrame F, et al. Selective IL-2 responsiveness of regulatory T cells through multiple intrinsic mechanisms supports the use of low-dose IL-2 therapy in type 1 diabetes. *Diabetes*. 2015;64: 2172-2183.
- Schuiveling M, Vazirpanah N, Radstake TRDJ, Zimmermann M, Broen JCA. Metformin, A New Era for an Old Drug in the Treatment of Immune Mediated Disease? [J]. *Curr Drug Targets*, 2017;18:1-15.

Table1. The changes of remission rate in the no-remission group during follow-up.

Follow-up period	Total patients	Remission	No-remission	Remission rate(%)
Baseline	92	0	92	0
3 Months	72	33	39	45.8 ^a
6 Months	74	42	32	56.8 ^a

a: Compared with baseline; b: Compared with 3 months.

Acknowledgments: We would like to express our sincere gratitude to all our coworkers and collaborators, Jing Luo, Xiangcong Zhao, Chen Zhang, Qi Wu, Congcong Liang, and Rui Fu for their technical support.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5801

FRI0172

THE INFLUENCE OF CALCINEURIN INHIBITORS ON DEVELOPMENT OF CANCER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE OBSERVATIONAL STUDY IN THE LUNA REGISTRY

K. Ichinose¹, T. Igawa¹, M. Okamoto¹, A. Takatani¹, N. Yajima², K. E. Sada³, R. Yoshimi⁴, Y. Shimojima⁵, S. Ono⁶, H. Kajiyama⁷, S. Sato⁸, M. Fujiwara⁹, A. Kawakami¹. ¹Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki, Japan; ²Showa University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Shinagawa-ku, Tokyo, Japan; ³Okayama University Graduate School of Medicine Dentistry and Pharmaceutical Sciences, Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama, Japan; ⁴Yokohama City University Graduate School of Medicine, Department of Stem Cell and Immune Regulation, Yokohama, Japan; ⁵Shinshu University School of Medicine, Department of Medicine (Neurology and Rheumatology), Matsumoto, Japan; ⁶Yokohama City University Medical Center, Center for Rheumatic Diseases, Yokohama, Japan; ⁷Saitama Medical University, Department of Rheumatology and Applied Immunology Faculty of Medicine, Saitama, Japan; ⁸Fukushima Medical University School of Medicine, Department of Rheumatology, Fukushima, Japan; ⁹Yokohama Rosai Hospital, Department of Rheumatology, Yokohama, Japan

Background: It has been reported that the incidence of cancer in patients with systemic lupus erythematosus (SLE) is higher than that in healthy individuals, but the findings are inconsistent¹. In the transplantation field, a few studies indicated an association between the use of immunosuppressants and an increased risk of cancer². Calcineurin inhibitors (CNIs), which include cyclosporine and tacrolimus, have been used for >30 years to treat renal and extrarenal manifestations of SLE, but the effects of exposure to CNIs among SLE patients have not been established.

Objectives: We investigated the incidence of various cancers (including cervical dysplasia) among SLE patients registered in the LUPus registry of NAtionwide institution (LUNA). We also investigate whether the registrants' exposure to CNIs increased the risk of cancer.

Methods: We calculated the standardized incidence ratio (SIR) of cancer among SLE patients based on the age-standardized incidence rate of cancer reported by Japan's Ministry of Health, Labour and Welfare. A multivariate analysis of the risk of cancer was performed using the covariates of age, smoking history, CNI treatment history, maximum steroid dose in the past, and Systemic Lupus International Collaboration Clinics/American College of Rheumatology Damage Index [SDI] value (excluding the occurrence of cancer) at the time of the patient's registration.

Results: We studied 714 patients (663 females; 88.9%). The median age at registry was 44 [interquartile range (IQR): 35–56] years. The median past max. steroid dose was 40 mg/day (IQR: 30–60 mg/day), and the SDI at registration was 1 (IQR 0–2). Smoking history was present in 248 patients (34.9%), and 53 patients (7.4%) experienced cancer complications. Gynecologic malignancies accounted for 71% of all cancers, including 12 cervical dysplasia cases. The standardized incidence rate of cancer in these SLE patients was 1.46 (95%CI: 1.07–1.85, p<0.01). The multivariate analysis showed that a CNI treatment history was not a risk factor for the development of cancer (OR 1.76, 95%CI: 0.63–4.88, p=0.30). After the covariance was adjusted for the propensity score, the risk of cancer in the CNIs group was not increased compared to the non-CNIs group (adjusted OR 2.46, 95%CI: 0.68–8.91, p=0.20).

Conclusion: The incidence of cancer in SLE was higher in the LUNA cohort than in the general population. Our results suggest that CNI treatment for individuals with SLE is not a risk factor for the development of cancer.

References:

- Ladouceur A. et.al, *Expert Rev Clin Immunol*. 2018 Oct;14(10):793-802.
- Gutierrez-Dalmau A. et.al, *Drugs* 2007;67(8):1167-98.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1379

FRI0173

IDENTIFICATION OF RISK FACTORS FOR DEVELOPMENT OF OSTEONECROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

R. Kallas¹, J. Li¹, M. Petri¹. ¹Johns Hopkins University School of Medicine, Baltimore, United States of America

Background: Patient with Systemic Lupus Erythematosus (SLE), particularly those who received corticosteroids are at a high risk of osteonecrosis (ON).

Objectives: In this analysis, we aimed at determining the predictors of ON in a longitudinal lupus cohort in which Caucasian and African-American ethnicities are well represented.

Methods: The data were reviewed from the initiation of the cohort in 1987 until October 2019. 2428 patients were included in the analysis based on 224295 person-months of follow-up. ON was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR) Damage Index. To calculate the rate of ON in each demographic and clinical subgroup, we calculated the number of ON events divided by the number of person-months at risk and converted this rate to rates per person-year. To assess the relationship between risk factors and rates of ON events, we used the pooled logistic regression. Rate ratios were adjusted for age. After identifying a set of variables related to ON incidence, we fit a final multivariable model to identify the most important risk factors for incident ON.

Results: 287 ON cases were identified, giving a point prevalence of 11%. ON cases that occurred before cohort entry were excluded. 122 incident events of ON occurred after cohort entry and were included in the final analysis. In the multivariable analysis, African-Americans were at twice the risk for ON compared to Caucasians. Male gender and smokers had about 80% and 50% increased risk of ON compared to females and non-smokers respectively. For every 10 year increase in the age there was a 20% reduced risk for ON. Patients diagnosed after the 1990's had a 50% reduced risk of ON compared to those diagnosed before 1990's. A highest daily dose of prednisone of 40 mg or higher, even when administered for a month or less, increased significantly the risk of ON. Use of pulse steroid was not associated with an increased risk of ON.

Conclusion: Ethnicity remains an important determinant in the risk of ON. African-American SLE patients are at double the risk of ON compared to Caucasians. APOL1 risk variants confer an increased risk of ON in this high-risk ethnic group. Oral prednisone more than 40mg daily administered for a month or less, at any point in the disease course, remains the most important predictor of ON. Prednisone-free or prednisone-limited regimens should be reinforced in SLE trials.

Table 1. Associations between ON rates and corticosteroids dose and duration based on a multivariable model

Predictor		RR (95% CI)	p-value
Max prednisone and duration	0- 40 mg/day for <=1 month	1.00 (Ref)	
	0- 40 mg/day for >1 month	1.49 (0.68, 3.26)	0.3162
	40-60 mg/day for <=1 month	2.76 (1.18, 6.39)	0.0182
	40-60 mg/day for >1 month	3.87 (1.73, 8.62)	0.0009
	>=60 mg/day for <=1 month	6.6 (3.37, 12.93)	<0.0001
	>=60 mg/day for >1 month	5.15 (2.55, 10.4)	<0.0001
Sex	Male (vs. Female)	1.79 (1.04, 3.10)	0.0373
Ethnicity	African American (vs. Caucasian)	1.94 (1.32, 2.83)	0.0007
Year of SLE diagnosis	1990 and after (vs. before 1990)	0.53 (0.36, 0.77)	0.0008
Age	Per 10 year increase	0.77 (0.66, 0.89)	0.0006
Smoking	Ever (vs. never)	1.51 (1.04, 2.19)	0.0293

Table 2. Associations between ON rates and pulse steroid stratified by max prednisone

Subgroup	No. of ONs	Person years	Rate per 1000 person years	Age-adjusted RR (95% CI)	Age-adjusted p-value
Pulse among those with maximum prednisone dose of <40 mg	No	21	6752.1	3.11	1.00 (Ref)
	Yes	2	387.8	5.16	1.69 (0.40, 7.20)
Pulse among those with maximum prednisone dose of >=40 mg	No	88	7202.3	12.2	1.00 (Ref)
	Yes	8	959.2	8.3	0.71 (0.35, 1.48)
Pulse among those with maximum prednisone dose of >=60 mg	No	64	4329.9	3.11	1.00 (Ref)
	Yes	7	622.4	5.16	0.79 (0.36, 1.72)

Acknowledgments: The Hopkins Lupus Cohort was funded by NIH Grant R01-AR069572

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5073

FRI0174

THE LONGER THE DELAY IN DIAGNOSIS, THE WORSE THE OUTCOME IN SLE – CROSS SECTIONAL ANALYSIS OF A GERMAN LONG-TERM STUDY (LULA COHORT)

A. Kernder¹, J. Richter¹, R. Fischer-Betz¹, B. Winkler-Rohlfing², M. Aringer³, M. Schneider¹, G. Chehab¹. ¹Department of Rheumatology & Hiller-Research Unit Rheumatology, Düsseldorf, Germany; ²German Lupus Self-Help

Community, Wuppertal, Germany; ³University Medical Center and Faculty of Medicine Carl Gustav Carus, Division of Rheumatology, Department of Medicine III, Dresden, Germany

Background: Patients with systemic lupus erythematosus (SLE), even compared to those with other rheumatic diseases, are thought to often experience a long delay from the onset of symptoms to diagnosis.

Objectives: Our aim was to study the association of this delay to the long-term outcome of the disease.

Methods: Information on demographics, onset of first symptoms, first physicians visit, time of diagnosis and organ involvement was assessed by self-reported questionnaires among SLE patients in Germany in 2011 (LuLa cohort, n=585). Disease related damage (Brief Index of Lupus Damage; BILD), disease activity (Systemic Lupus Activity Questionnaire; SLAQ) and health related quality of life (SF-12) were chosen as proxies for outcome. The association to the outcome of the disease was analyzed by linear regression analysis, adjusted for age, disease duration, organ involvement and sex.

Results: In our cohort, the mean reported duration between the onset of symptoms and the diagnosis of SLE was 46 months (SD 73), which includes 13 months (SD 41) between the onset of symptoms and the first physicians visit. The participating patients were diagnosed between 1960 and 2004.

Linear regression analysis revealed that longer time to diagnosis was associated with (i) higher disease activity (SLAQ, p<0.0001, β =0.199), (ii) higher disease-related damage (BILD, p=0.002, β =0.137) and (iii) lower health-related quality of life (SF-12 physical p=0.004, β =-0.136, SF-12 mental p=0.004, β =-0.143) in the year 2011. The organ involvement at the time of diagnosis did not alter these results.

Conclusion: A delay in diagnosis was associated with a worse outcome in SLE (disease activity, disease-related damage and health-related quality of life). Therefore, an early diagnosis seems to be important to improve the long-term outcome of the disease. It will be interesting to see whether adopting the new EULAR/ACR 2019 classification criteria can contribute to a faster diagnosis and a better outcome in consequence.

The LuLa study is supported by unrestricted grants from GlaxoSmithKline and UCB Pharma.

Disclosure of Interests: Anna Kernder Grant/research support from: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Jutta Richter Grant/research support from: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Rebecca Fischer-Betz Consultant of: UCB, Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celgene, Chugai, GSK, Janssen, Lilly, Medac, MSD, Novartis, Roche, UCB, Pfizer., Borge Winkler-Rohlfing: None declared, Martin Aringer Consultant of: Boehringer Ingelheim, Roche, Speakers bureau: Boehringer Ingelheim, Roche, Matthias Schneider Grant/research support from: GSK, UCB, Abbvie, Consultant of: Abbvie, Alexion, Astra Zeneca, BMS, Boehringer Ingelheim, Gilead, Lilly, Sanofi, UCB, Speakers bureau: Abbvie, Astra Zeneca, BMS, Chugai, GSK, Lilly, Pfizer, Sanofi, Gamal Chehab Grant/research support from: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study.

DOI: 10.1136/annrheumdis-2020-eular.1595

FRI0175

SEMI-DYNAMIC MRI OF THE EXTENSOR DIGITORUM TENDONS IN JACCOUD ARTHROPATHY

T. Kirchgesner¹, M. Stoeniou¹, N. Michoux¹, X. Libouton¹, F. Houssiau¹, B. Vande Berg¹. ¹Cliniques Universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium

Background: Jaccoud arthropathy (JA) is a rare joint deformity mostly associated with systemic lupus erythematosus (SLE) (1). JA may be defined as a reversible deformity of the hands during flexion with ulnar deviation and swan neck deformities of the fingers. The physiopathology and the mechanisms leading to JA still remain to be elucidated.

Objectives: To test the hypothesis that Jaccoud arthropathy (JA) in systemic lupus erythematosus (SLE) patients is associated with abnormal extensor digitorum (ED) tendons displacement during flexion of the metacarpophalangeal (MCP) joints.

Methods: 16 SLE patients with JA (JA+), 12 SLE patients without JA (JA-) and 24 control subjects were included in the study. Transverse spin echo T1-weighted MR sequences of the MCP joints in flexion and in extension were obtained in each hand of SLE patients and in one randomly-selected hand of control subjects. Two radiologists separately measured the amplitude and the direction of the displacement of the ED tendons with respect to the midline at the level of the MCP joints. Statistical analysis included two-way ANOVA with random effects to assess differences in amplitude (p<0.0083), Fisher-Freeman-Halton exact test to