References:

- [1] Yoshimura Y, Ishijima M, Ishibashi M, Liu L, Arikawa-Hirasawa E, Machida S, Naito H, Hamada C, Kominami E. *J Orthop Sci.* 2019 Nov;24(6):1094-1104. doi: 10.1016/j.jos.2019.08.009. Epub 2019 Sep 3.
- [2] Siu PPY, Cheung PWH, Cheung JPY. *J Orthop Sci.* 2019 Nov;24(6):1110-1117. doi: 10.1016/j.jos.2019.07.012. Epub 2019 Aug 14.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3625

AB0197

INCREASED CIRCULATING ADIPONECTIN IS AN INDEPENDENT DISEASE ACTIVITY MARKER IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY USING THE KURAMA DATABASE

M. Katsushima¹, M. Hashimoto², M. Shirakashi¹, T. Yoshida³, W. Yamamoto⁴, K. Murakami¹, K. Murata², K. Nishitani², M. Tanaka², H. Ito², S. Matsuda⁵.

¹Kyoto University, Department of Rheumatology and Clinical Immunology, Kyoto, Japan; ²Kyoto University, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan; ³Kyoto Prefectural University of Medicine, Department of Nursing, Kyoto, Japan; ⁴Kurashiki Sweet Hospital, Department of Health Information Management, Kurashiki, Japan; ⁵Kyoto University, Department of Orthopedic Surgery, Kyoto, Japan

Background: Adiponectin is a major adipokine with pleiotropic effects on inflammatory conditions including rheumatoid arthritis (RA). Adiponectin generally has anti-atherogenic effects, and its serum level inversely correlates with body mass index (BMI) and visceral fat area (VFA). On the other hand, several studies have indicated a deleterious role of adiponectin in RA progression [1]. Recently, both low BMI and increased serum adiponectin have been reported as poor prognostic factors of RA [2, 3]. However, large-scale surveys have not been done focusing on both BMI and serum adiponectin, and it is unclear which factor provides further contribution to RA disease activity. In addition, the effects of biological disease-modifying antirheumatic drugs (bDMARDs) and Janus kinase (JAK) inhibitors on serum adiponectin are largely unknown.

Objectives: To clarify the relationship among serum adiponectin, body composition, current disease activity and therapeutic agents of RA.

Methods: We conducted a cross-sectional study in RA patients under treatment with agents including bDMARDs and JAK inhibitors. A total of 351 subjects from the Kyoto University RA Management Alliance cohort (KURAMA) were enrolled. We classified the participants into five body composition groups (overweight with or without visceral adiposity, normal with or without visceral adiposity, and underweight), according to the cut-off points for obesity and visceral fat used in Japan: BMI, 18.5 kg/m² for underweight and 25.0 kg/m² for obesity, and VFA, 100 cm² for visceral adiposity. Differences of continuous variables among the five groups were assessed by the Steel-Dwass test or one-way analysis of variance (ANOVA). We adopted a multiple standardized linear regression model to analyze effects of serum adiponectin level on DAS28-ESR.

Results: Serum adiponectin levels (20.9±12.5 vs. 14.7±8.4 µg/ml, $p < 0.001$) and DAS28-ESR (3.04±1.0 vs. 2.63±0.9, $p = 0.017$) in the underweight group were significantly higher than those in the others. In multiple regression analysis, serum adiponectin level, but not BMI, was positively correlated with DAS28-ESR (estimate = 0.0127, $p = 0.0258$). Subanalysis also showed that the use of bDMARD or JAK inhibitor did not have an obvious influence on circulating adiponectin.

Conclusion: In the multiple regression analysis we revealed a positive and independent correlation between serum adiponectin and DAS28-ESR in Japanese RA patients. Thus, serum adiponectin is an potential marker reflecting high disease activity of RA regardless of current medications.

References:

- [1] Frommer KW, Zimmermann B, Meier FM, Schroder D, Heil M, Schaffler A, et al. Adiponectin-mediated changes in effector cells involved in the pathophysiology of rheumatoid arthritis. *Arthritis Rheum.* 2010;62(10):2886-99.
- [2] Kaufmann J, Kielstein V, Kilian S, Stein G, Hein G. Relation between body mass index and radiological progression in patients with rheumatoid arthritis. *Journal of Rheumatology.* 2003;30(11):2350-5.
- [3] Ebina K, Fukuhara A, Ando W, Hirao M, Koga T, Oshima K, et al. Serum adiponectin concentrations correlate with severity of rheumatoid arthritis evaluated by extent of joint destruction. *Clin Rheumatol.* 2009;28(4):445-51.

Acknowledgments: We would like to thank to Ms. Sumie Nakagawa for management of blood specimens, Ms. Noriko Kitayama and Ms. Maki Yoneyama for support of the patients. We also thank Drs. Takao Fujii, Chicashi, Terao,

Masahide Hamaguchi, Hiroyuki Yoshitomi, and Masahiro Ishikawa for their thoughtful comments.

Disclosure of Interests: Masao Katsushima: None declared, Motomu Hashimoto Grant/research support from: Bristol-Myers Squibb, Eisai, and Eli Lilly and Company., Speakers bureau: Bristol-Myers Squibb and Mitsubishi Tanabe Pharma., Mirei Shirakashi: None declared, Tamami Yoshida: None declared, Wataru Yamamoto: None declared, Kosaku Murakami Speakers bureau: AbbVie, Eisai, and Mitsubishi Tanabe Pharma., Koichi Murata Grant/research support from: KMurata belong to a department that has been financially supported by four pharmaceutical companies (Mitsubishi-Tanabe, Chugai, AYUMI and UCB Japan)., Employee of: KMurata belong to a department that has been financially supported by four pharmaceutical companies (Mitsubishi-Tanabe, Chugai, AYUMI and UCB Japan)., Speakers bureau: KMurak has received speaking fees, and/or consulting fees from Eisai Co. Ltd, Chugai Pharmaceutical Co. Ltd., Pfizer Japan Inc, Bristol-Myers Squibb, Mitsubishi-Tanabe Pharma Corporation, UCB, Daiichi Sankyo Co. Ltd. and Astellas Pharma Inc., Kohei Nishitani Grant/research support from: KN belong to a department that has been financially supported by four pharmaceutical companies (Mitsubishi-Tanabe, Chugai, AYUMI and UCB Japan)., Masao Tanaka Grant/research support from: AbbVie, Asahi Kasei Pharma, Astellas Pharma, Ayumi Pharmaceutical, Chugai Pharmaceutical, Eisai, Mitsubishi Tanabe Pharma, Taisho Pharmaceutical, and UCB Japan.

Speakers bureau: AbbVie, Asahi Kasei Pharma, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Eli Lilly and Company, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma, Novartis Pharma, Pfizer, Taisho Pharmaceutical, Takeda Pharmaceutical, and UCB Japan., Hiromu Ito: None declared, Shuichi Matsuda: None declared

DOI: 10.1136/annrheumdis-2020-eular.3001

AB0198

SMOKING AND POSITIVITY OF RHEUMATOID FACTOR AND ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY IN THE GENERAL POPULATION

G. Kidoguchi¹, S. Fukui¹, T. Nakai¹, S. Kawaai¹, H. Ozawa¹, Y. Ikeda¹, A. Koido¹, Y. Ohara¹, H. Shimizu¹, K. Yamaguchi¹, H. Tamaki¹, M. Okada¹.

¹St. Luke's International Hospital, Immuno-Rheumatology Center, Chuo City, Japan

Background: It is well known that rheumatoid arthritis (RA) occurs due to environmental risk factors in addition to genetic risk factors. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) are strongly associated with RA, and these biomarkers could turn to be positive before development of clinical symptoms. While smoking, particularly Brinkman index (BI) is well known as a risk factor for RA and ACPA positivity, it is still unclear whether smoking intensity or smoking duration contribute more to positive RF and ACPA.

Objectives: This study aims to evaluate risk factors for RF and ACPA positivity in the general population. It also describes whether smoking intensity, duration, and BI are significant.

Methods: This is a cross-sectional, observational, single center study. We reviewed the baseline characteristics of the general population who checked RF and ACPA at Preventive Medicine Center in St. Luke's International Hospital, Tokyo, Japan from January 2004 to December 2018.

The data for basic demographics, dietary habit, smoking intensity, smoking duration, BI, and blood tests including RF and ACPA were extracted. The data was analyzed statistically.

Results: A total of 127472 people who checked RF are included. Of these 127472 people, 64504 (50.6%) are male and the mean age was 44.9 years. RF was positive in 11477 people (9.0%). Among these, 1667 (1.2%) were checked for ACPA, and 21 people (1.3%) had positive ACPA. None of variables demonstrated significant association with RF positivity. In contrast, BI and smoking duration was significantly associated with an increased risk of ACPA positivity (13.3 years vs 7.49 years, p value = 0.023), although the number of cigarettes smoked was not. The smoking duration for 10 years or more was associated with an increased risk of ACPA positivity even after adjusted for age and sex (adjusted hazard ratio: 2.47 [95% confidence interval: 1.04-5.87]; $p=0.04$).

Conclusion: In this study, no significant risk factor for positive RF was found. Even smoking was not associated with RF positivity. On the other hand, smoking duration, not smoking intensity was significantly associated with an increased risk of ACPA positivity.

References:

- [1] Verpoort KN. Association of smoking with the constitution of the anti-cyclic citrullinated peptide response in the absence of HLA-DRB1 shared epitope alleles. *Arthritis Rheum* 2007;56:29138.

Table 1. Patient characteristics with RF and ACPA positivity

	RF positive (n=11477)	RF negative (n=115995)	p value	ACPA positive (n=21)	ACPA negative (n=1646)	p value
Age	44.86 (12.32)	44.94 (12.47)	0.54	37.90 (9.07)	45.26 (12.58)	0.008
Male (%)	5659 (49.3)	57309 (49.4)	0.845	11 (52.4)	834 (50.7)	1
Body Mass Index	22.33 (3.38)	22.35 (3.40)	0.521	21.64 (3.28)	22.34 (3.37)	0.346
Smoker, total (%)	4509 (39.3)	45738 (39.4)	0.772	12 (57.1)	642 (39.0)	0.115
Current smoker (%)	1959 (17.1)	20483 (17.7)	0.114	8 (38.1)	277 (16.8)	0.017
Previous smoker (%)	2550 (22.2)	25255 (21.8)	0.271	4 (19.0)	365 (22.2)	1
Brinkman index	144.8 (299.3)	145.2 (313.8)	0.897	280.9 (409.7)	145.3 (300.3)	0.041
Number of cigarettes (/day)	17.7 (18.5)	17.4 (13.3)	0.166	19.8 (12.0)	17.4 (12.1)	0.511
Smoking Duration (years)	7.43 (11.68)	7.45 (11.66)	0.851	13.33 (14.11)	7.49 (11.68)	0.023
Alcohol Drinker (%)	6972 (60.7)	70010 (60.4)	0.418	10 (47.6)	1005 (61.1)	0.261
Alcohol Intake (g/ day)	13.67 (21.88)	13.58 (21.32)	0.676	16.70 (26.89)	14.06 (22.16)	0.59
Exercise $\geq$ 3 times/ week (%)	2792 (24.3)	28293 (24.4)	0.882	5 (23.8)	402 (24.4)	1
White blood cell (103/ μ L)	5.32 (1.46)	5.35 (1.50)	0.13	5.59 (2.05)	5.37 (1.54)	0.52
Hemoglobin (g/dL)	13.82 (1.44)	13.82 (1.45)	0.753	14.12 (1.03)	13.83 (1.43)	0.36
Creatinine (mg/dL)	0.73 (0.20)	0.73 (0.25)	0.194	0.76 (0.16)	0.73 (0.18)	0.586
AST (U/L)	21.89 (9.39)	21.93 (11.65)	0.782	20.95 (6.02)	21.68 (8.29)	0.69
LDL cholesterol (mg/dL)	115.41 (30.90)	115.48 (30.77)	0.815	112.62 (33.26)	115.36 (31.03)	0.688
Triglyceride (mg/dL)	97.63 (78.46)	97.70 (80.36)	0.929	100.57 (63.40)	97.85 (78.37)	0.874
Uric Acid (mg/dL)	5.32 (1.42)	5.33 (1.42)	0.623	5.76 (1.34)	5.34 (1.42)	0.172

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.4134

AB0199

**GENES PREDICTIVE ON THE EFFICACY OF
INFLIXIMAB IN THE TREATMENT OF RHEUMATOID
ARTHRITIS: A PROSPECTIVE, MULTI-CENTRE,
CLINICAL PERFORMANCE EVALUATION STUDY FOR
AN IN-VITRO DIAGNOSTICS MEDICAL DEVICE**

E. Kiss¹, G. Poór¹, G. Zahuczky², K. Tauberné Jakab³, M. Sebeszta³, T. Ponyi³, Z. Holló³. ¹National Rheumatology and Physiotherapy Institute, Budapest, Hungary; ²UD-GenoMed Medical Genomic Technologies Ltd, Debrecen, Hungary; ³Egis Pharmaceuticals PLC, Budapest, Hungary

Background: Approximately 30% of rheumatoid arthritis (RA) patients fail to respond to first biological therapy, thus treatment selection of biologic therapy for patients with RA is of high importance. The lack of biomarkers to predict specific biological treatment response, in the case of non-responder (NR) patients leads to unnecessary exposure, delay of adequate therapy, progression of the disease and therapy cost increase. Predicting the patient's responsiveness to the first biological therapy is still an unmet need in the clinical setting. Predictive in vitro testing would have a significant effect on the administration of biological therapy, on the real life implementation of cost effective personalized therapy.

Objectives: The purpose of this in vitro diagnostic medical device study was to demonstrate that particular gene expression profiles as genomic biomarkers (i.e. the IVD medical device) predict therapeutic response to infliximab, discriminate between responders and non-responders to infliximab treatment. Responders were defined if they reached DAS target value DAS28 $\leq$ 3.2 at 6 month (M6).

Methods: 110 bionaire patients were enrolled with moderate-high activity RA (DAS28-CRP >3.2), who have responded inadequately to DMARDs (including methotrexate), after they have been assigned to infliximab treatment. All patients received commercially available infliximab, procured according to SmPC, local guidelines and regulations in this non-interventional clinical study. The clinical response was evaluated according to the change from baseline in disease activity at M6. Clinical characteristics (RA duration, smoke, steroid treatment, etc.) and serological parameters (RF, ACPA, aCVM) were collected. A 3rd visit scheduled around week 22 (M6) and change of DAS28-CRP value from the baseline has been evaluated. Gene expression profiling was performed from blood samples taken at month 0 (M0); - just before the first infliximab infusion. Global gene expression profiling was performed to identify differentially expressing genes using RNA sequencing. The set of differentially expressing genes were further reduced with a combination of machine learning modelling and various feature elimination methods. The expression of the reduced gene set was confirmed and further analysed using reverse-transcription and quantitative real-time PCR.

Results: A total of 250 genes were identified by a combination of differential gene expression analyses, feature elimination techniques and various machine learning modelling methods of which 44 genes showed significant differences between NR and good responder groups. Preliminary interim analysis identified associations between gene expression and clinical response/ non-response to infliximab therapy.

Table. Three models containing gene expression + clinical data sets illustrates some statistical characteristics

Modell building_ID	Accuracy	Sensitivity	Specificity	Modell Verification	Accuracy	Sensitivity	Specificity
00232	100.00	100.00	100.00	00232	88	88.89	87.50
00249	98.82	96.55	100.00	00249	84	77.78	87.50
00270	98.82	96.55	100.00	00270	88	77.78	93.75

Conclusion: Our preliminary analysis shows that this set of genes and selected clinical parameters are predictive markers for infliximab specific response in RA patients. Ongoing work involves the clinical validation of these results in an independent patient cohort (n=60). This approach provides the opportunity to develop an in vitro diagnostic test method for the prediction of infliximab treatment responsiveness in bionaire rheumatoid arthritis patients, hence to personalize infliximab therapy for these patients.

Disclosure of Interests: Emese Kiss Consultant of: EK has received consultancy fees from Egis., Gyula Poór Consultant of: GyP has received consultancy fees from Egis and he was the coordinating investigator in this study, Gábor Zahuczky Grant/research support from: Egis, Katalin Tauberné Jakab Employee of: Egis., Miklós Sebeszta Employee of: Egis., Tamás Ponyi Employee of: Egis., Zsolt Holló Employee of: Egis.

DOI: 10.1136/annrheumdis-2020-eular.5849

AB0200

**SHORT AND MID-TERM OUTCOME OF FOREFOOT
SURGERY FOR PATIENTS WITH RHEUMATOID
ARTHRITIS**

R. Kurose¹. ¹Hirosaki Memorial Hospital, Hirosaki, Japan

Background: Patients with rheumatoid arthritis (RA) have frequently painful foot deformities. These deformities including hallux valgus, dorsal dislocation of the metatarsophalangeal (MTP) joints and hammer toe deformity of the lesser toes are associated with disability in daily activities.

Objectives: The aim of this study is to investigate short and mid-term outcome of forefoot surgery for patients with RA.

Methods: We investigated 28 patients with 39 foets who underwent forefoot surgery between January 2010 and December 2018 and followed for more than one year after surgery. Swanson implant arthroplasty or metatarsal osteotomy was performed for big toe, and shortening oblique osteotomy (SOO) was performed for the II-V toes. Examination items were as follows; plain X-ray changes in the angle of hallux valgus (HVA), the angle between the first and second metatarsal bones (M1/2), and the angle between the first and fifth metatarsal bones (M1/5) after surgery. The progress of painful hyperkeratosis and bunions, Japanese Society for Surgery of the foot standard rating system (JSSF scale), the recurrence of deformity and bone fusion, complications, and patient satisfaction were also examined.

Results: The patients followed were 24 women with 34 feet and 4 men with 5 feet, and average age at the time of surgery was 66.1 years. HVA improved from average of 39.7 degrees to 20.2 degrees one month after surgery, but increased slightly to 23.5 degrees one year after surgery. Painful hyperkeratosis and bunions tended to disappear one month after surgery, and JSSF scale significantly improved at the final observation. One year after surgery, the bone fusion rate of big toe was 100%, but 7.8% of the metatarsal bone underwent SOO had non-union. The complications after surgery were one infection at the surgical site, one necrosis at the tip of the toe, and one infection of Swanson implant. Patient satisfaction at the final observation was high.

Conclusion: Forefoot surgery for RA has problems such as recurrence, non-union, and infections, but it is considered to be a useful treatment because that pain by hyperkeratosis and bunions disappears and ADL improves.

References:

- [1] Sung IH, Sung YK, Huh DR, Kim SJ. A comparative study on the results of the modified Ludloff osteotomy for hallux valgus deformities with minimal erosion of the metatarsophalangeal joints in rheumatoid patients versus non-rheumatoid patients.. Mod Rheumatol 2015; 25(5): 694-700.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5023