later (w16), with respect to the 5 clustering PROs as well as for coping behavior, illness perceptions and social support.

Results: Analyses revealed 3 distinct clusters. Details are depicted in Table 1. Of 140 patients, 77.9% were assigned to the 'concordant to disease activity' cluster, 9.3% to the 'dominant fatigue' cluster and 12.9% to the 'dominant pain and fatigue' cluster. When comparing the concordant cluster with both discordant clusters, differences at BL and w16 were shown, with small effects on patients' evaluation of their disease at year 1, such as more negative beliefs about the consequences of RA at w16 in patients reporting dominant pain and fatigue at year 1. Few differences with medium effects were identified, such as a moderately higher use of avoidance as a coping style at w16 and a stronger belief that symptoms can be explained by RA at w16, in patients reporting dominant fatigue at year 1 compared to patients in the concordant cluster. Large differences between patients in concordant and discordant clusters were found for pain and fatigue levels, which were already higher after 4 months of treatment for those patients reporting persistent pain and fatigue at year 1.

Abstract THU0103 –Table 1.

Table 1. Mean scores at year 1 of the patient-reported outcomes used to assign patients to a cluster (n=140 persistent responders)

	Clusters		
	Concordant to disease activity n=109 (77.9%)	Dominant fatigue n=13 (9.3%)	Dominant pain and fatigue n=18 (12.9%)
Pain (VAS 0-100)	7	15	45
Fatigue (VAS 0-100)	10	70	42
Functionality (HAQ 0-3)	0.07	0.24	0.26
RA-related quality of life (RAQoL 0-30)	3.92	6.21	5.55
Sleep quality (PSQI 0-21)	5	6	5

Note: RA: Rheumatoid arthritis; VAS: Visual Analog Scale; HAQ: Health Assessment Questionnaire; RAQoL: Rheumatoid Arthritis Quality of Life questionnaire; PSQI: Pittsburgh Sleep Quality Index; Higher scores indicate worse pain, worse fatigue, more functional loss, worse health-related quality of life and worse sleep quality. Clinical response was defined as achieving a disease activity score (DAS28CRP) <2.6. Persistent response was defined as an early clinical response at week 16, sustained between week 16 and year 1.

Conclusion: Three distinct groups of persistent responders with early RA were identified based on their 1-year PRO profile. The majority of patients were well-synchronized, reporting very low pain and fatigue levels in concordance with their well-controlled disease activity. One in 5 persistent responders, however, seemed to have unmet needs. In view of early identification of patients at risk of poor wellbeing despite good disease control, early pain and fatigue levels and certain coping behavior and illness perceptions were recognized as potential targets for future interventions.

Disclosure of Interests: Kristien Van der Elst: None declared, Patrick Verschueren Grant/research support from: Unrestricted Pfizer Grant for Early RA research, Diederik De Cock: None declared, An De Groef: None declared, Veerle Stouten: None declared, Sofia Pazmino: None declared, Johanna Vriezekolk: None declared, Johan Joly: None declared, Philip Moons: None declared, Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead

DOI: 10.1136/ANNRHEUMDIS-2019-EULAR.3629:

THU0104 HIGH-PERFORMANCE CHEMICAL ISOTOPE LABELING LIQUID CHROMATOGRAPHY MASS SPECTROMETRY FOR DISCOVERY OF METABOLITE BIOMARKERS OF RHEUMATOID ARTHRITIS

Xiaohang Wang¹, Joel Paschke², Rana Dadashova², Edna Hutchings², Li Liang¹, Walter P Maksymowych². ¹University of Alberta, Chemistry, Edmonton, Canada; ²CaRe Arthritis, Edmonton, Canada

Background: Early diagnosis of rheumatoid arthritis (RA) is hampered by suboptimal accuracy of currently available serological biomarkers. Recent advancements in metabolomic profiling include liquid chromatography mass spectrometry (LC-MS) and in-depth profiling of amine/phenol and carboxyl submetabolomes, resulting in 1000-fold increase in detection sensitivity, and universal metabolome-standard methodology to facilitate metabolome comparisons among different data sets.

Objectives: We aimed to identify a metabolite signature with consistently high accuracy for RA.

Methods: Sera from 2 RA cohorts were analyzed: Cohort A samples were from 50 RA patients, 39 female (mean age 49.9), 11 male (mean age 47.8), symptom duration <3 years, DAS >3.7, naïve to b-DMARD, and 50 age and sex-matched healthy controls. Cohort B samples were from 50 RA patients, 40 female (mean age 53.4), 10 male (mean age 57.2), symptom duration <5 years, samples from both pre- and post- (3 months) treatment with TNFi and a second set of 50 age and sex-matched healthy controls. Amine/phenol- and carboxyl-containing metabolites were labeled by ¹²C-dansyl (Dns) chloride and ¹²C-dimethylaminophenacyl (DmPA) bromide, respectively. A pooled sample was generated and labeled by ¹³C-Dns and ¹³C-DmPA, respectively. LC-UV quantification was applied for sample normalization. After mixing individual ¹²C-labeled serum with the ¹³C-labeled pool in equal amounts, the mixtures were analyzed by LC-QTOF-MS for relative quantification.

Results: A total of 3415 amine/phenol and 2114 carboxyl metabolites were commonly detected in more than 80% of the samples. For amine/phenol submetabolome profiling, partial least squares discriminant analysis (PLSDA) showed a clear separation of the groups for each cohort (R²=0.98;Q²=0.92 for cohort A and R²=0.93;Q²=0.79 for cohort B). Similarly, for carboxyl submetabolome profiling, a clear separation between RA and controls was demonstrable (R²=0.93;Q²=0.80 for cohort A and R²=0.84;Q²=0.55 for cohort B). 13 positively identified amine/phenol-containing metabolites, including o-phosphoethanolamine and glycyl-valine, were both significant in cohort A and cohort B, and each of these metabolites showed similar fold changes between RA and controls for both cohorts. 5 carboxyl-containing metabolites, with 1 positively identified, azelaic acid, and 4 unidentified, were both significant in 2 cohorts. The ROC AUC (95%CI) of the 13 amine/phenol-containing metabolite panel were 0.99 (0.94-1.00), 0.98 (0.92-1.00) and 0.98 (0.95-1.00) for cohort A and cohort B (pre- and post-treatment), respectively, with sensitivity/specificity of 94%/96%, 94%/95%, 94%/94%. The ROC AUC (95%CI) of the 5 carboxyl metabolite panel were 0.92 (0.86-0.97), 0.96 (0.91-0.99), 0.89 (0.82-0.95), respectively, with sensitivity/specificity of 86%/86%, 90%/91%, 80%/80%. The combined panel of 18 metabolites demonstrated ROC AUC>0.99 with sensitivity and specificity>95% for each cohort. None of these biomarker metabolites correlated with age, gender, or symptom duration.

Conclusion: Consistent discrimination in metabolite profiles between discovery and verification cohorts generated high priority candidates for further biomarker validation in RA.

Disclosure of Interests: Xiaohang Wang: None declared, Joel Paschke: None declared, Rana Dadashova: None declared, Edna Hutchings: None declared, Liang Li: None declared, Walter P Maksymowych Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis

DOI: 10.1136/annrheumdis-2019-eular.4474

THU0105 DIVERSE DISEASE ACTIVITY MEASURES DEMONSTRATE THAT THE INITIATION OF TOFACITINIB LEADS TO SUSTAINED CLINICAL RESPONSES IN THE MAJORITY OF RHEUMATOID ARTHRITIS PATIENTS IN A CLINIC UTILIZING A TREAT TO TARGET STRATEGY

Craig Wiesenhuber^{1,2}. ¹University of Washington, Department of Medicine, Seattle, United States of America; ²Coeur d'Alene Arthritis Clinic, Coeur d'Alene, United States of America

Background: Treating Rheumatoid Arthritis (RA) patients to target (T2T) has been shown to result in better outcomes in patients with RA [1] and offers the opportunity to analyze clinical responses and changes in certain laboratory parameters after treatment with specific therapeutic agents.

Objectives: To determine the frequency, magnitude, and duration of clinical responses and changes in certain laboratory parameters after initiating Tofacitinib in a single community rheumatology clinic (author's) utilizing a T2T strategy.

Methods: Patients at a community based rheumatology clinic undergo disease activity measure assessments (DAMs) on a routine basis as part of the implementation of the T2T strategy. These assessments include the disease activity score in 28 joints (DAS28CRP), and the more objective

measures, the power Doppler joint count (UPDJC), which demonstrates hyper vascularization of the synovium, and the 12-multiparameter disease activity test (MBDA), which incorporates 12 biomarkers in an algorithm leading to a single disease activity score. The UPDJC includes scoring at six dorsal wrist and six dorsal MCP sites [2]. The average duration of RA in patients at this clinic is > 10 years.

Results: Fifty two patients were found to be in inadequate control at the clinic and were started on Tofacitinib. Ten patients discontinued treatment with Tofacitinib within the first year, four because of an inadequate response, and four because of adverse effects (two deaths, one with lung cancer and one with colon cancer), and two because of noncompliance or loss to follow up.

Forty two patients remained on treatment with Tofacitinib for at least one year, and at this point in time, 21 patients have remained on the drug for two or more years. The DAM assessments and selected changes in certain laboratory parameters for two yearly time points are shown for these patients in Table 1.

Clinical significance was determined by Paired-samples T tests.

Conclusion: Patients showed sustained significant clinical responses for two or more years by all three diverse DAMs and several other common measures of clinical response. The initiation of Tofacitinib in a Rheumatology clinic utilizing a T2T strategy clearly showed sustained clinical responses for up to two years for a significant number of patients. Significant changes in some of the cytokine components of the MBDA were also noted, including increases in leptin levels.

The use of the T2T strategy offers a unique opportunity to obtain real time data on patients treated with specific therapeutic agents at a community rheumatology clinic.

Abstract THU0105 –Table 1.

	Baseline	Year One	Year One	Year Two	Year Two
	Data	N	Data	Data	Prob*
USPDJC ¹	8.7 +/- 3.8	35	6.2 +/- 2.2	20	6.6 +/- 2.2 **
DAS28CRP	4.97 +/- 1.01	26	3.55 +/- 1.00	15	3.12 +/- 1.28 ***
DAS28ESR	5.37 +/- 0.83	21	3.91 +/- 1.28	15	3.94 +/- 1.15 ***
CDAI	30.1 +/- 11.5	25	14.7 +/- 7.8	15	14.3 +/- 10.3 ***
MBDA ²	48.5 +/- 12.2	39	42.4 +/- 10.4	24	38.2 +/- 11.5 **
Dr Global	4.8 +/- 1.3	35	2.9 +/- 1.0	19	3.0 +/- 1.3 ***
Pt Global	5.3 +/- 2.7	33	3.8 +/- 2.7	18	3.1 +/- 2.4 *
TCI ³	13.1 +/- 6.6	36	7.2 +/- 6.6	20	6.3 +/- 6.8 ***
SIC ⁴	7.9 +/- 3.8	36	3.4 +/- 4.5	19	3.2 +/- 2.1 ***
CRP	8.4 +/- 8.5	24	4.3 +/- 2.8	12	3.5 +/- 3.5 NS
ESR	24.4 +/- 15	32	22.9 +/- 16	19	20.6 +/- 15 NS
VCAM1	0.70 +/- 0.22	25	0.60 +/- 0.14	15	0.57 +/- 0.11 *
TNFR1	1.7 +/- 0.5	24	1.4 +/- 0.4	15	1.4 +/- 0.5 *
YKL40	114 +/- 72	26	85 +/- 55	14	75 +/- 38 *
Leptin	36.5 +/- 35	23	40 +/- 32	17	39 +/- 26 ***
prob<0.05*			prob<0.01**		prob<0.001***
Ultrasonography Joint Count ⁵			Multi-Biomarker Disease Activity Score ⁶		
Tender Joint Count ⁷			Swollen Joint Count ⁸		

REFERENCES:

- [1] Smolen, J. et al. Treating Rheumatoid Arthritis to Target: Recommendations of an International Task Force. *Ann. Rheum. Dis* 2010;69:631-6372.
- [2] Shin-ya Kawashiri et. All. The power Doppler Ultrasonography Score from 24 Synovial Sites or 6 Synovial Sites, including the MCP joints, reflects the Clinical Disease Activity and Level of Serum Biomarkers in Patients with RA. *Rheumatology* (2011) 50 (5): 962-965.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.2012

THU0106

SYSTEMIC IMMUNE-INFLAMMATION INDEX IN RHEUMATOID ARTHRITIS PATIENTS: RELATION TO DISEASE ACTIVITY

Takahiro Yoshikawa, Tetsuya Furukawa, Masao Tamura, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui. *Hyogo college of Medicine, Division of Rheumatology, Department of Internal Medicine, Nishinomiya-city, Japan*

Background: Among the immune system elements, neutrophils, lymphocytes and platelets play a role in the regulation of inflammation while also undergoing changes secondary to inflammation. Recently, the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been used as markers of systemic inflammation including rheumatoid arthritis (RA). It was reported that systemic immune-inflammation

index (SII) is positively correlated with neutrophil and platelet counts and inversely correlated with lymphocyte count.

Objectives: We investigated whether SII in RA patients and compare between active cases and those in remission.

Methods: This research is a cross-sectional study. In 734 RA patients registered in the database of our department from January to April in 2016, a total of 574 eligible RA patients were included in this study, excluding 160 patients whose neither RA disease activity or laboratory data were available. Correlations of SII with the disease activity of RA were evaluated. SII was calculated by the following calculation formula; SII = Neutrophils (%) / Lymphocyte (%) * Platelets (G/L).

Results: The median age of patients was 65.0 (IQR: 53.0-73.0) years and the median of disease duration was 9.0 (6.0-14.0) years. The DAS28-ESR was median 2.65 (1.90 - 3.37). SII was 612.0 (400.6 - 951.8). There was a significant correlation between SII and DAS28-ESR ($r=0.322$, $P<0.0001$), and SII was significantly elevated as disease activity increased (median 513.6 in remission group, 605.7 in low disease activity group, 793.8 in moderate disease activity group and 1367.1 in high disease activity group, respectively; $P<0.00001$). In contrast to SII, in NLR no significant difference was observed in all groups. The cut-off of SII was 635.9, 688.6 and 912.5 for DAS28-ESR remission, low disease activity and high disease activity. In multiple regression analysis of LogSII, compared to conventional DMARDs treatment, anti-cytokine therapy such as anti-IL-6 receptor inhibitor or anti-TNF inhibitor showed a significant negative correlation, but no significant differences were observed with abatacept or JAK inhibitor.

Conclusion: In this study, for the first we demonstrated that SII was more strongly related to disease activity than NLR. SII is an emerging inflammatory biomarker which could be used to evaluate disease activity in RA patients. A larger scale longitudinal study is recommended to confirm the present results and further demonstrate the relation to medications received and disease outcome.

Disclosure of Interests: Takahiro Yoshikawa: None declared, Tetsuya Furukawa: None declared, Masao Tamura: None declared, Teppei Hashimoto: None declared, Mai Morimoto: None declared, Naoto Azuma: None declared, Masayasu Kitano: None declared, Kiyoshi Matsui Grant/research support from: Asahi Kasei, Astellas

DOI: 10.1136/annrheumdis-2019-eular.4481

THU0107

BARIATRIC SURGERY DOES NOT PREVENT THE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN OBESE SUBJECTS

Yuan Zhang¹, Anna Rudin¹, Cristina Maglio¹, Lena Carlsson². ¹University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden; ²University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden

Background: Obesity is among the risk factors for rheumatoid arthritis (RA)^{1,2}. In subjects with RA, bariatric surgery-induced weight loss has been associated with a lower disease activity, a decrease in inflammatory markers and a lower use of disease-modifying antirheumatic drugs³. However, the effect of bariatric surgery on the prevention of RA is not known. We have previously shown that bariatric surgery reduces the risk of gouty arthritis and psoriasis in obese subjects^{4,5}.

Objectives: By exploiting a longitudinal study enrolling more than 4000 obese subjects, we aim to determine if bariatric surgery prevents the incidence of RA.

Methods: The Swedish Obese Subjects (SOS) study is a longitudinal controlled trial on the effect of bariatric surgery on the incidence of obesity-related diseases. It includes 4047 obese subjects: 2010 underwent bariatric surgery and 2037 constituted the matched control group⁶. Seven Swedish local ethics review boards approved the study protocol. SOS study participants who developed RA were identified by searching the Swedish National Patient Register. Eleven subjects with prevalent RA at baseline are excluded by the analyses. Patients were followed up until diagnosis of RA, death, migration or end of follow-up (December 2016).

Results: During a follow-up for up to 29 years, 92 subjects developed RA. Fifty-one individuals (55%) had a seropositive RA (serostatus was unknown for 17 subjects). Forty-seven subjects (2.3%) developed RA in the surgery group compared to 45 subjects (2.2%) in the control group. Bariatric surgery was not associated with the incidence of RA during follow up (log-rank $P=0.88$; unadjusted Hazard Ratio-HR 1.03, 95% Confidence Interval-CI 0.69-1.55, $P=0.88$, Figure 1). Similar results were