sex/age-matched healthy controls: 50 in Cohort 1, 50 in Cohort 2, and 100 in Cohort 3. Among these 446 subjects, 75% were females and the average age was 52.5 years. Amine/phenol-containing metabolites were labeled by ^{12}C -dansyl chloride to improve the LC-MS detection. For each cohort, a pooled sample was prepared and labeled by ^{13}C -dansyl group to serve as the reference sample for relative quantification. Then the individual samples and the pooled sample were mixed 1:1. Finally, an LC-QTOF-MS platform analyzed the mixtures and output the intensity ratios of $^{12}\text{C}/^{13}\text{C}$ peak pairs.

Results: 1,149 amine/phenol-containing metabolites were commonly detected across the three sample sets. Among them, 134 were positively identified by our dansyl-labeling standard library, and 141 were matched to predicted retention times and mass values of dansyl-labeled human metabolites. Visualized by the partial least squares discriminant analysis (PLS-DA), the overall amine/phenol-submetabolome demonstrated clear and consistent differences between healthy controls and the RA groups, with cross-validation $Q^2 = 0.765, 0.745, 0.793$, respectively. The selection of significant metabolites was conducted according to the fold change and false-discovery-rate-adjusted Welch's t-test. Cohort 1 demonstrated 85 metabolites having higher concentrations in the RA samples than the controls, and 89 metabolites with lowered concentrations. The numbers of increased/decreased metabolites in Cohort 2 and 3 were 87/26 and 90/53, respectively. Importantly, there were 59 significantly discriminatory metabolites commonly found in the three data sets (49 increased and 9 decreased). We picked the top three with the highest univariate classification performance to form a biomarker panel. We implemented the linear support vector machine (SVM) to build the classifier and the receiver operating characteristic (ROC) analysis to measure the performance. The area-under-the-curve (AUC) values (95% confidence interval) were 1.000 (1.000-1.000), 0.992 (0.967-1.000) and 0.902 (0.858-0.945) for the three cohorts, respectively. The results revealed the importance of examining multiple sample sets and even in the worst case (Cohort 3), our biomarker candidates could differentiate RA at 82.5% sensitivity and 82.5% specificity. Particularly, in Cohort 3, there were 30 RA patients negative for anti-cyclic citrullinated peptide and rheumatoid factor, and our metabolite panel demonstrated consistently high performance for differentiating these specific subjects from healthy controls.

Conclusion: Metabolites showing significant and consistent changes associated with RA have been identified with high discriminative power.

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THU0106

PREDICTORS OF FLARE IN RHEUMATOID ARTHRITIS PATIENTS WITH LOW DISEASE ACTIVITY

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Background: Low disease activity (LDA) in patients with rheumatoid arthritis (RA) are usually recognized as stable state. In according to most guidelines for RA, monotherapy of disease modifying anti-rheumatic drug (DMARD) was recommended for RA patients with LDA. But some of patients with LDA suffer from flare in their disease course. Until now, we don't have enough data on factors that can predict flare in RA patients with LDA.

Objectives: The aim of this study is to evaluate predictor of flare in RA patient with LDA from long-term (3 year) cohort data.

Methods: Korean observational study network for arthritis (KORONA) registry is a nationwide Korean RA specific cohort registry that collecting data annually from 5,376 RA patients in 23 centers across South Korea. We include the data from 1,801 RA patients with LDA (28 -joint disease activity score (DAS 28) < 3.2 at enrollment) who had consecutive data of DAS28 for 3 years. Flare was defined as an increase in DAS28 compared with baseline of >1.2 or >0.6 if concurrent DAS28 ≥3.2. Cox regression analysis was used to identify baseline predictors of flare.

Results: Among 1,801 RA patients, 673 patients (37.4%) experienced flare in 3 years. When we compare the baseline characteristics of both flare and non-flare group, more women and more non-adherent patients for medication were observed in flare group. Flare group had longer disease duration, lower EuroQol 5D score, higher health assessment questionnaire (HAQ) score, and higher

erythrocyte sedimentation rate (ESR) than non-flare group at baseline. In multivariate analysis, physician's VAS, HAQ score, ESR, and poor adherence for medication were significant predictors of flare (Table 1).

Table 1. Multivariate analysis of prediction of flare with baseline variables

Measure	Hazard ratio	95% Confidence Interval	P-value
Female	1.130	0.906-1.409	0.280
Age	0.996	0.988-1.005	0.414
Physician's VAS	1.008	1.002-1.013	<0.01
Pain VAS	1.002	0.998-1.006	0.34
EQ5D	0.952	0.534-1.696	0.87
HAQ	1.407	1.109-1.786	<0.01
ESR	1.008	1.002-1.014	<0.01
Poor adherence	1.272	1.047-1.545	<0.05

VAS: Visual Analogue Scale; EQ5D: EuroQol 5D; HAQ: Health Assessment Questionnaire; ESR: Erythrocyte Sedimentation Rate

Conclusion: RA patient who have risk factors for flare, even though their disease activity was low, require more proactive treatment.

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THU0107

OBSESITY PREDICTS RESPONSE TO NOT ALL BUT CERTAIN BIOLOGICAL / TARGETED DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS - RESULTS FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATIC DISEASE PATIENTS (ANSWER COHORT)

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Background: A number of previous reports suggested that obesity is one of the baseline factors indicates refractory to biologic disease-modifying antirheumatic drugs (bDMARDs). However, difference of the significant responses appears on obesity patients depending on each kind of drug is yet unclear. However, it is yet unclear how the significant responses on obesity patients vary on each kind of drug.

Objectives: To assess whether obesity affects clinical outcome in rheumatoid arthritis (RA) treated with each molecular-targeted agent including bDMARDs and tofacitinib.

Methods: In Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, which was the real-world retrospective cohort of clinical database for rheumatic diseases, RA patients who initiated biological / targeted disease modifying anti-rheumatic drugs were included and consecutively followed. Obesity was defined as BMI over than 25, and patients were divided between

obese ("Ob") and non-obese ("non-Ob") patients. SDAI (simplified disease activity index) was compared between non-Ob and Ob at month 0, 3, 6, 9, 12 after the indicated drugs were administered. Using logistic regression analysis, odds ratio (OR) and their corresponding 95% confidence intervals (95% CIs) were further calculated to estimate achievement rate of SDAI remission defined as lower than 3.3 by obesity and other relevant clinical parameters. Once after the drugs were discontinued by any unfavorable reason, disease activities were no more scored and the Last Observation Carried Forward (LOCF) imputation method was used for SDAI at month 3 and thereafter.

Results: A total of 1936 patients met in the inclusion criteria were under the analysis. In each drug, SDAI remission rate (non-Ob, Ob, p-value by Chi-square test) at month 12 was as follows; Infliximab (IFX, n=135): 43%, 38%, NS (not significant); Etanercept (ETN, n=188): 44%, 19%, p=0.0122; Adalimumab (ADA, n=169): 50%, 56%, NS; Golimumab (GLM, n=315): 36%, 30%, NS; Certolizumab pegol (CZP, n=131): 33%, 56%, p=0.0287; Tocilizumab (TCZ, n=423): 41%, 29%, p=0.0456; Abatacept (ABT, n=144): 26%, 23%, NS; Tofacitinib (TOF, n=69): 27%, 23%, NS. In multivariate analysis to predict SDAI remission at month 12, obesity was an independent protective factor in CZP (OR: 0.29, 95% CIs: 0.10 – 0.83), but was an independent risk factor in TCZ (OR: 1.9, 95% CIs: 1.01 – 3.61) irrespective of age, sex, disease duration, SDAI at month 0 or number of previous bDMARDs. Any other drug including ETN did not show significant result between non-Ob and Ob in the multivariate analysis.

Conclusion: Obese patients were more resistant to TCZ but more effective in CZP than non-obese patients.

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THU0108

REAL-WORLD RADIOGRAPHIC PROGRESSION IN RA WITH BIOLOGIC DMARDS

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Background: As structural damage is irreversible and strongly associated with functional disability¹, it is an important outcome to be prevented in rheumatoid arthritis (RA). Acute phase markers, rheumatoid factor (RF) and anti-citrullinated protein (anti-CCP) positivity are important predictors of erosive disease². Previous studies conducted in real life setting have divergent results regarding the role of disease activity in radiographic progression^{3,4}.

Objectives: To evaluate the impact of disease activity and biologic disease modifying anti-rheumatic drugs (bDMARDs) on radiographic progression of established RA in clinical practice in southern Brazilian public health system.

Methods: Longitudinal retrospective study including patients with RA (1987 ACR criteria) treated with bDMARDs and followed from 2015 to 2019. Clinical and demographic data were collected at baseline. Radiographs of hands and feet were performed yearly. X-rays were scored according to the van der Heijde-modified total Sharp method (vdH-mTSS) in known chronological order. Clinical relevant radiographic progression (CRRP) was defined as an increase ≥ 3 units on the score per year⁵. Demographic, clinical, and radiographic characteristics of RA patients with or without relevant progression were compared with Fisher exact and Mann-Whitney test.

Results: Seventy-five patients were included. The patients' characteristics are shown in table 1. Twenty three (30%) patients presented CRRP at any time point of the follow up (figure 1). Mean DAS28-ESR at baseline was higher in patients who progressed radiographically, than those who did not progress (4.8 ± 1.1 vs 3.5 ± 1.1 ; $p < 0.001$). No patient in remission at baseline presented with CRRP. Radiographic progression occurred in 15% of patients in low disease activity, 34% of patients in moderate disease activity and 57% of patients in high disease activity at baseline, depicting a linear relation between categories of disease activity and CRRP. RF, anti-CCP, disease duration, educational level, smoking status, total vdH-mTSS at baseline, number and duration of biologic DMARDs were not associated with CRRP. No single biologic DMARD was associated with worse radiological prognosis.

Table 1. Baseline characteristics and bDMARD treatment during 5 years of follow up

Characteristics	N = 75
Age, yrs, mean $\pm$ SD	58.1 $\pm$ 10.1
Female, n (%)	65 (86.6)
Disease duration, yrs, mean $\pm$ SD	16.2 $\pm$ 7.6
IgM RF positivity, n (%)	69 (92)
Anti-CCP positivity, n (%)	27 (75) *
DAS28-ESR, mean $\pm$ SD	4.2 $\pm$ 1.0
Educational level, n(%)	
Elementary school ($\leq$ 8years)	49 (65)
Intermediate school (9-12 years)	23 (30.6)
University/college degree	3 (4)
Smoking	
Current or former	31 (41.3)
Never	44 (58.7)
vdH-mTSS, median (IQR)	21 (5-53)
Number of bDMARD, mean $\pm$ SD	2.4 $\pm$ 1.1
Duration of bDMARD, yrs, mean $\pm$ SD	7.4 $\pm$ 2.6
Methotrexate use, n, %	61 (81)
Biologic DMARD	184**
TNF inhibitors, n, %	106 (57.6)
Tocilizumab, n, %	30 (16.3)
Abatacept, n, %	25 (13.6)
Rituximab, n, %	23 (12.5)

RF rheumatoid factor anti-CCP anti-citrullinated protein bDMARD biologic disease-modifying anti-rheumatic drug ESR erythrocyte sedimentation rate DAS28 disease activity in 28 joints vdH-mTSS van der Heijde-modified total Sharp score IQR interquartile range *information available from 36 patients **all bDMARD treatments

Conclusion: In contrast to controlled clinical trials, real-world studies have shown that patients with RA treated with bDMARD still develop radiological progression. We observed that despite prognostic factors, achievement of treatment target is the most important factor to prevent articular damage in RA.

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