Figure 1. Rate of radiographic progression (RP) by MBDA category for patient groups based on concordance or discordance of Patient Global Assessment (PGA) and Evaluator Global Assessment (EGA).

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POS0455

EFFECT OF ANTI-RO/SSA ANTIBODIES FOR TREATMENT RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Background: Several previous observational studies have suggested that patients with anti-Ro/SSA antibody-positive rheumatoid arthritis (RA) may respond poorly to treatment, including tumor necrosis factor inhibitors¹. However, its influence on methotrexate (MTX) treatment, which is the anchor drug of treat-to-target strategy in RA treatment, remains unclear.

Objectives: We compared the clinical response to MTX in both anti-Ro/SSA antibody-positive and -negative patients with MTX-naïve RA and investigated the reasons for the difference in response.

Methods: We recruited 210 consecutive patients with RA who were newly started on MTX in this retrospective cohort study. The effect of the presence of anti-Ro/SSA antibodies on achieving low disease activity (LDA) of DAS28-CRP at six months after initiating MTX was investigated by using logistic regression analysis. CDAI, SDAI, concomitant using DMARDs and painkillers, patient's and evaluator's VAS, tender joint counts, and swollen joint counts at six months were also compared between the anti-Ro/SSA-positive patients and -negative

patients. Missing data were imputed by using multiple imputations before multivariate analysis.

Results: 32 anti-Ro/SSA antibody-positive patients and 178 anti-Ro/SSA antibody-negative patients were included. The rate of achieving DAS28-LDA at six months was significantly lower in the anti-Ro/SSA antibody-positive patients than those in the anti-Ro/SSA antibody-negative patients (56.2% versus 75.8%, $P=0.03$). In the logistic regression analysis, the presence of anti-Ro/SSA antibodies was an independent negative predictor for achieving DAS28-LDA at six months (OR:0.431, 95%CI: 0.190-0.978, $P=0.044$) (Table1). Anti-Ro/SSA antibody-positive patients had significantly higher patient's VAS at six months (median [IQR]: 22 [15-41] vs 19 [5-30], $P=0.038$), and prescribed NSAIDs (37.5% vs 18.0%, $P=0.018$). CDAI and SDAI after six months were not significantly different between the group.

Conclusion: The presence of anti-Ro/SSA antibodies might be one of the predictive factors for the insufficient response to treat to target strategy in RA treatment. Residual pain was suspected as one of the mechanisms contributing to the lesser clinical response of MTX in anti-Ro antibody-positive RA.

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Table 1. Logistic regression analysis for the rate of achieving DAS28 low disease activity at six months.

Risk factor	Odds ratio	95%CI	P value
Age at onset	0.993	0.968-1.018	0.586
Sex (woman)	0.643	0.300-1.384	0.258
RF-positive	1.962	0.853-4.511	0.112
ACPA-positive	0.552	0.225-1.351	0.192
Anti-Ro/SSA antibody-positive	0.431	0.190-0.978	0.044

Disclosure of Interests: None declared

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POS0456

EXTERNAL VALIDATION OF A MULTI-BIOMARKER-BASED CARDIOVASCULAR DISEASE RISK PREDICTION SCORE FOR RHEUMATOID ARTHRITIS PATIENTS

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Background: A novel score for predicting 3-year risk for CVD events in RA patients combines age, four traditional CVD risk factors (diabetes, hypertension, smoking, history of high-risk CVD event), a personalized assessment of RA-related inflammation based on the multi-biomarker disease activity (MBDA) score and, individually, 3 of its 12 biomarkers, TNF-R1, MMP-3 and leptin (log-transformed). This score was developed and internally validated using patient data from the Medicare database.

Objectives: The purpose of this analysis was to externally validate the MBDA-based CVD risk prediction score in a younger cohort from the Symphony claims database.

Methods: A cohort of patients greater than or equal to 18 years old with RA diagnosis from a rheumatologist and evidence of an RA-specific treatment, excluding patients with malignancy, past myocardial infarction (MI) or stroke, was created by a third party (Symphony) by matching medical and pharmaceutical claims and linking them to MBDA scores from a database of tests done for routine care. Medicare patients were excluded to avoid overlap with the internal validation cohort. Only the first MBDA test was used for each patient. The study endpoint was time from MBDA testing to first CVD event within a 3-year time horizon. CVD event was defined as MI or stroke, based on ICD-9 or ICD-10 diagnosis codes in hospital claims. Analyses focused on relative risk, not absolute risk, because CVD event data in Symphony may be incomplete. A univariate Cox proportional hazards regression model was fit with the MBDA-based CVD risk score as the sole predictor of time to CVD event to obtain a hazard ratio (HR) estimate (95% CI) and p-values from a likelihood ratio test (LRT). Sensitivity analyses determined HR for patient subgroups, with p-values determined for the interaction between subgroups and the MBDA-based CVD risk score. Using a multivariate Cox proportional hazard regression model, the MBDA-based CVD risk score was compared to a simpler model that included only age, sex, diabetes, hypertension, history of other CVD, smoking and CRP (log-transformed) for ability to predict time to a CVD event.

Results: 48,868 patients with 337 CVD events met eligibility criteria and had linked biomarker data. Mean age was 54.4 years. 81.7% were female (Table 1).

Mean follow-up was 24.4 months. The MBDA-based CVD risk score (mean 3.3, IQR 2.8–3.8) was highly significant in univariate analysis, with HR = 3.99 (95% CI: 3.52–4.51, $p = 4.4 \times 10^{-95}$); i.e., for every 1-unit increase in risk score, the CVD event rate in this cohort was ~4 times as high. Similar results were seen in the subset of 44,379 patients <65 years old, with HR=4.26 (95% CI: 3.53–5.14, $p = 1.2 \times 10^{-47}$). In sensitivity analyses, after adjusting for multiple comparisons, there were no significant differences between HR of complementary subgroups (Figure 1). The MBDA-based CVD risk score added significant prognostic information to a simpler, clinical model (HR=2.28 [95% CI: 1.69–3.08, $p = 1.6 \times 10^{-7}$] after accounting for all other factors).

Conclusion: The MBDA-based CVD risk prediction score has been externally validated in a cohort that is younger than and independent of the Medicare cohort used previously for test development and internal validation.

Table 1. Cohort characteristics of RA patients with linked biomarker data and at risk for CVD events.

Variable	Median (IQR) or N (%)
Total patients	48,868()
Age, years	54 (46–60)
Sex, male	8,940 (18.3%)
Diabetes	7,974 (16.3%)
Hypertension	19,132 (39.2%)
History of high-risk CVD event	6,713 (13.7%)
Smoking	7,487 (15.3%)
CRP, mg/L	4.1 (1.4–11.5)
Leptin, ng/mL	24.3 (10.6–47.1)
MMP-3, ng/mL	21.1 (14.3–36.2)
TNF-RI, ng/mL	1.4 (1.1–1.7)
MBDA score	40 (31–48)
MBDA-based CVD risk score	3.3 (2.8–3.8)

Figure 1. Hazard ratios for CVD event over 3 years in the external validation dataset (N=48,868). Vertical dashed line indicates the hazard ratio for all patients.

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POS0457

CHANGES OF RF ISOTYPE PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM 10 YEARS FOLLOW-UP STUDY

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Background: Presence of autoantibodies such as anti-cyclic citrullinated peptide (anti-CCP2) and rheumatoid factor (RF) is of considerable diagnostic and prognostic value in patients with rheumatoid arthritis (RA). Limited data are available for autoantibody profile changes over time in patients with RA.

Objectives: Thus, we compared the presence of anti-CCP2 and different RF isotypes in individual RA patients at baseline and during 10 years follow-up.

Methods: A total of 320 RA patients from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) case-control study was included in this study. The presence of anti-CCP2, IgM RF, IgG RF, and IgA RF at baseline and at later time point (± 10 years) were determined using enzyme-linked immunosorbent assays, with identical techniques in paired samples. Seropositive RA is defined by the presence of at least one autoantibody, whilst seronegative RA is defined by the absence of all investigated autoantibodies.

Results: The proportion of seropositive RA were higher for the follow-up samples ($n=263$, 82.2%) as compared to the baseline samples ($n=251$, 78.4%). Among the baseline samples, 105 (41.8%) were positive for anti-CCP2 and all RF isotypes. Of these individuals, 85 (81.0%) remained positive for all antibodies at the follow-up, while 20 (19.0%) lost one or more RF isotypes (4 IgM RF, 19 IgG RF and 13 IgA RF). Interestingly, 14 (5.6%) RA patients who were seropositive at baseline became totally seronegative after follow-up. Among the 69 patients seronegative at baseline, 26 (37.7%) acquired one or more autoantibodies at follow-up (14 IgM RF, 2 IgG RF, 9 IgA RF and 8 anti-CCP2) (Figure 1).

Conclusion: Anti-CCP2 present at baseline usually remained at follow-up. Among Malaysian RA patients, changes in status were mainly found for RF of all isotypes.

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