Table 1. Patient characteristics at the start of a JAKi, TNFi or csDMARD.

	ALL PATIENTS			HIGH RISK PATIENTS*		
	JAKi	**TNFi**	**csDMARD**	**JAKi**	**TNFi**	**csDMARD**
# treatment starts	2030	2338	871	1215	1254	508
Age	59.9 ± 11.6	57.6 ± 13.0	59.5 ± 12.7	64.3 ± 8.9	63.5 ± 8.9	64.4 ± 9.2
Women	1573 (77.5)	1707 (73.0)	627 (72.0)	907 (74.7)	864 (68.9)	355 (69.9)
Disease duration	12.6 ± 9.6	8.9 ± 8.5	5.7 ± 6.6	13.3 ± 9.9	9.7 ± 9.1	6.0 ± 7.0
Rheumatoid factor/ ACPA positive	1531 (79.2)	1672 (74.2)	548 (66.3)	917 (79.7)	890 (73.7)	321 (66.5)
# previous bDMARDs	2.0 ± 1.8	0.7 ± 1.2	0	2.0 ± 1.8	0.7 ± 1.2	0
DAS28-ESR	4.2 ± 1.4	4.5 ± 1.4	4.2 ± 1.3	4.4 ± 1.5	4.7 ± 1.3	4.3 ± 1.3
Percentage of full physical function	63.3 ± 24.1	68.6 ± 22.4	72.3 ± 21.9	60.3 ± 24.2	64.4 ± 23.3	69.6 ± 22.7
Glucocorticoids ≥10 mg/d	170 (17.5)	239 (21.5)	49 (12.4)	112 (18.6)	142 (22.3)	23 (10.0)
BMI >30 kg/m^2	565 (28.2)	631 (27.4)	271 (31.7)	383 (31.8)	413 (33.3)	180 (36.0)
Sum of comorbidities	2.9 ± 2.5	2.6 ± 2.4	2.2 ± 2.2	3.7 ± 2.6	3.5 ± 2.5	3.1 ± 2.3
Current smokers	461 (26.3)	617 (28.5)	274 (33.5)	355 (33.5)	466 (39.5)	202 (42.3)
Previous smokers	551 (31.4)	692 (31.9)	230 (28.1)	300 (28.3)	338 (28.6)	114 (23.9)

Values are given as mean ± standard deviation or number (percentage). *Age ≥50 years and ≥ 1 CV risk factor (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, current smoking)

disease-modifying anti-rheumatic drugs (csDMARDs - bionaive) in patients with rheumatoid arthritis (RA) observed in daily rheumatological care.

Methods: Data from patients enrolled in the biologics register RABBIT with treatment episodes from 01/2017 - 04/2021 were included. Incidence rates (IR) of MACE per 100 patient-years (PY) with 95% confidence intervals (CI) and adjusted risk ratios (RR) were calculated for all and for high-risk patients (age ≥ 50 years and ≥ 1 CV risk factor). Poisson regression analysis was adjusted for age, sex, smoking, disease activity, prior therapies, glucocorticoids and comorbidities.

Results: Starting from 2017, 2030 JAKi, 2338 TNFi and 871 csDMARD initiations were documented. Patients with a JAKi start were slightly older, more often women and had a longer RA disease duration (Table 1). The proportion with positive autoantibodies was higher than in the TNFi and csDMARD group, the physical function was lower, and they had received more previous biologic treatments. Characteristics of high-risk patients are also given in the Table 1.

In total, 28 incident MACE were reported. Patients under treatment with JAKi, TNFi and csDMARD showed comparable IR for MACE between 0.26 and 0.41 events per 100 PY (Figure 1). High-risk patients showed higher IRs. The median time under treatment was 10 months on JAKi and TNFi, and 12 months on csDMARDs. The majority of events were reported in the first year after treatment start. In the adjusted analyses, JAKi (RR 0.94 [95% CI 0.39; 2.28]) and csDMARDs (RR 0.85 [0.25; 2.88]) did not show a significantly increased risk for MACE compared with TNFi in unselected patients, and also not in high-risk patients (JAKi: RR 0.90 [0.37; 2.17]; csDMARDs: RR 0.61 [0.16; 2.28]).

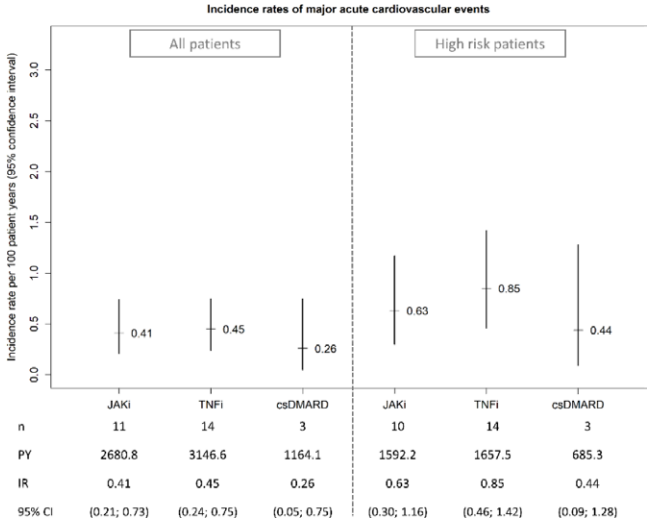

Figure 1. Incidence rates of MACE per 100 patient years by treatment group.

Conclusion: IR of MACE in patients receiving JAKi in a real-world setting was lower than the IR reported for tofacitinib in the Oral Surveillance study. We found no evidence of an increased risk of MACE with JAKi compared to TNFi, although patients in the JAKi group were older and had longer disease duration.

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OP0136

SERUM CHOLESTEROL LOADING CAPACITY ON MACROPHAGES AND INTERACTIONS WITH TREATMENTS ON CORONARY ATHEROSCLEROSIS BURDEN AND EVENT RISK IN RHEUMATOID ARTHRITIS

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Background: Cholesterol loading capacity (CLC) describes the ability of serum to deliver cholesterol to cells. It is linked to foam cell formation, a pivotal step in atherosclerotic plaque development. Rheumatoid arthritis (RA) serum promoted foam cell formation significantly more than control serum. Likewise, RA patients display greater plaque burden and higher-risk features than non-RA controls. bDMARDs and statins lower cardiovascular risk by reducing new coronary plaque formation, promoting regression, altering the composition and stabilizing prevalent atherosclerotic lesions.

Objectives: To evaluate the associations between CLC, coronary plaque burden and cardiovascular event risk in patients with RA. We further explored the conditioning effects of RA treatments on these relationships.

Methods: 140 patients underwent coronary CT angiography for atherosclerosis evaluation and were prospectively followed for cardiovascular events over 6.0±2.4 years. Coronary artery calcium score (CAC), number of segments with plaque (segment involvement score [SIS]) and plaque composition were assessed. CLC was the macrophage cholesterol content, measured by fluorometric assay, after a 24-hour incubation with whole serum. Robust linear regression examined the effects of CLC and the interaction between CLC and bDMARD use on SIS and CAC. Negative binomial regression evaluated CLC and CLC × bDMARD interaction effects on number of high-risk (low-attenuation) plaques. With data discretized into 1-month intervals, weighted pooled logistic regression models with robust variance estimation evaluated CLC and time-varying bDMARD use as predictors of event risk, and the effect of CLC × time-varying bDMARD use on risk. Stabilized inverse probability of treatment and censoring weights were estimated as a function of ASCVD risk, SIS, RA duration, and baseline and time-varying CRP and statin use.

Results: Mean (SD) CLC was 12.67 (2.83) μg/mg protein. In analyses adjusting for ASCVD score, HDL, prednisone and statin use, CLC (per 1-SD unit) was not related to SIS (β -0.05 [95%CI -1.19,0.09]), number of high-risk plaques (rate ratio [RR] 1.20 [95%CI 0.80-1.80]) or ln-transformed CAC (β 0.017 [95%CI -0.133,0.147]). However, in analyses stratified by baseline bDMARD use, CLC

(per 1-SD unit) was positively related to number of high-risk plaques (RR 2.14 [95%CI 1.04-4.40]) and ln-transformed CAC (β 0.21 [95%CI 0.01-0.41]) among bDMARD-naïve individuals (Figure 1). In addition, CLC inversely associated with SIS (per SD increment; β -0.16 [95%CI -0.32, -0.01]) only in bDMARD-treated patients. Baseline statin use did not significantly modify the effect of CLC on coronary plaque (not shown). CLC associated with cardiovascular event risk (per SD increment; adjusted odds ratio 2.02 [95%CI 1.27-3.50], p=0.011) covarying for ASCVD score and time-varying bDMARD use. The CLC × time-varying bDMARD use interaction also predicted event risk (p =0.010); current bDMARD use associated with lower event risk at higher (1 SD above the mean) CLC levels (p=0.037) but not average or lower (1 SD below the mean) CLC levels (p=0.064 and 0.756, respectively).

Conclusion: CLC associated with greater CAC score and high-risk plaque burden in bDMARD-naïve RA patients and lower total plaque burden in bDMARD-treated patients at baseline. CLC also predicted long-term cardiovascular risk and its effect was mitigated by bDMARD use.

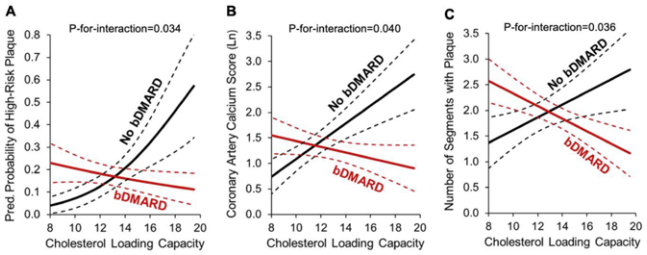

Figure 1 Impact of CLC on coronary atherosclerosis burden in RA and mitigation by bDMARDs

Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi-Genzyme-Regeneron, Janssen, Bristol-Meyer-Squibb, Consultant of: Sanofi-Genzyme-Regeneron, Janssen, Bristol-Meyer-Squibb, Grant/research support from: Pfizer, Bianca Papotti: None declared, Sarah Ormseth: None declared, Marcella Palumbo: None declared, Elizabeth Hernandez: None declared, Cinzia Marchi: None declared, Francesca Zimetti: None declared, Matthew Budoff Consultant of: Pfizer, Nicoletta Ronda: None declared

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OP0137

ABDOMINAL OBESITY MAY CONFOUND THE ACCURACY OF CARDIOVASCULAR RISK PREDICTION IN RHEUMATOID ARTHRITIS; CAN CORONARY ATHEROSCLEROSIS IMAGING AND BIOMARKERS HELP?

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Background: Accurate cardiovascular risk stratification is essential in rheumatoid arthritis (RA) care. RA patients who are underweight incur greater total and cardiovascular mortality compared to those who are overweight or obese.

Objectives: We explored whether abdominal obesity impaired the accuracy of risk prediction estimates in RA patients without known cardiovascular disease (CVD). We further interrogated the potential utility of coronary atherosclerosis assessment and serum levels of related cardiac damage biomarkers to optimize risk prediction in obese RA patients.

Methods: In a single center observational study, 150 participants with coronary CT angiography for atherosclerosis evaluation and prospective follow-up for cardiovascular events over 6.0±2.4 years were assessed. Framingham cardiovascular risk score was computed at baseline. Obesity was defined as waist circumference >88 cm in females and >102 cm in males. Segment involvement score (SIS) described the number of coronary segments with plaque. Serum highly-sensitive cardiac troponin I (hscTnI)-related both to coronary plaque burden and event risk in RA- was measured with Erenna immunoassay. Serum leptin, which is closely related to obesity, was measured with radioimmunoassay. CVD risk estimates were contrasted in non-obese vs. obese patients and those with low vs. high leptin correspondingly using area under the curve (AUC) comparisons. Improvements in risk estimate accuracy in obese patients were explored by sequentially adding hscTnI information and coronary plaque burden estimates to a baseline model of Framingham score and evaluating sequential change in AUC, net reclassification index (NRI) and integrated discrimination improvement (IDI).

Results: A significant interaction between Framingham cardiovascular risk score and obesity was observed (p=0.032). Lower estimates were seen in obese [AUC 0.660, 95%CI 0.487-0.832] vs. non-obese RA patients [AUC 0.952, 95%CI 0.897-1.007, p=0.002, Figure 1A]. Likewise, risk estimates were lower in patients with higher (>22.1 ng/ml) vs. lower (<22.1 ng/ml) leptin [AUC 0.618, 95%CI 0.393-0.842 vs. 0.874, 95%CI 0.772-0.976 respectively, p=0.042, Figure 1B]. In obese patients, sequential addition of the highest hscTnI tertile values and extensive atherosclerotic plaque presence (SIS>5) to a base model including Framingham risk score, significantly improved risk prediction estimates based on changes in NRI [1.093 95%CI 0.517-1.574], IDI [0.188, 95%CI 0.060-0.526], as well as AUC [0.179, 95%CI 0.058-0.378, p=0.02]. The final, combined model accurately predicted 83.9% of incident cardiovascular events (Figure 1C).

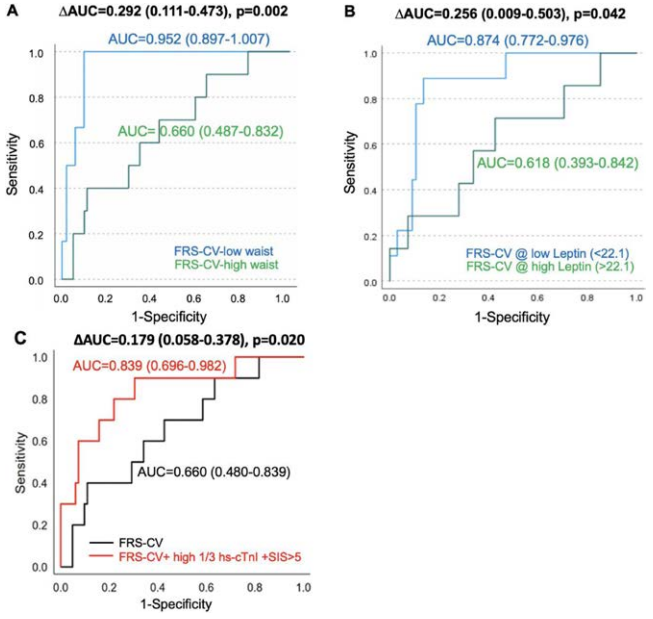

Figure 1. **A** and **B.** Obesity attenuates accuracy of clinical cardiovascular risk estimates in RA. **C.** Addition of information from hs-cTnI measurements and coronary atherosclerosis assessment significantly improve risk prediction

Conclusion: Obesity significantly reduced cardiovascular risk estimate accuracy in patients with RA. The optimization of cardiac risk stratification with the help of non-invasive assessment of coronary atherosclerosis burden and related cardiac damage biomarkers in the serum may warrant further study.

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OP0138

RISK OF CANCER AFTER BIOLOGIC AND TARGETED SYNTHETIC DMARDS INITIATION IN PATIENTS WITH RHEUMATIC DISEASES AND A HISTORY OF PRIOR MALIGNANCY: DATA FROM THE BIOBADASER REGISTRY

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Background: Patients with a history of cancer are routinely excluded from randomized controlled trials. As consequence, data on the safety of biologic disease modifying antirheumatic drugs (bDMARDS) and targeted synthetic (ts) DMARDs are limited. Although real world data from various national registries have not provided evidence of increased cancer recurrence, additional data from real-world registries may help to confirm safety of non-TNFi bDMARDs and tsDMARDs regarding cancer recurrence to guide treatment decisions.

Objectives: To compare the risk of incident malignancy with exposure to different bDMARDs and tsDMARDs in patients with rheumatic diseases and a prior malignancy.