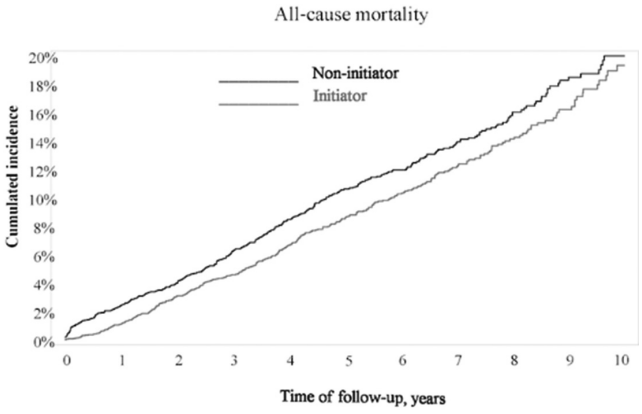

Conclusions: The beneficial properties on survival seen with HCQ use in other inflammatory diseases seem also applicable to RA patients. These results needs confirmation in a randomised setting but justifies the use of HCQ in combination with other conventional synthetic disease-modifying antirheumatic drugs even though the effect of HCQ, *per se*, on RA disease activity is limited.

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Disclosure of Interest: None declared

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OP0192 METHOTREXATE USE AND THE RISK FOR CARDIOVASCULAR DISEASE AMONG RHEUMATOID PATIENTS INITIATING BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

F. Xie, L. Chen, H. Yun, E. Levitan, P. Muntner, J.R. Curtis. *University of Alabama at Birmingham, Birmingham, USA*

Background: Methotrexate (MTX) has been associated with reduced risk for CVD in several studies conducted among rheumatoid arthritis (RA) patients never exposed to biologic disease-modifying antirheumatic drugs (bDMARDS). Effect of concomitant MTX use on CVD risk among RA patients initiating bDMARDS remains unknown.

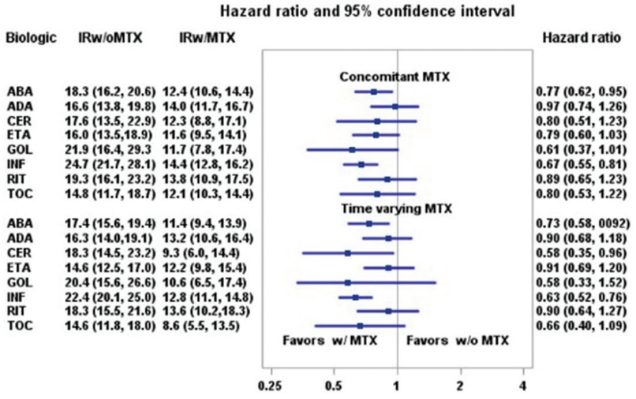
Objectives: The objective of this study was to assess the CVD risk associated with MTX use among RA patients initiate bDMARDS, overall, and by each bDMARDS initiated.

Methods: A retrospective cohort study was conducted using 2006–2015 Medicare claims data for RA patients. Follow up started at initiation (index date) and ended at earliest of 1) end of exposure of the specific bDMARDS agent (days of supply plus 90 days extension), 2) switched to other bDMARDS or tofacitinib, 3) CVD event, 4) death date, 5) loss of Medicare coverage, 6) end of study (September 30, 2015). MTX use was defined as 1) concomitant MTX use, with prescription for MTX within 120 days after index date and 2) time varying MTX, defined as prescription date to prescription date plus days of supply without extension. For sensitivity analysis, a 90 day extension was added to days of supply. The primary outcome was composite of incident MI, incident stroke and fatal CVD. Fatal CVD were identified by a claims based algorithm with PPV $\geq$80%.

Incidence rates (IR) and 95% confidence intervals (CI) were calculated using Poisson regression. Overall association between MTX use (versus no MTX) and risk of CVD were assessed using Cox regression. Given that the interactions between MTX and background bDMARDs was significant, we performed contrast (MTX Yes vs No) to examine the association between MTX and risk for CVD for each underlying bDMARDS in one model. A subgroup analysis limited the cohort to RA patients with previous exposure to MTX was conducted to ensure consistency of findings.

Results: A total of 88,255 DMARDS initiations (64 218 patients) were included in this study. The average age at initiation was 64.6 (12.3) years, 84.0% were female, 68.2% were non-Hispanic white. The crude IRs for CVD were 13.1 (95% CI: 12.2 to 14.0) and 18.7 (95% CI: 17.6 to 19.9) events per 1000 person years for RA patients with and without concomitant MTX respectively. The crude IRs for CVD were 12.1 (95% CI: 11.1 to 13.2) and 17.9 (95% CI: 16.9 to 18.8) events per 1000 person years for RA patients with and without time varying MTX respectively. IRs for individual bDMARDS are shown in figure. P-value for interaction between concomitant MTX and background bDMARDS was 0.0189 and p-value for interaction between time varying MTX and background bDMARDS was 0.0030. The contrast HRs for concomitant MTX ranged from 0.61 (0.37, 1.01) for golimumab initiators to 0.97 (0.74, 1.26) for adalimumab initiators (figure 1). The contrast HRs for time varying MTX ranged from 0.58 (0.35, 0.96) for certolizumab initiators to 0.90 (0.68, 1.18) for adalimumab initiators.

Results were robust in sensitivity and subgroup analyses.



Conclusions: Our observational study suggests an overall 23% reduction of CVD risk associated with concomitant MTX use. The effect sizes vary among background bDMARDS.

Disclosure of Interest: F. Xie: None declared, L. Chen: None declared, H. Yun Grant/research support from: BMS, E. Levitan Grant/research support from: Amgen, Consultant for: Amgen, Novartis, P. Muntner: None declared, J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB

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OP0193 TOCILIZUMAB AND THE RISK FOR CARDIOVASCULAR DISEASE EVENTS AMONG RHEUMATOID ARTHRITIS PATIENTS: A DIRECT COMPARISON IN REAL WORLD SETTING

F. Xie, H. Yun, E. Levitan, P. Muntner, J.R. Curtis. *University of Alabama at Birmingham, Birmingham, USA*

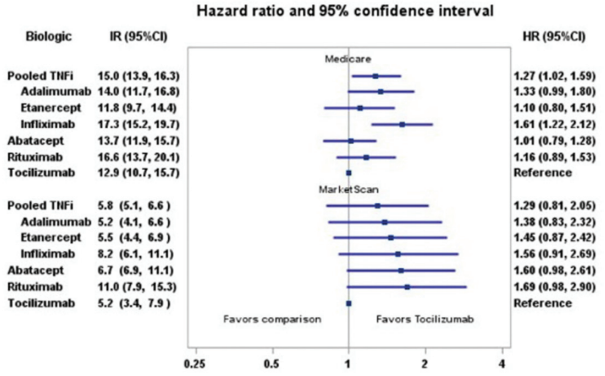
Background: Multiple studies have observed unfavourable changes in lipid profile associated with tocilizumab (TCZ, anti-IL6 receptor antagonists) and some other rheumatoid arthritis (RA) therapies. The real-world cardiovascular disease (CVD) risk associated with the first anti IL-6R medication for RA, TCZ, remains uncertain.

Objectives: The objective of this study was to assess the CVD risk associated with TCZ compared to individual tumour necrosis inhibitor (TNFi) therapies, as well as to other biologics used for RA (e.g. rituximab, abatacept).

Methods: Using 2006–2015 Medicare and MarketScan claims data, we conducted a retrospective cohort study among RA patients who initiated biologic disease-modifying antirhematic drugs (bDMARDS) after January 1, 2010 and had at least 365 days medical and pharmacy coverage before initiation. The primary outcome was a composite of myocardial infarction (MI), stroke, and fatal CVD assessed using a validated method. Subgroups analyses were done for RA patients experienced to other bDMARDs before initiation and by stratifying patients with respect to key CVD risk factors to identify both higher and lower CVD risk patients. We provided descriptive statistical for each exposure group. Incidence rates and 95% confidence intervals were calculated using Poisson regression. COX regression was used to generate unadjusted and adjusted hazard ratio.

Results: We identified 3 54 486 (Medicare 206,275+MarketScan 148,211) RA patients and 4 63 446 (Medicare 271,832+MarketScan 191,614) initiations of bDMARDS. After applying inclusion and exclusion criteria, the final cohort contained 88 463 (Medicare 46,648+MarketScan 41,815) RA patients and 1 17 493 (Medicare 61,715+MarketScan 55,778) episodes. The mean (SD) age was 64.7 (12.1) in Medicare and 52.2 (12.3) in MarketScan. The majority of patients were female (83.9% in Medicare and 80.5% in MarketScan), and 68.6% were non-Hispanic White in Medicare. TCZ users were similar to abatacept and rituximab users except that TCZ users were less likely to be naïve to bDMARDS. Compared to TNFi users, TCZ users were more likely to be white, with history of CVD (other than MI or stroke), heart failure, atrial fibrillation, hospitalisation and had more

physician visits in baseline. TCZ users were less likely to be diabetic, use methotrexate in the baseline, and to be naïve to bDMARDS.
The crude incidence rate (IR) per 1000 patient-years for composite CVD among Medicare patients ranged from 13.3 (95% CI: 11.1 to 16.0) for etanercept to 19.4 (95% CI: 16.3 to 20.9) for rituximab users. The crude incidence rate for pooled TNFi users was 16.4 (15.2–17.7). Compared to TCZ, the adjusted hazard ratios were 1.03 (0. 82–1.29) for abatacept, 1.25 (0.96–1.61) for rituximab, 1.13 (0.84–1.52) for etanercept, 1.33 (0.99–1.80) for adalimumab, and 1.57 (1.21–2.05) for infliximab (figure 1). There were no significant differences in CVD risk between tocilizumab and any other biologic using MarketScan data. Results were robust in numerous subgroup analyses.



Abstract OP0193 – Figure 1. Incidence rates and adjusted hazard ratios of CVD events in RA patients

Conclusions: Consistent with findings of a recently completed safety trial in RA, tocilizumab was associated with a comparable CVD risk compared to etanercept, as well as a number of other RA biologics, in two large data sources.
Disclosure of Interest: F. Xie: None declared, H. Yun Grant/research support from: BMS, E. Levitan Grant/research support from: Amgen, Consultant for: Amgen, Novartis, P. Muntner: None declared, J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB
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OP0194 THE ASSOCIATION BETWEEN SERUM URIC ACID AND ARTERIAL STIFFNESS IN A LOW-RISK, LARGE POPULATION OF MIDDLE-AGED KOREAN

J. Hwang[1], J.H. Hwang[2], Y. Eun[3], H. Kim[3], J. Lee[3], J.K. Ahn[4]. *[1]Department of internal medicine, National Police Hospital; [2]Center for health promotion, Samsung Medical Center; [3]Department of medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine; [4]Department of internal medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic Of*

Background: Arterial stiffness occurs because of biologic ageing and arteriosclerosis, and is most commonly measured by pulse-wave velocity. Several studies have reported that high serum uric acid may contribute to the development of a number of metabolic and haemodynamic abnormalities, and multivariate analyses in epidemiologic studies have suggested that hyperuricemia is an independent risk factor for arterial stiffness in those with comorbidities such as diabetes, hypertension, and chronic kidney disease. However, there are few reports about the association between SUA and arterial stiffness in apparently healthy populations.
Objectives: We aimed to investigate the association between serum uric acid (SUA) and arterial stiffness as evaluated by brachial ankle pulse wave velocity (baPWV) in a low-risk, large, middle-aged Korean population.
Methods: We conducted a cross-sectional study of 66,917 Koreans (38 170 men, 28 747 women) who received yearly screening with available PWV and SUA results. None of the participants had coronary heart disease, diabetes, or hypertension. SUA was divided into quintiles for assessment of its association with baPWV by multiple linear regression analysis.
Results: The average SUA level was 5.23±1.4 mg/dl, and SUA values were higher in men than in women (6.1±1.2 mg/dl vs 4.1±0.8 mg/dl). In multiple regression analysis, PWV was significantly higher in SUA quintiles 2–5 compared to the lowest group (reference) (coefficient=11.52, 18.19, 24.73, and 31.02 cm/s, respectively). In female subjects, the average difference (cm/s) of PWV between quintiles 2–5 and quintile 1 of SUA was 13.1, 22.9, 34.6, and 32.1, respectively. Fully adjusted linear coefficient β (S.E.) was 6.62 (0.70) and 12.43 (1.33) in all participants and female subjects, respectively (p<0.001). In contrast, there was a J-shaped association between PWV and SUA quintile among males. When modelled continuously, each 1 mg/dl higher SUA level was associated with 0.27 higher baPWV (p<0.001) in the adjusted analysis.
Conclusions: These findings indicate that higher SUA levels could have an unfavourable impact on arterial stiffness as measured by baPWV in a low-risk, large, middle-aged Korean population.
Disclosure of Interest: None declared
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OP0195 ROLE OF SEROPOSITIVITY ON MORTALITY IN RA AND THE IMPACT OF TREATMENT WITH DMARDS

E. Alemao[1], Z. Guo[1], M.E. Weinblatt[2], N.A. Shadick[2]. *[1]Bristol-Myers Squibb, Princeton; [2]Brigham and Women's Hospital, Boston, USA*

Background: Previous studies showed that RF positivity (+) in RA was associated with increased overall mortality, and that cause-specific mortality rates differed by autoantibodies. Anti-citrullinated protein antibodies (ACPAs) have been associated with cardiovascular death, and RF with death due to neoplasm and respiratory disease.[1]
Objectives: To evaluate the association of serostatus (in particular, antibody [Ab] titres) with mortality and its modification by DMARDs.
Methods: Administrative claims data from Optum Clinformatics Data Mart and Humana databases (2006–2016) were used. Inclusion criteria: 2 diagnosis codes for RA plus 1 DMARD prescription; age ≥18 years (y);≥6 months (M) baseline (BL;+/–3 M from index date). Index date was the first test date for ACPA or RF (main analysis) or the DMARD prescription date (DMARD effect on mortality analysis). Patients (pts) with ankylosing spondylitis, Crohn's disease, lupus, psoriatic arthritis or ulcerative colitis at/before index date were excluded. Based on BL Ab test, pts were categorised into Ab status of ACPA+/–, RF +/–and double +/–. Ab +pts were then categorised into 2 groups based on Ab titres. DMARD-exposed pts were categorised into biologic (b)DMARD (use of any bDMARD) and conventional (c)DMARD (use of a cDMARD but never a bDMARD) cohorts. Crude mortality rates per 1000 pt-y, as well as adjusted analysis using traditional multivariate regression and disease risk score methods, were used. Covariates were age, sex, region, physician office visits in past 3 M, indicator variable for RA diagnosis before ACPA/RF testing, past hospitalisation, medication use (steroids, NSAIDs, salicylates), DMARD use and co-morbidities.
Results: A total of 53 849 and 79 926 pts with RA had evaluable ACPA and RF status, respectively. The average (SD) age was 61.4 (15.2) and 61.8 (15.6) y in the ACPA and RF cohorts, respectively. For both ACPA and RF, mortality rates were significantly higher in Ab +vs Ab– pts, and were highest in pts with the highest Ab titres (table 1). The hazard ratios (HRs) for mortality were highest in pts with double positivity (figure 1A). HRs were higher in Ab +vs Ab– pts exposed to cDMARDs. There was no difference in mortality between Ab +vs Ab– pts in the bDMARD-exposed group (figure 1B).

Abstract OP0195 – Table 1 Crude mortality rates and HRs in patients categorised by serostatus

	Patients, n	Deaths, n	Pt-y	Crude mortality, incidence rate/1000 pt-y (95% CI)	Adjusted HR (95% CI)	P value
ACPA–	36 667	1798	1 26 451	14.2 (13.6–14.9)	1.00	
ACPA+	17 182	1276	57 719	22.1 (20.9–23.4)	1.48 (1.37–1.60)	<0.001
ACPA +Group 1*	8321	606	29 518	20.5 (18.9–22.2)	1.38 (1.25–1.52)	<0.001
ACPA +Group 2*	8861	670	28 201	23.8 (22.0–25.6)	1.60 (1.45–1.76)	<0.001
RF–	46 376	2522	1 79 247	14.1 (13.5–14.6)	1.00	
RF+	33 550	2688	1 18 583	22.7 (21.8–23.5)	1.44 (1.36–1.53)	<0.001
RF +Group 1*	16 758	1098	60 393	18.2 (17.1–19.3)	1.18 (1.09–1.27)	<0.001
RF +Group 2*	16 792	1590	58 190	27.3 (26.0–28.7)	1.79 (1.51–2.11)	<0.001

*Based on antibody titre: Group 1=lower titre; Group 2=higher titre