Objectives: To evaluate serum calprotectin S100 protein (A8 and A8/A9) levels in a South African RA Cohort in relation to disease severity at presentation in comparison with traditional RA-associated autoantibodies.

Methods: This was an observational, single-centre study, involving patients attending the Rheumatology Clinic of the Department of Internal Medicine, Chris Hani Baragwanath Academic Hospital (CHBAH) and University of the Witwatersrand, South Africa. The cohort consisted of 128 ethnic black RA DMARD-naïve patients. The study was approved by the local ethics committee and patients gave informed consent to participate.

Results: The baseline demographics and clinical data of the cohort are summarized in table 1. Calprotectin S100 A8 demonstrated a statistically significant association with disease severity (both SDAI ($p=0.005$) and DAS 28 ($p=0.016$)) by linear regression analysis. Calprotectin S100A8/A9 also showed significant associations with SDAI ($p=0.010$) and DAS28 ($p=0.022$) figure 1.

Table 1 Clinical and demographic data of patients with RA

Sex	Freq	Percent	Cum
Male	23	17.97	17.97
Female	105	82.03	100.00
DAS 28	25	19.53	19.53
Inactive			
DAS 28	57	44.53	64.06
Moderate			
DAS 28	46	35.94	100.00
Very Active			
SDAI	9	7.03	7.03
Remission			
SDAI	16	12.50	19.53
Low DA			
SDAI	45	35.16	54.69
Mod DA			
SDAI	58	45.31	100.00
High DA			
CCP	10	7.81	7.81
Negative			
CCP	118	92.19	100.00
Positive			
RF	8	6.25	6.25
Negative			
RF Positive	120	93.75	100.00
MCV	7	5.47	5.47
Negative			
MCV	121	94.53	100.00
Positive

Conclusions: Unlike those of traditional autoantibodies, serum levels of calprotectin correlate strongly with disease severity of RA patients. These findings suggest that calprotectin S100 is a promising biomarker for assessment and monitoring of disease activity in RA.

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FR10663

THE FINE SPECIFICITY OF ANTI-DRUG ANTIBODY RESPONSES TO ORIGINATOR AND BIOSIMILAR INFlixIMAB: ANALYSES ACROSS FIVE DISEASES FROM THE 52-WEEK RANDOMIZED NOR-SWITCH STUDY

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Background: Norway's government funded the NOR-SWITCH study to investigate switching from originator infliximab (INX) to biosimilar CT-P13 in Crohn's disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and chronic plaque psoriasis (Ps). Previously, the main analyses have been published¹. Immunogenicity is associated with treatment failure and is of particular concern in switching².

Objectives: To evaluate the consistency and fine specificity of anti-drug antibody (ADAb) responses to INX and CT-P13, in arthritis and IBD patients, after switching from INX to CT-P13.

Methods: The study included adult patients with CD, UC, SpA, RA, PsA or Ps¹. Assays for drug serum levels and ADAb have been described¹. ADAb positive sera were tested for cross-reactivity to 5 batches of INX and CT-P13. We quantified IgG4 ADAb, testing for functional inhibition. Infliximab peptides were used to compare epitope recognition of positive sera. Immunogenic infliximab-epitopes were identified by ELISA and sera compared across diseases.

Results: We tested 15 controls, 15 arthritis, 21 IBD patients. No Ps patients had ADAb in our study. All 23 anti-CT-P13 and 13 anti-INX sera cross-reacted with INX and CT-P13, respectively. ADAb concentrations to INX or CT-P13 correlated strongly (r values between 0.92 and 0.99, $p<0.001$ for all experiments, Spearman's correlation test). Sera negative for CT-P13 ADAb (10 healthy controls, 5 RA patients) were also anti-INX negative. IgG4 ADAb in all sera recognized 5 different batches of CT-P13 and INX. All positive sera had similar functional inhibition of CT-P13 or INX TNF-binding capacity, showing reduced binding to CT-P13 in the presence of 5 different batches of CT-P13 and INX. 60%-79% of patients recognized 7 synthetic peptides corresponding to major anti-infliximab epitopes, with no significant differences between CT-P13 and INX ADAb. Three minor epitopes in framework regions of infliximab showed reduced antibody reactivity in 30%-50% of patients. Stratifying by diagnosis, we found two epitopes in the variable and constant heavy-chains of infliximab specifically recognized in IBD patients but not rheumatic patients.

Conclusions: ADAb to INX also recognize CT-P13, with similar epitopes. We found no consistent difference in ADAb epitope specificity between diagnoses. However, two specific minor epitopes are only recognized by IBD patients which might reflect the importance of HLA background for ADAb.

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FRI0664

BIOMARKERS FOR RELAPSE IN PATIENTS WITH ADULT ONSET STILL'S DISEASE TREATED WITH IL-6 INHIBITOR.

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Background: Symptoms and laboratory data in patients with adult onset Still's disease patients (AOSD) at relapse are often non-specific. Especially in AOSD patients treated with tocilizumab, IL-6 receptor inhibitor, inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are almost normal despite flared disease activity.

Objectives: To identify useful biomarkers for assessing disease activity and relapse in AOSD patients treated with tocilizumab.

Methods: Consecutive AOSD patients diagnosed by Yamaguchi's criteria in our institution from January 2007 until January 2018 were reviewed. Clinical information was collected from their medical charts. Relapse was defined as a case who required immunosuppressive treatment intensification for AOSD according to their attending physicians. Biomarkers were compared between before relapse and at relapse.

Results: Forty eight patients with AOSD were enrolled. Thirty relapses during the observation period of 3.5 years were identified. At relapse, white blood cell count (WBC), CRP, ESR, serum ferritin levels, and serum lactate dehydrogenase (LDH) levels significantly increased compared to before relapse (WBC, 12123 ± 1238 / μ L vs 7184 ± 607 / μ L, $P=0.002$; CRP, 4.37 ± 1.08 mg/dL vs 0.32 ± 0.18 mg/dL, $P=0.003$; ESR 39.1 ± 7.78 mm/hr vs 6.67 ± 1.46 mm/hr, $P=0.001$; ferritin, 78.9 ± 30.9 ng/mL vs 24.9 ± 3.8 ng/mL, $P=0.036$; LDH, 374.8 ± 48.1 IU/mL vs 214.7 ± 16.8 IU/mL, $P=0.005$). Six patients were identified to experience relapse with fever, active synovitis, rash or lymphadenopathy while treated with tocilizumab. In patients treated with tocilizumab, while neither CRP nor ESR increased in all patients at relapse (CRP <0.30 mg/dL in all; ESR, 4.50 ± 1.04 mm/hr vs 3.75 ± 1.18 mm/hr, $P=0.893$), LDH was significantly elevated at relapse compared to before relapse (451.2 ± 92.1 IU/mL vs 211.2 ± 24.6 IU/mL, $P=0.04$). WBC and serum ferritin levels tended to increase but with no significant difference (WBC: 14620 ± 1547 / μ L vs 9500 ± 2285 / μ L, $P=0.21$; ferritin, 236.4 ± 91.2 ng/mL vs 49.2 ± 24.2 ng/mL, $P=0.091$).

Conclusions: Instead of CRP and ESR, LDH level was a useful clinical biomarker for relapse of AOSD, especially in those treated with tocilizumab.

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FRI0665

IMPACT OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE RESULTS ON WHETHER RHEUMATOLOGISTS CHANGED BIOLOGIC THERAPY FOR RA PATIENTS

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Background: The multi-biomarker disease activity (MBDA) score is a validated test used to assess disease activity for patients with rheumatoid arthritis (RA). How it is used in clinical practice in the U.S. is unclear.

Objectives: We evaluated the likelihood that rheumatologists would add or switch biologic therapies based on the MBDA test result.

Methods: Using previously published methods, we linked results of MBDA tests obtained as part of routine clinical care to 2012–2014 Medicare fee for service claims data for RA patients. We characterized patients as being on a biologic or targeted synthetic DMARD in the 90 days prior to the MBDA test and evaluated biologic/to facitininb treatment changes in the 90 days following the MBDA test. MBDA test scores were classified as low (<30), moderate (30–44), and high (>44). The unit of analysis was the 90-day interval before and after each MBDA test score. Alternating logistic regression was used to compute odds ratios (OR) to quantify the likelihood that patients made any change (add or switch), accounting for the clustered nature of the data (intervals nested within patients, and patients nested within doctor practices) and physician-level variability, controlling

for patient age and sex. Sensitivity analyses used a 6-month interval for outcome ascertainment after the MBDA test.

Results: Using previously validated methods, a total of 27,621 unique RA patients were linked to 44,438 MBDA test scores. For the 27,256 intervals where RA patients were not on biologic therapy when the MBDA score was obtained, a total of 13.2% of patients added a biologic. Patients with high MBDA scores were significantly more likely to add a biologic (table 1). For the 17,182 intervals where RA patients were already on a biologic, a total of 19.1% of patients switched or stopped the biologic that they were taking. Patients with lower MBDA scores were significantly more likely to stay on their therapy, whereas those with higher scores were more likely to stop and/or switch biologics. After adjustment, results from the regression analyses showed that patients with moderate MBDA scores were 1.47 (95% 1.29–1.67)-fold more likely to add or switch biologics, and those with high MBDA scores were 2.54 (95% CI 2.19–2.94)-fold more likely to add or switch biologics. Men (OR=0.90, 95% 0.82–0.98) and older patients (OR=0.92 per 5 year increment, 95% CI 0.91–0.93) were less likely to add or switch therapy, even after controlling for variability between physicians (OR=1.10, 95% CI 1.02–1.19). These results were robust and ORs were numerically larger when extending the interval to 6 months.

Table 1 Proportion of patients who added or switching biologics after the MBDA test

MBDA Score	Non-biologic users who added a biologic after the MBDA test N=27,256	Biologic Users Who Switched or Stopped their Current Biologic after the MBDA test N=17,182
Low (<30)	8.4%	14.0%
Moderate (30–44)	10.8%	16.2%
High (>44)	16.3%	23.1%
Chi-square p value	<0.0001	<0.0001

Conclusions: Results from the MBDA score were significantly associated with the likelihood that a physician added or switched biologic therapies, with either type of change being more frequent when the MBDA score was high. Further evaluation of outcomes after switching, conditional on the MBDA score, is warranted.

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FRI0666

CIRCULATING MIR-99B-5P AS A PREDICTOR OF EROSION PROGRESSION IN EARLY RHEUMATOID ARTHRITIS: A 1-YEAR FOLLOW-UP STUDY BY HR-pQCT

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Background: Bone erosion is a key feature of RA reflecting both disease severity and progression. HR-pQCT is an in-vivo clinical imaging system allowing detailed analysis of bone structure, including bone erosion. Several circulating microRNAs have already been suggested as potential biomarkers in RA.

Objectives: To determine whether plasma cell-free circulating miRNAs are 1) associated with bone erosion at presentation and 2) predictive of erosion progression at 12 months as determined by HR-pQCT in patients with early rheumatoid arthritis (ERA).

Methods: In this prospective study, 124 ERA patients were treated with a tight control protocol aiming at remission by using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). The second metacarpophalangeal joint (MCP2) was assessed for erosions by HR-pQCT at baseline and after 12 months. Plasma cell-free circulating miRNAs at baseline were identified by microRNA array in 10 treatment-naïve ERA patients with maximal erosion volume at MCP2; in 10 treatment-naïve ERA patients without erosion; and in 6 age- and sex-matched healthy controls. The 4 most dysregulated miRNAs were identified by TaqMan[®] qRT-PCR in these same 20 ERA patients. Thereafter, the expression of these 4 selected miRNAs was validated in all 124 ERA patients at baseline.

Results: Of the 377 screened miRNAs, 155 miRNAs were detectable. 94 (60.6%) of these detectable miRNAs were upregulated in ERA patient with erosions, with 13 (8.4%) upregulated more than twofold. 61 (39.4%) miRNAs were