Disclosure of Interest: A. Lila: None declared, L. Denisov: None declared, T. Plaksina: None declared, S. Smakotina: None declared, E. Kunder: None declared, N. Soroka: None declared, A. Kastanayan: None declared, O. Nesmeyanova: None declared, O. Antipova: None declared, E. Ilvanova: None declared, A. Eremeeva Employee of: JSC BIOCAD, E. Dokukina Employee of: JSC BIOCAD, E. Chernyaeva Employee of: JSC BIOCAD, R. Ivanov Employee of: JSC BIOCAD

DOI: 10.1136/annrheumdis-2018-eular.2332

THU0194 CD4+ T CELLS, IMMUNOGLOBULINS AND RISK OF INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER MULTIPLE CYCLES OF RITUXIMAB

F. Martins¹, A. Bensalem², T. Bejan-Angoulvant^{2,3}, A. Lhommas¹, J. Mélet^{1,2}, S. Mammou¹, G. Thibault^{2,4,5}, L. Bernard⁶, P. Goupille^{1,2}, D. Mulleman^{1,2}.

¹Rheumatology, CHRU de Tours; ²EA GICC, University of Tours; ³Clinical Pharmacology, CHRU de Tours; ⁴CNRS ERL 7001, University of Tours;

⁵Immunology; ⁶Infectious diseases, CHRU de Tours, Tours, France

Background: Rituximab (RTX) may be responsible for infectious event in RA patients. Immunological markers may be associated with the occurrence of infections.

Objectives: To evaluate lymphocyte counts and immunoglobulin concentrations over multiple cycles of RTX in RA patients, and to analyse the relationship between these markers and the occurrence of infections.

Methods: Retrospective monocentric study on 94 RA patients treated with RTX. At baseline and during follow up, lymphocyte phenotyping (CD4+, CD3+, CD19 +cells), gammaglobulin, IgG, IgM and IgA concentration were assessed. Patients were dichotomized according to the absence or presence of infectious events. A student's test was used to compare the continuous variables and a Chi2 test or the Fisher test was used for the dichotomous variables.

Results: A total of 119 infectious events occurred during follow-up, of which only 11 were serious, with respective incidences of 65 per 100 patient-years and 6 per 100 patient-years. Low IgM concentration at RTX initiation and low IgG concentration (<5 g/L) throughout follow-up were associated with an increased risk of infection. Both gammaglobulin and IgG concentrations decreased along with successive cycles of RTX in patients with infection, while they remained stable in patients without infection. Twelve patients had a CD4 +cell count<200/mm³ during follow up, of which one with a CD4 +cell count 233/mm³ at baseline, who subsequently presented an opportunistic infection.

Conclusions: Gammaglobulin, IgM and IgG concentrations and CD4 +cell count are valuable before RTX initiation in RA patients. IgG or gammaglobulin concentration should also be monitored before each cycle. CD4 +lymphocytes monitoring should be considered in patients with low value at initiation.

Disclosure of Interest: F. Martins: None declared, A. Bensalem: None declared, T. Bejan-Angoulvant: None declared, A. Lhommas: None declared, J. Mélet: None declared, S. Mammou: None declared, G. Thibault: None declared, L. Bernard: None declared, P. Goupille Consultant for: Abbvie, Biogaran, BMS, Hospira, Janssen-Cilag, MSD, Pfizer, Sanofi-Genzyme and UCB, D. Mulleman Grant/research support from: Abbvie and Nordic Pharma, Consultant for: MSD, Novartis, UCB and Pfizer

DOI: 10.1136/annrheumdis-2018-eular.7030

THU0195 PREVALENCE OF OCCULT HEPATITIS B CARRIER STATUS AND ITS ASSOCIATED FACTORS IN PATIENTS WITH RHEUMATIC DISEASES UNDERGOING BIOLOGICAL THERAPIES

C.C. Mok¹, L.Y. Ho¹, K.L. Chan¹, S.M. Tse¹, C.H. To². ¹Medicine, Tuen Mun Hospital; ²Medicine, Pok Oi Hospital, HK, Hong Kong

Objectives: To study the prevalence of occult hepatitis B carrier status and its associated factors in patients with rheumatic diseases undergoing biological therapies

Methods: Consecutive adult patients with various rheumatic diseases who were currently receiving biological therapies between November 2016 and April 2017 were recruited in this cross-sectional study. Blood was taken for evidence of hepatitis B infection (HBsAg, anti-HBs, anti-HBc-IgG). For patients tested positive for HBsAg or anti-HBc-IgG, assay of serum HBV-DNA level was also performed. Occult hepatitis B carrier was defined as patients who were HBsAg negative but anti-HBc-IgG positive. Logistic regression was performed to study factors independently associated with occult hepatitis B carrier status in these patients.

Results: 310 Chinese patients were studied (60% women, age at biological therapy 44.0±13.0 years). The underlying rheumatic diseases requiring biological therapies were rheumatoid arthritis (46%), spondyloarthritis (31%), psoriatic

arthritis (12%) and systemic lupus erythematosus (8.1%). The biologics being used were the TNF inhibitors (66%), tocilizumab (16%), abatacept (2.9%), rituximab (7.7%), belimumab (5.8%) and tofacitinib (1.3%). Hepatitis B carrier (HBsAg +) status was detected in 11 (3.5%) patients and they were all put on preemptive anti-viral therapy (entecavir). A total of 105 patients (34%) were occult hepatitis B carriers (HBsAg- but anti-HBc-IgG+). Anti-HBs was present in 83/105 (79%) of these patients. Occult hepatitis B carriers were significantly older than the non-carriers (49.9±11.1 vs 40.9±13.3 years; p<0.001), and were more frequently identified in rheumatoid arthritis than other rheumatic diseases (45% vs 25%; p<0.001). However, there was no gender difference in the prevalence of the occult hepatitis B carrier status (37% in women vs 28% in men; p=0.10). Logistic regression revealed that older age (RR 1.05 [1.03–1.08] per year; p<0.001) was the only independent factor significantly associated with occult hepatitis B infection. Rheumatoid arthritis was not significantly associated with occult hepatitis B carrier status after adjustment for age and sex. Of the occult hepatitis B carriers, 9 (8.6%) had detectable HBV-DNA levels but all were very low titers (<100 IU/ml). Five (56%) patients with detectable HBV-DNA levels received entecavir treatment during biological therapies, while 19 (20%) patients without detectable HBV-DNA were put on preemptive entecavir treatment (including all patients who were receiving rituximab). None of the overt (HBsAg+) or occult hepatitis B (HBsAg-anti-HBc-IgG+) carrier patients developed clinical reactivation of hepatitis B during a mean of 5.0±3.7 years of biological therapies.

Conclusions: Occult hepatitis B carrier status was present in one-third of Hong Kong Chinese patients with various rheumatic diseases undergoing biological therapies. Older age was the only independent factor associated with occult hepatitis B infection. Despite the relatively low rate of preemptive anti-viral treatment in these patients, clinical reactivation of hepatitis B was not reported over 5 years of biological therapies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4333

THU0196 DO CONTEXTUAL FACTORS INFLUENCE SURVIVAL ONDRUG OF BIOSIMILARS IN CLINICAL PRACTICE?

D. Di Giuseppe¹, T. Frisell², E. Lindqvist³, L. Jacobsson⁴, C. Turesson³, C. Sjöwall¹, J. Askling¹, on behalf of ARTIS group. ¹Department of Medicine Solna, Karolinska Institutet; ²Department of Medicine Solna, SRQ, Stockholm; ³Lund University and Skåne University Hospital, Malmö; ⁴Sahlgrenska Academy, University of Gothenburg, Gothenburg; ⁵Linköping University, Linköping, Sweden

Background: The introduction of biosimilars has been linked to concerns regarding their effectiveness and safety compared to their originator products. Whilst randomized controlled trials may address their relative efficacy, the outcome of biosimilars in clinical practice may be influenced by contextual factors, such as the treating rheumatology unit's experience with biosimilars and non-medical switching.

Objectives: To analyze whether contextual factors, such as department size and use of biosimilars, and calendar period of treatment start, influence time until treatment discontinuation (i.e. drug survival) of biosimilars as compared to corresponding originator products.

Methods: We used data from the Swedish Rheumatology Quality register to identify all patients with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, or other spondyloarthropathies who started infliximab between March 1st 2015 and Sept 30th 2017 or etanercept between April 1st 2016 and Sept 30th 2017, as their first ever biologic. Kaplan-Meier curves and Cox models were used to assess the association between drug survival and the size of the rheumatology unit, its use of biosimilars (extent of biosimilar use above/below national median at teach time point), and whether the treatment start occurred soon after biosimilar introduction (infliximab: first 12 months, etanercept: 6 months counting from first date of availability of the biosimilar in question). To avoid artefacts, patients were censored if switching from the originator to a biosimilar (or vice versa).

Results: During the study period, 368 and 738 patients started infliximab originator or biosimilar, and 125 and 2079 started etanercept originator or biosimilar, as first ever biological treatment. Overall, the hazard ratio (HR) of discontinuing treatment (comparing the biosimilar vs its originator) was 1.21 (95% CI: 0.96–1.51) for infliximab and 0.88 (95% CI: 0.57–1.35) for etanercept, adjusted for indication, age (quartiles), gender, region, and HAQ (quartiles), DAS28 (quartiles) and global health (quartiles) at treatment start. Patients treated in large clinics (more than 1695 patients (75th percentile) at the end of the study period) were at a lower risk of drug discontinuation (table 1). We noted no association between overall biosimilar use in the rheumatology clinic in question and survival on drug (neither originator nor biosimilar). By contrast, those who started infliximab biosimilar later had a lower risk of discontinuing (HR: 0.65 (95% CI: 0.50–0.85)) compared to those who started in the first year of availability. For etanercept biosimilar, no such association was noted.

Abstract THU0196 – Table 1. Hazardratios among patients starting their first biologic treatment during the studyperiod according to contextual factors

	Infliximab originator	Infliximab biosimilar	Etanercept originator	Etanercept biosimilar
Number of patients	368	738	125	2079
Number of discontinuations	165	265	23	392
Dept. size				
Low (quartile I & II)	0.88 (0.37-2.11)	1.47 (0.88-2.46)	30.66 (6.16-152.68)	1.69 (1.12-2.55)
Medium (quartile III)	1.29 (0.81-2.08)	1.90 (1.36-2.65)	10.96 (2.13-56.49)	1.40 (1.08-1.82)
High (quartile IV)	Ref	Ref	Ref	Ref
Dept. use of biosimilars				
Low	Ref	Ref	Ref	Ref
High	0.88 (0.58-1.34)	1.20 (0.82-1.75)	1.90 (0.64-5.70)	1.00 (0.77-1.29)
Period of biologic start*				
Early period	Ref	Ref	Ref	Ref
Later period	0.98 (0.67-1.42)	0.65 (0.50-0.85)	0.06 (0.01-0.53)§	0.94 (0.76-1.17)

*Additionally adjusted for department size and use of biosimilar;

§ Only 2 discontinuation in the later period of etanercept originator

Conclusions: Contextual factors, presumably related to expectations and differences in clinical monitoring, influence the observed survival on drug of biologics, including biosimilars, and must be considered when the comparative effectiveness of biosimilars is evaluated.

Disclosure of Interest: D. DiGiuseppe: None declared, T. Frisell: None declared, E. Lindqvist: None declared, L. Jacobsson Consultant for: received lecture and consulting fees from Pfizer, Abbvie and Novartis, C. Turesson Grant/research support from: Abbvie, Bristol Myers-Squibb, Roche, Consultant for: MSD, Bristol Myers-Squibb, Roche, Paidinstructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, C. Sjöwall: None declared, J. Askling Grant/research support from: has or has had research agreements with Abbvie, BMS, MSD, Pfizer, Roche, Astra-Zeneca, Eli Lilly, Samsung Bioepis, and UCB, mainly in the context of safety monitoring of biologics via ARTIS. Karolinska Institutet has received remuneration for JA participating in advisory boards arranged by Pfizer and Eli Lilly.

DOI: 10.1136/annrheumdis-2018-eular.4464

THU0197**EFFECTS OF TOCILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR ANTIBODY, ON SERUM LIPID AND ADIPOKINE LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

E. Hoffman¹, M.A. Rahat^{1,2}, J. Feld³, M. Elias³, I. Rosner^{1,4}, L. Kaly⁴, I. Lavi⁵, D. Zisman^{1,3}. ¹The Ruth and Bruce Rappaport Faculty of Medicine, Technion; ²The Immunotherapy Laboratory; ³Rheumatology Unit, Carmel Medical Center; ⁴Rheumatology Unit, Bnai Zion Medical Center; ⁵Department of Community Medicine and Epidemiology, Carmel Medical Center, Haifa, Israel

Background: Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease.¹ Dyslipidemia is a known adverse reaction to tocilizumab (TCZ), the anti-interleukin-6 receptor antibody, used in RA treatment.

Objectives: To assess the effect of TCZ on lipid and adipokine levels in the serum of RA patients

Methods: Forty RA patients with active disease initiating TCZ treatment and 40 healthy matched controls were included. Height, weight, disease activity score (DAS28), lipid profile and atherogenic indices (AI) were measured before and four months after TCZ treatment initiation. Serum concentrations of leptin, adiponectin, resistin, interleukin-6 and high sensitivity CRP were measured by ELISA in both study groups.

Statistical analysis: The differences in clinical and laboratory data of RA patients between baseline and follow up were assessed by paired t-test and by linear mixed models with repeated measures for adipokines levels after adjustment to BMI, statin treatment and disease duration. To compare the adipokines levels between RA and control groups adjusted to baseline BMI and statin treatment we used ANCOVA models. HsCRP and IL-6 were compared between the two groups by two-tailed Mann Whitney test. The results were considered statistically significant when p≤0.05.

Results: The average age of the study population was 57.5±11 years, 82.5% were women, with a disease duration of 8.7±5.6 years. The majority of the patients responded to TCZ and reduced their diseases activity from DAS28 score of 5.45±1.06 to 3.46±1.37 (p<0.0001). Following treatment, a significant elevation of total cholesterol (199±52 to 221±53 mg/dl, p<0.01), HDL (55±19 to 59±23 mg/dl, p<0.01) and triglycerides (140±69 to 168±107, p=0.04), and no significant changes in weight, BMI, low density lipoprotein (LDL) and AI were found. Significantly higher adiponectin levels (5.59±2.39 vs. 3.75±1.63 ng/ml, p<0.0001), lower resistin levels (16.25±7.17 vs. 21.53±8.19 pg/ml, p=0.007) and leptin/adiponectin ratio (6.44±6.44 vs. 5.52±6.08, p=0.03) were measured in the RA group compared to controls after adjustment to BMI and statin treatment. Four months after TCZ treatment a statistically significant decrease in adiponectin (4.53±2.12 ng/ml p<0.0001), resistin levels (20.42±8.06 pg/ml, p=0.01) and leptin/adiponectin ratio (7.99±7.84, p=0.002) were measured after adjustment to BMI, statin treatment and disease duration. The levels of hsCRP decreased significantly

(3.37±2.0 vs 0.74±1.36 mg/dl, p<0.001) and IL-6 increased significantly (13.15±25.43 vs 99.80±97.97 pg/ml, p<0.001) following treatment.

Conclusions: The impact of TCZ treatment on lipid metabolism is complex. The elevation in HDL without change in AI, and the tendency toward normalisation of the adipokine profile observed, suggests a protective role of TCZ treatment against the cardiovascular burden in RA patients.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4418

THU0198**IMMUNOGENICITY ASSOCIATED WITH A TRANSITION FROM ADALIMUMAB REFERENCE PRODUCT TO ABP 501 IN PATIENTS WITH RHEUMATOID ARTHRITIS**

E. Krishnan, D. Mytych, N. Zhang, H. Wang, A. Kaliyaperumal. *Biosimilars Development, Amgen Inc., Thousand Oaks, USA*

Background: In clinical practice, patients treated with an originator product may be transitioned to a biosimilar. Therefore, it is important to ensure that such transition is safe and is not associated with increased immunogenicity.

Objectives: To study the incidence of binding anti-drug antibodies (bADAs) and neutralising anti-drug antibodies (nADAs) after patients with rheumatoid arthritis (RA) are transitioned from adalimumab reference product (RP) to ABP 501, an approved biosimilar for adalimumab.

Methods: We analysed data from the open-label extension (OLE) of a randomised 26 week phase 3 study (NCT 01970475) comparing ABP 501 and adalimumab. In this OLE study (NCT02114931), patients originally randomised to ABP 501 in the parent study continued on ABP 501 while patients originally randomised to adalimumab (RP) were switched to ABP 501 so that all patients received ABP 501. Specifically, we studied the incidence of new ADAs in patients who were ADA negative at the time of entry into the OLE study. The incidence after excluding transiently elevated ADAs was also examined.

Results: The Table summarises the incidence of ADAs.

Abstract THU0198 – Table 1

Original randomization arm	ABP 501/ ABP 501	Adalimumab RP/ ABP 501
Number of patients with negative bADA at OLE baseline	147	149
New cases of +bADA post OLE baseline	50	35
New cases of +nADA post OLE baseline	20	12
Transient cases of +bADA	33	13
Transient cases of +nADA	8	2
Overall incidence of new cases of +bADA	34.0%	23.5%
Overall incidence of new cases of +nADA	13.6%	8.1%
Incidence of non-transient cases of +bADA	11.6%	14.8%
Incidence of non-transient cases of +nADA	8.2%	6.7%

Conclusions: Transitioning from adalimumab reference product to ABP 501 was not associated with increased immunogenicity over the observational period of 72 weeks.

Disclosure of Interest: E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc., D. Mytych Shareholder of: Amgen Inc., Employee of: Amgen Inc., N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., H. Wang Shareholder of: Amgen Inc., Employee of: Amgen Inc., A. Kaliyaperumal Shareholder of: Amgen Inc., Employee of: Amgen Inc.

DOI: 10.1136/annrheumdis-2018-eular.7225

THU0199**A PILOT STUDY TO ASSESS THE RELATIONSHIP BETWEEN SMOKING AND DRUG INEFFECTIVITY IN RHEUMATOID ARTHRITIS – PART OF A QUALITY IMPROVEMENT PROJECT AIMED AT SMOKING CESSATION**

G. Starritt, D. Brennan. *Rheumatology, Musgrave Park Hospital, Belfast Health and Social Care Trust, Belfast, UK*

Background: It has long been known that patients with rheumatoid arthritis who smoke have more severe disease. This results in greater joint destruction and disability, and further increase in cardiovascular risk¹. Patients' disease may be more difficult to control with disease modifying anti-rheumatic drugs (DMARDs) and biologic drugs. Smoking may also interfere with the pharmacokinetics of biologic