52.8% over 2.0 years of exposure to GLM and 45.2% over 1.6 year of exposure to GLM-IV.

Conclusion: In this real-world study of Canadian patients with RA, differences in baseline characteristics between patients treated with an anti-TNF over time and between agents shows potential selection biases when selecting a given therapy and may impact the proportion of patients achieving a target-specific outcome. Treatment significantly reduced disease activity and improved functionality in a similar fashion and were also safe and well tolerated.

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FRI0110 RITUXIMAB BIOSIMILAR NON-MEDICAL SWITCH – DOES IT WORK?

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Background: Since the introduction of anti-TNF biosimilars in routine clinical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. Rituximab biosimilar was granted marketing authorisation by the EMA in February 2017. Our Trust was one of the first centres to embrace a CQUIN which required adoption of biosimilar within three months for new patients and one year for switchers. This could help deliver significant savings to the NHS whilst achieving similar clinical outcomes.

Objectives: We report our early experience of introducing rituximab biosimilar in people with RA.

Methods: A list of all patients prescribed rituximab was extracted through our database. A 'switch' letter was drafted and sent to all patients including Truxima information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch. Patients were reviewed as originally planned by their respective clinicians.

Results: 44 patients with RA on 2 g dose six-monthly were identified established on rituximab. Four had stopped treatment prior to switching. All 40 agreed to switch to Truxima that was completed by February 2018. Mean age of switchers was 58.6 (range 26-80 years). Eight were men and remaining 32 (80%) were women. Fourteen (35%) were Asian, one Afro-Caribbean and the rest (62%) were White Caucasian. DAS28 scores were available for all participants. Prior to the switch median DAS28 was 3.0 (range 0.6-5.1). Following the switch it was 2.95 (range 1.5-5.7). Amongst these, eight (20%) reported adverse effects. Four had serum sickness reaction within the first week of the second dose with loss of efficacy. One required admission to ED (<24 hrs) for further management. All decided against further biosimilar and three were swapped back to the originator with no further concerns. In one case the clinician decided to change the class of drug to a TNF inhibitor. Three patients had mild intolerance and agreed to continue Truxima with no further issues. One patient developed military tuberculosis and was taken off biologic therapy.

Adverse events related to Rituximab biosimilar switch

Age	Gender	Previous Mabthera Cycles	Prior DAS28	Post switch DAS28	Adverse effects	Final drug choice
39	F	1	3.5	5.1	Gen unwell, achy, flu like symptoms	Humira
70	M	3	2.1	1.8	Itchy scalp, brain fog	Truxima
49	F	2	4.4	2.8	Vomiting, diarrhoea	Mabthera
48	F	2	3.1	5.5	Palpitations, dizziness	Mabthera
48	F	4	1.8	2.8	Headache, flushing	Truxima
58	F	4	4.5	5.1	Nausea, flushing, headache	Truxima
37	F	5	3.5	4.5	Body pains, headache, distaste, lethargy (hospitalised)	Mabthera
76	F	1	2.2	2.5	Miliary TB	Biologic withdrawn

Conclusion: Our experience of switching rituximab patients is certainly not as smooth as it was for infliximab and etanercept. All were happy to switch after receiving a letter and having the opportunity to contact if necessary. Substantial annual cost savings of nearly £140,000 were achieved once the switch process completed. At group level there were no major differences in disease outcomes. However, 10% had severe serum sickness reaction with loss of efficacy and loss of confidence in the drug. One patient developed military TB despite having one previous originator cycle with no issues. We support the routine switching from originator to biosimilar rituximab however close monitoring is required certainly in the first few weeks of dose administration.

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FRI0111 ASSOCIATION BETWEEN RHEUMATOID FACTOR STATUS AND DISCONTINUATION OF TUMOR NECROSIS FACTOR INHIBITORS DUE TO INEFFECTIVENESS IN RHEUMATOID ARTHRITIS

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Background: As for the treatment of rheumatoid arthritis (RA), the influence of rheumatoid factor (RF) positivity on the long-term efficacy of tumor necrosis factor inhibitors (TNFi) is controversial.

Objectives: We conducted an exploratory study in a large cohort of RA patients to evaluate the relationship between RF status and the discontinuation of TNFi treatment due to ineffectiveness in a clinical setting.

Methods: This study included bio-naïve RA patients enrolled in the Tsurumi Biologic Communication Registry in Japan. The crude comparison of TNFi discontinuation due to ineffectiveness between seropositive and seronegative patients was analyzed using the cumulative incidence function of competing events and Gray test. We assessed the associations between baseline patient characteristics and discontinuation of TNFi therapy due to insufficient response using Fine-Gray proportional hazard regression. Fine-Gray proportional hazard analysis considered competing events of interest, including insufficient response, adverse event, palliation, and personal reasons.

Results: Demographic and clinical characteristics of each group are described in Table 1. There was a higher discontinuation rate due to insufficient response in RF positive patients than in RF negative patients using Gray test (Figure). RF positivity was significantly predictive of the discontinuation of TNFi therapy due to ineffectiveness using Fine-Gray proportional hazard regression analysis after adjusting for baseline characteristics, including age, sex, stage, class, disease activity at baseline, methotrexate use, and prednisolone use (Table 2).

Conclusion: Using Fine-Gray proportional hazard regression, we demonstrated that RF positivity was related to a higher discontinuation rate of TNFi therapy due to ineffectiveness in bio-naïve RA patients.

Figure. Cumulative incidence of competing events and Gray test.

Discontinuation of tumor necrosis factor inhibitors therapy due to ineffectiveness, stratified by rheumatoid factor (RF) status ($P = 0.14$ by Gray test).

Table 1. Characteristics of RA patients at baseline by RF status.

	RF (n = 1151; 3407 patient-years)		
	RF positive (n = 913)	RF negative (n = 238)	P†
Age, years (SD)	56.6 (13.5)	53.1 (14.7)	<0.001
Female, no. (%)	737 (80.8)	195 (82.3)	0.64
DAS28ESR (SD)	5.28 (1.33)	4.87 (1.38)	<0.001
Stage I+II/III+IV, no. (%)	312/569 (35.4/ 64.6)	103/120 (46.2/ 53.8)	0.0032
Class I+II/III+IV, no. (%)	543/338 (61.6/ 38.4)	174/49 (78/22)	<0.001
Current MTX treatment, no. (%)	584 (82.7)	191 (90.1)	0.009
Current PSL treatment, no. (%)	383 (58.1)	98 (51.0)	0.083

Data are presented as mean, unless otherwise stated. SD: standard deviation; RA: rheumatoid arthritis; RF: rheumatoid factor; MTX: methotrexate; PSL: prednisolone; DAS28ESR: Disease Activity Score in 28 joints calculated with erythrocyte sedimentation rate. † Chi-square test for categorical variables and t-test for continuous variables.

Table 2. Fine-Gray proportional hazard regression.

Model including RF status (n = 643)		
Variable	HR (95% CI)	P
RF positive	1.73 (1.07-2.80)	0.023
Age at baseline	0.98 (0.97-0.99)	0.035
Sex (referent: male)	0.89 (0.58-1.38)	0.63
Methotrexate use	1.68 (0.96-2.96)	0.069
Prednisolone use	1.20 (0.83-1.75)	0.31
Stage III + IV (referent: I + II)	0.99 (0.98-1.01)	0.97
Class III + IV (referent: I + II)	1.00 (0.98-1.02)	0.67
DAS28ESR at baseline	1.31 (1.14-1.51)	<0.001

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FRI0112 INCREASED RISK OF SEVERE INFECTION RECURRENCE IN PATIENTS WHO DEVELOPED SEVERE INFECTIONS DURING bDMARDs THERAPY: A STUDY OF THE MIRAI COHORT

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Background: One of the most important complications of biological disease-modifying antirheumatic drugs (bDMARDs) is severe infection, and management of patients who develop severe infection during treatment with bDMARDs is a great concern. However, no consensus exists regarding bDMARDs readministration following treatment for bDMARDs-associated infection.

Objectives: We elucidated risk factors associated with severe infection recurrence in patients who developed severe infections during bDMARDs therapy. Severe infection was defined as an infection requiring hospitalization. Moreover, we analyzed whether bDMARDs readministration after severe infection in patients with rheumatoid arthritis (RA) was a risk for severe infection recurrence.

Methods: The study sample comprised patients with RA who were examined and prescribed bDMARDs at Osaka Minami Medical Center between January 2010 and December 2017, as part of the MIRAI cohort. The patients who developed severe infections during bDMARDs treatment were followed-up for 12 months. Logistic regression analysis was performed using baseline disease activity, baseline treatment, and disease activity and treatment during the 12-month period.

Results: Severe infections developed in 164 of a total of 1192 patients who were treated with bDMARDs during the study period, and the severe infection rate was 5.73/100 patients-years. Among the 164 patients, bDMARDs were readministered in 130 (79.3%), whereas treatment with bDMARDs was discontinued in 34 patients (20.7%). We observed 31 cases of patients with severe infections during the follow-up period (18.9/100 patients-years), of which 20 patients (15.4/100 patients-years) belonged to the bDMARDs readministration group and 11 (32.4/100 patients-years) belonged to the bDMARDs discontinuation group. The adjusted odds ratio (OR) for severe infection recurrence within 12 months in the bDMARDs readministration group was 0.39 [95% confidence interval (CI) 0.16–0.96]. At 12 months after infection, high-dose prednisolone treatment (adjusted OR 1.35, 95%CI 1.08–1.69), high C-reactive protein level (adjusted OR 1.28, 95%CI 1.02–1.62), and low serum albumin levels (adjusted OR 0.30, 95%CI 0.01–0.89) were associated with high risk of severe infection recurrence (Figure).

Figure. Adjusted odds ratio for severe infection recurrence within 12 months (adjusted for age and sex)

Conclusion: Patients who developed severe infection during bDMARDs treatment were at an extremely high risk for severe infection irrespective of the readministration or discontinuation of bDMARDs after infection. Discontinuation of bDMARDs, high dose of prednisolone 12 months after infection, high levels of C-reactive protein 12 months after infection, and low levels of albumin 12 months after infection were identified as risk factors for severe infection recurrence in these patients. However, bDMARDs readministration did not increase the risk of severe infection recurrence.

REFERENCE:

- [1] Ramiro et al, Ann Rheum Dis 2017;76:1093-1101.