csDMARDs were introduced: methotrexate (MTX), leflunomide (LFN), sulfasalazine (SSZ) and hydroxychloroquine (HCQ). In addition, the following bDMARDs were used: abatacept, adalimumab (ADA), certolizumab, etanercept (ETN), golimumab, infliximab (INF), rituximab and tocilizumab. Finally, small doses of steroids were used. During follow-up the clinical, laboratory findings as well as the treatment decisions and strategies were all recorded. In addition, the adverse drug reactions, the reason of termination or changing strategies, disease complications and comorbidities were all recorded. Finally, disease activity was measured with the 28 joint count, Disease Activity score-28 (DAS-28) using the erythrocyte sedimentation rate.

Results: All patients have received one csDMARD, at least for 6 months. The csDMARD of first choice was MTX (58%), followed by LFN (32%), HCQ (8%), and SSZ (2%) with or without small doses of steroids. The bDMARD of first choice was INF (37%) followed by ETN (32%) and ADA (31%). During the follow up period, 14 patients were lost. In addition, 7 patients never received bDMARDs due to various comorbidities. Thus, the final results are referred to 517 patients. Among those patients, 324 (66%) were treated with csDMARDs as monotherapy or in combination therapy with or without the use of steroids with significant clinical improvement and sustained LDA. However, eleven patients (3,2%) from this group neither achieved LDA, nor received bDMARDs, due to comorbidities. On the other hand, 175 patients (34%) were treated with bDMARDs with or without csDMARDs or/and steroids. The majority of them demonstrated sustained LDA for a long period of time. From this group 31 patients (17,7%) never achieved LDA, despite that they switched and received all bDMARDs. Thus a total of 20,9% of our patients never achieved LDA.

Conclusions: Using the EULAR and ACR recommendations for RA therapy we successfully treated the majority of our patients. However, we found that the size of gap and the unmet needs for RA treatment is about twenty per cent. This is the first study aiming to estimate the gap and the size of unmet needs for RA treatment in a large patient population followed-up in a tertiary university centre.

Disclosure of Interest: None declared

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FRI0102

REDUCTION OF ANTIDRUG ANTIBODY LEVELS AFTER SWITCHING TO RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH PREVIOUS FAILURE TO INFILIXIMAB OR ADALIMUMAB

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Background: Rituximab (Rtx), a monoclonal antibody against CD20+, induces transient depletion of B cells and was approved for the treatment of patients with active rheumatoid arthritis (RA). Previous data¹ showed that Rtx is particularly effective on autoimmune diseases in which auto-antibodies (auto-Ab) are produced. Based on this, it is hypothesised that auto-Ab produced by short-lived plasma cells expressing CD20 are targets of Rtx. Given this scenario, the immunogenicity related to the use of Infliximab (Ifx) or Adalimumab (Ada) could be cleared by Rtx.

Objectives: First, to analyse the persistence of anti-drug antibodies (ADA) after switching to either a 2nd biological therapy (TNFi or Rtx) after 12 months of follow-up. Second, to evaluate whether the reduction of ADA levels are influenced by the mechanism of action of the second biological therapy (BT).

Methods: Dataset from a prospective cohort including all patients with RA starting BT at the Unit of Complex Therapy in a tertiary hospital was used. For this study, data from 21 patients who had experienced previous failure to Ifx (57%) or Ada (43%) related to ADA detection and then switched to a 2nd TNFi (Ifx, Ada, Etanercept or Certolizumab) or to Rtx was analysed. Additionally, patients should have both determinations of ADA levels: at the end of the first BT and 12 months after switching. ADA were determined by a bridging ELISA. The proportion of patients with ADA positive levels at 12 months was determined. Also, the relative reduction (in median) of ADA levels between patients switching to a 2nd TNFi vs Rtx in both visits was compared.

Results: Out of 21 ADA positive patients with RA, 15 (71%) switched to a 2nd TNFi and 6 (29%) to Rtx. Demographic characteristics of patients are shown in table 1.

ADA remained positive in 80% of patients at 12 months after switching BT. The percentage of patients with undetectable ADA levels at 12 months was higher in

the group of patients treated with Rtx compared with patients receiving a 2nd TNFi (33% vs 13%, respectively). The median ADA levels (AU/ml) values at baseline and at 12 months were 536 and 123 for Rtx and 3625 and 1842 for TNFi. The relative reduction of median ADA levels between baseline and 12 months visits was higher in patients with Rtx than in patients treated with TNFi (-78% vs -50%, respectively).

Abstract FRI0102 – Table 1. Demographics characteristics of the 21 patients according to the second biologic.

Switch to:	TNFi(n=15)	RTX(n=6)
Women, n(%)	13 (87%)	6 (100%)
Age, years, median(IQR)	47 ^(37–56)	50.5 (42.5–65.5)
Smoking status, n(%)	2 (13%)	1 (17%)
IMC, Kg/m ² , median(IQR)	23.6 (19.3–28.6)	34.1 (25.2–32.5)

Conclusions: Despite discontinuing TNFi, ADA titers remain positive in a high proportion of patients with RA after one year. Over time, ADA levels decrease in patients who switch to a second BT, being this effect more pronounced in patients receiving Rtx than a 2nd TNFi. This effect could be explained by the intrinsic action mechanism of Rtx on plasmatic CD20+ cells.

REFERENCE:

- [1] Huang H, et al. Rituximab specifically depletes short-lived autoreactive plasma cells in a mouse model of inflammatory arthritis. PNAS2010 Mar 9;107(10):4658–63.

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FRI0103

ONE-YEAR FOLLOW-UP OF A NATIONWIDE COHORT OF PATIENTS WITH INFLAMMATORY ARTHRITIS, WHO SWITCHED FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT, FOCUSING ON PATIENTS WHO SWITCHED BACK TO ORIGINATOR. AN OBSERVATIONAL DANBIO STUDY

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Background: In Denmark, patients (pts) treated with originator etanercept (ETA) 50 mg SC conducted a mandatory non-medical switch to biosimilar SB4 in April 2016 (switchers). Pts treated with 25 mg ETA or 50 mg powder-solution were not mandated to switch (non-switchers). Some switchers resumed ETA during follow-up (back-switchers).

Objectives: To investigate the frequency of back-switching after the non-medical switch from ETA to SB4, and in back-switchers to study, 1) baseline characteristics at the time of initial switch (ETA->SB4), 2) reasons for SB4 withdrawal, 3) changes in disease activity during treatment with SB4 and after back-switching.

Methods: Patient data were retrieved from the DANBIO registry (censored August 2017). For back-switchers, disease activity at the start of SB4 (=baseline) and at the time of back-switching to ETA were compared, and changes in disease activity between the two time points were calculated (=delta values), stratified by indication (RA/PsA/AxSpA). Baseline characteristics of back-switchers were compared to the rest of the switch population (Chi-sq, Mann-Whitney U-test). Abbreviations are shown in table 1.

Results: 1641 pts switched from ETA to SB4. Of these, 299 (18%) withdrew SB4 therapy during 1 year follow-up and either switched back to ETA (n=120, 7%), started another bDMARD (n=104), died (n=9), were lost to follow-up (n=1) or did not re-start bDMARDs (n=65).

Among the 120 back-switchers, SB4 was withdrawn due to LOE (52%), AE (39%), or other/unknown reasons (9%). The reasons for withdrawal of SB4 in back-switchers are listed in table 1. No major safety events occurred. The median time on SB4 before back-switching was 120 (IQR 73–193) days, and the time

between stop of SB4 and re-start of ETA was 1^{1-1} days. Baseline characteristics of back-switchers vs the rest of the switch population were similar (all $p>0.05$). Among back-switchers who stopped SB4 due to LOE, PGA increased during SB4 treatment, whereas CRP and SJC were largely unchanged (table 1). At the date of censoring, 104/120 back-switchers (87%) were still treated with originator ETA (median treatment duration 236 (155–302) days).

Abstract FRI0103 – Table 1. Description of ETA-SB4-ETA back-switchers (n=120)

	RA, n=80	PsA, n=20	AxSpA, n=20
Characteristics upon start of SB4, n=120			
Female, %	73	55	35
Age, years	59 (52-70)	45 (36-56)	43 (38-56)
SJC, n	0 (0-1)	0 (0-0)	-
CRP, mg/L	3 (1-8)	1 (1-5)	3 (1-6)
PGA, mm	27 (12-54)	25 (13-63)	23 (13-44)
Characteristics upon re-start of ETA in pts who back-switched due to LOE, n=62			
Pt number, n	38	11	13
SJC, n	2 (0-5)	0 (0-2)	-
CRP, mg/L	3 (2-11)	3 (2-7)	4 (1-6)
PGA, mm	64 (50-76)	78 (18-90)	42 (35-63)
Delta-values among pts who stopped due to LOE and back-switched, n=62**			
Delta-SJC, n	1 (0-4)	0 (0-0)	-
Delta-CRP, mg/L	0 (-1-5)	1 (0-2)	0 (0-4)
Delta-PGA, mm	30 (12-52)	15 (7-77)	25 (19-35)
Pts stopped due to AE, n=47: Arthralgia 1 pt, bladder dysfunction 1, blurred vision 1, diarrhea 4, dizziness 2, dyspnea 2, erectile dysfunction 1, hair loss 1, headache/migraine 4, hyperhidrosis 2, hypertension 1, hypotension 1, infections 2, leg cramps 1, local injection problems 3, myalgia 1, nausea 2, neuropathies 1, psoriasis/pustulosis 1, rash/itching 9, not stated 21 (total =62 events)			
Numbers are medians (IQR) unless otherwise stated, *DAS28<2.6 (RA, PsA), ASDAS<1.3 (AxSpA)			
** Disease activity at time of re-start ETA minus SB4 start			
Abbreviations: AE: adverse event, CRP: C-reactive protein, ETA: originator etanercept, LOE: lack of effect, PGA: patient global score, SB4: biosimilar etanercept, SJC: swollen joint count			

Conclusions: In a nationwide cohort of 1621 arthritis patients that were switched from ETA to SB4, 7% switched back to ETA. Back-switchers had no distinct clinical or disease characteristics upon start of SB4. AEs prior to back-switching were largely unspecific. In pts who withdrew SB4 due to LOE, PGA had increased. Reasons for back-switching appeared to be predominantly subjective rather than objective (nocebo effect). Originator drug was still available (25 mg or 50 mg powder-solution), which may have encouraged back-switching.

REFERENCES:

- [1] Glinborg, et al. Arthritis Rheum 2017;69(suppl 10).
- [2] Glinborg, et al. Abstract, EULAR 2018.

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FRI0104

PREDICTORS FOR THE RESPONSE TO ANTI-TNF THERAPY AND THE IMPACT OF SMOKING IN RHEUMATOID ARTHRITIS- RESULTS ON A GROUP OF PATIENTS IN ROMANIA

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Background: 20%–40% of the patients are declared nonresponders to at least one of the biologic agents.

Objectives: to test the possible predictive role of RF type IgM and IgA, anti-CCP, anti-MCV, 14–3–3eta protein and COMP on a group of patients treated with anti-TNFα agents. We also followed the evolution of serum titres of these biomarkers under biologic therapy and the impact of smoking regarding response to treatment.

Methods: prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. Clinical assessment was performed at 0, 6 and 12 months according to ACR criteria and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder).

Results: Following baseline immunological parameters titres and the response at 6 months, tests for identifying differences between the groups showed that lower titres of both RF isotypes, anti-CCP, 14–3–3eta protein and COMP had predictive value on achieving a good EULAR response at 6 months. Grouping patients in 2 categories (responders/nonresponders), just 14–3–3eta protein and anti-CCP maintained their predictive value for the response at 6 months.

For the visit at 12 months, lower baseline titres for RF type IgM (92.93±120.22 U/ml, $p=0.010$) and IgA (49.96±98.08 U/ml, $p=0.002$) had predictive value for achieving a good response at 12 months. We didn't obtain other informations grouping patients in 2 categories.

The status pretreatment influenced the good response for COMP at 6 months ($p=0.001$) and RF IgA at 12 months ($p=0.004$).

Using multivariate logistic regression methods we obtained a statistical model for predicting the response at 6 months including normal values for 14–3–3eta protein, anti-CCP and COMP (Hosmer and Lemeshow according test $\chi^2=5.795$, $p=0.670 \geq 0.05$ with a predictive response accuracy of 89.1%).

Smoking had a negative impact on the EULAR response as well as on 2 groups response at 6 months of treatment ($p=0.017$).

	6 Months response nonresponders	6 Months response moderate	6 Months response good
Smoking	2/7 (28.6%)	29/38 (76.3%)	17/19 (89.5%)
No	0/6 (0.0%)	3/38 (7.9%)	1/19 (5.3%)
Past	5/7 (71.4%)	6/38 (15.8%)	1/19 (5.3%)
Yes			

0.046 (Likelihood Ratio corrected Bonferroni)

Following the evolution of serum levels, we noticed a reduction for all biomarkers tested, statistically significant at 6 and/or 12 months from baseline.

Abstract FRI0104 – Table 1. Description of ETA-SB4-ETA back-switchers (n=120)

	Nonresponder	Moderate response	Good response	p value	Nonresponder	Responder	p value
No.	7	38	19		7	57	
RF type	132.35±99.602	157.22±131.47	51.36±95.359	0.016	132.35±99.602	121.93	0.571
Ig M						±129.92	
RF type	122.81±99.876	102.08±128.33	22.45±61.256	0.033	122.81±99.87	75.54	0.307
Ig A						±116.282	
Anti-MCV	74.04±47.951	80.06±149.543	33.77±113.069	0.459	74.04±47.951	64.63	0.860
14–3–3 eta protein	0.99±0.888	0.28±0.469	0.51±0.580	0.045	0.99±0.888	±139.174	
Anti-CCP	146.16±41.688	113.65±50.448	60.82±26.331	0.000	146.16±41.68	0.36±0.515	0.040
COMP	1042.2±181.71	1032.8±188.67	746.04±130.09	0.000	1042.2±181.717	937.27	0.028
						±218.10	0.227