Figure 1 – Persistence in 1st bDMARD (months) for elderly and adults

Efficacy and safety	Total	Adults	Elderly	P value
EULAR response at 3 month (Lundex corrected) %	77.8 (51)	78.4 (51)	75 (51)	
EULAR response at 6 month (Lundex corrected) %	80.6 (50)	81.7 (52)	76 (45.2)	
EULAR response at 12 month (Lundex corrected) %	81.5 (35.6)	83.8 (37)	71.5 (29.3)	0.01
N patients with AE during 1st bDMARD	409	319	90	
AE infection – N (%) N=407	237 (58.2)	176 (55.3)	61 (68.5)	0.03
AE opportunistic infection – N (%) N=408	30 (7.4)	21 (6.6)	9 (10)	
AE allergic reaction – N (%) N=407	71 (17.4)	59 (18.6)	12 (13.5)	
Severe AEs – N (%) N=391	82 (21)	64 (21)	18 (20.9)	
Hospitalization – N (%) N=407	56 (13.8)	42 (13.2)	14 (15.7)	
bDMARD suspension due to AE – N (%) N=407	171 (42)	130 (40.9)	41 (46.1)	
bDMARD reintroduction after AE – N (%) N=211	61 (28.8)	48 (30)	13 (25.5)	

Figure 2 – Efficacy and safety. AE: adverse event. When p value > 0.05 no value is presented.

Disclosure of Interests: None declared

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SAT0144

UNDERSTANDING THE LONG-TERM OUTCOME OF RITUXIMAB – IMPLICATIONS FOR MANAGEMENT

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Background: In patients with rheumatoid arthritis (RA), rituximab (RTX) is often prescribed after loss of response to TNF inhibitors; however, little is known about the long-term outcome of patients receiving treatment with RTX. Previous work [1,2] has shown that aiming for “complete B-cell depletion with clinical response” (CD-R) leads to an optimal management of the disease but unfortunately not all patients maintain this status. Whether CD-R can be regained with RTX retreatment remains unclear.

Objectives: To assess the outcome of RA patients treated with consecutive cycles of RTX, focusing on those who achieved complete B-cell depletion with clinical response.

Methods: A prospective 12 year observational study was conducted in RA patients who were treated with RTX in Leeds. Consecutive cycles of RTX consisting of 2 infusions of 1000mg were administered either on clinical relapse or a 6-monthly basis. B-cells were measured using highly sensitivity flow cytometry at 0 and 2 weeks post-RTX. Complete depletion (CD) was defined by total B-cell count $<0.0001 \times 10^9/L$ at week 2. Clinical response was defined by EULAR response criteria and CD-R was seen as the optimal outcome.

Results: 755 patients participated in the study of which 723 had complete data (see fig.1). The mean (range) number of RTX cycles administered was 3.8 (1-14). 76% (549/723) of patients reached CD-R at some stage during therapy while 24% (174/723) never did. The latter patients had a shorter period of RTX treatment vs CD-R with an OR of 7.98 after adjusting for age, gender, prior therapy with TNF-I and concomitant DMARDs (95% CI 5.86-10.86); $p < 0.001$ (see fig.2). 84% of those who were retreated with RTX recovered CD-R (77% of them did it in the following cycle). Half of the patients that reached CD-R maintained it in prospective cycles but 47% lost it subsequently. A third of the patients that lost either clinical response or B-cell depletion were switched to other medication without receiving further cycles. Overall, at the end of the study, 55% of all patients treated with RTX (400/723) remained in CD-R.

Conclusion: Most patients treated with RTX will achieve CD-R, but approximately half of them will lose this optimal status at some point. In patients who achieve CD-R but subsequently lose it, retreatment with

RTX appears to be an effective strategy since 80% of them will regain it and will maintain long-term treatment with therapy

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Figure 1

Figure 2

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SAT0145

ON TAPERING THERAPY FOR RA PATIENTS IN CLINICAL REMISSION; FLARE ON CS-DMARDs IS PREDICTED BY CLINICAL PARAMETERS AND ULTRASOUND, WHEREAS T-CELL ABNORMALITIES ARE PREDICTIVE FOR B-DMARD TAPERING

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Background: Tapering of disease-modifying therapy (DMARDs) is recommended by EULAR/ACR for rheumatoid arthritis (RA) patients who achieve sustained remission on stable therapy(1,2). However, there is no guidance on how to manage this in clinical practice.

Objectives: We aimed to assess flare over 12 months in RA patients in sustained remission who were offered structured tapering of either conventional synthetic (cs) or biologic (b) DMARDs.

Methods: RA patients (ACR/EULAR 2010) prospectively attending a remission clinic were recruited when fulfilling the criteria of stable remission as defined by 3-variable DAS28CRP < 2.6 for ≥ 6 months (stable therapy & no corticosteroids). Patients were offered tapering according to a structured protocol (Figure 1). For patients receiving combination cs/b-DMARDs, only the b-DMARD was tapered. Clinical, ultrasound (US) + immunological (T-cell subsets: naïve, Treg (both age-corrected) and

inflammation related cells, IRC) data were collected. Flare over a period of 12 months was assessed using several definitions in order to evaluate their relevance for clinical outcomes. Associations with baseline characteristics were assessed using univariate statistics (Mann-Whitney-U and Chi-square). No correction for multiple testing was attempted.

Results: 98 patients (cs-DMARDs n=66, b-DMARDs n=32) accepted tapering and achieved at least 12 months follow-up. In the cs-DMARD group 55% were female; the median age was 64 years and median remission duration 25 months. For b-DMARDs 63% were female; the median age was 61 years and median remission duration 28 months. There was great heterogeneity in terms of flare rate according to the definitions used (Figure 2). Flare on tapering b-DMARDs was more commonly observed (29-70%) compared to cs-DMARDs (24-52%). Demographics were not associated with flare by any definition (except longer disease duration for cs-DMARD patients who lost Boolean remission status). Clinical (notably seropositivity) and US measures were associated with flare for cs-DMARDs. Reduced Treg and higher IRC's at baseline were associated with flare in patients tapering b-DMARDs.

Conclusion: Flare rate varied with the definition used and was more common when tapering b-DMARDs compared to cs-DMARDs. Flare was predicted in the latter patients by clinical and US (including seropositivity) findings, whereas T-cell abnormalities predicted flare in b-DMARD patients. These results will help formulate further tapering strategies.

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Figure 1. Tapering Protocol

Order*	Drug	Baseline Dose	Taper 1	Taper 2	Taper 3	Taper 4	Taper 5
1	Hydroxychloroquine	400mg od	200mg od	stop	-	-	-
2	Sulfasalazine	1.5g bd	1g bd	1.5g od	500mg bd	500mg od	stop
3	Methotrexate	25mg/week	15mg/week	7.5mg/week	no change	stop	-
N/A	Etanercept	50mg/week	25mg/week	25mg/ every 4 weeks	stop	-	-
N/A	Adalimumab	40mg/ every other week	40mg/ every 4 weeks	40mg/ every 8 weeks	40mg/ every 16 weeks	stop	-
N/A	Infliximab	Variable	Double dose	Double time interval	Double time interval	stop	-
N/A	Certolizumab	200mg/ every other week	200mg/ every 4 weeks	200mg/ every 8 weeks	200mg/ every 16 weeks	stop	-
N/A	Golimumab	Variable	Every month	Every 2 months	Every 4 months	stop	-

NI: Patients were seen 3-monthly, if they remain in remission, they proceed to the next taper unless there is a significant clinical reason not to taper at the time of assessment (as per standard care). * Order of cs-DMARD therapy tapered if on dual/triple therapy

Figure 2. Rate of flare according to different definitions and associations with baseline characteristics

Flare Definition	csDMARD (n=66)	bDMARD (n=32)
	Hydroxychloroquine n=13, Sulfasalazine n=4, Methotrexate n=49, (on monotherapy n=43, Combination therapy n=23)	Etanercept n=17, Adalimumab/Infliximab/ Certolizumab/Golimumab n=15
Physician Judgement (Increase in therapy +/- prescription of corticosteroids)	47% flare Higher total PD (p=0.005) RF positive (p=0.010) Higher total GS (p=0.012) ACPA positive (p=0.041)	50% flare Reduced Treg (p=0.0001)
DAS28 flare (Increase in 3wDAS >1.2)	24% flare RF positive (p=0.007) Higher total PD (p=0.018)	29% flare Reduced Treg (p=0.001)
Loss of remission (3wDAS28 >2.6)	38% flare Higher TIC28 (p=0.0001) Higher total PD (p=0.003) Higher CRP (p=0.006) RF positive (p=0.009)	44% flare Reduced Treg (p=0.001) Increased IRC (p=0.008)
Loss of LDA (3wDAS28 >3.2)	27% flare Higher TIC28 (p=0.0001) Higher CRP (p=0.01)	37% flare Reduced Treg (p=0.004) Increased IRC (p=0.008) RF positive (p=0.014)
Loss of Boolean remission* (TIC, SJC & CRP all <1)	53% flare Longer disease duration (p=0.008) Higher CRP (p=0.002)	70% flare No associations

* Considering only patients who were in Boolean remission at baseline: 46 for DMARDs and 30 for biologics. Patient global health assessment omitted due to missing data.

Abbreviations: Rheumatoid Factor (RF), Anti-Citrullinated Protein Antibodies (ACPA), Power Doppler Synovitis (PD), Gray Scale Synovial Hypertrophy (SS), Tender/Swollen Joint Counts (TJC28/SJC28), Age-corrected T-regulatory cells (Treg), Inflammatory Related Cells (IRC).

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SAT0146

COMPARING DRUG SURVIVAL FOR BIOSIMILAR SB4 ETANERCEPT IN RHEUMATOID ARTHRITIS BOTH ETANERCEPT NAÏVE AND NON-MEDICAL SWITCH PATIENTS WITH ETANERCEPT REFERENCE DRUG IN A NORWEGIAN OUT-PATIENT CLINIC. PRELIMINARY RESULTS FROM A MULTI-CENTER STUDY

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Background: In Norway encouraged by the health authorities non-medical switch from reference drug to biosimilar drug has been performed in most patients on biologic reference drugs with biosimilar drugs available, including etanercept. There is a need for real life data understanding the effect of biosimilar drugs when these drugs are introduced in clinical practice.

Objectives: To explore drug survival for biosimilar SB4 etanercept in RA patients, both etanercept naïve and non-medical switch patients, and compare with the etanercept reference drug.

Methods: Preliminary 2 years drug survival data from one center in a 5 center study in Norway exploring drug survival for etanercept reference drug and biosimilar etanercept SB4 is presented. At this outpatient clinic RA patients as part of standard clinical care has been monitored systematically since 2003. Drug survival for SB4 etanercept, both the etanercept naïve and the non-medical SB4 switch group, was compared with patients treated with the etanercept reference drug in the period 2003-2018. Baseline demographic, clinical and treatment data were retrieved and analyzed. Kaplan-Meier survival curves were used to explore 2 years drug survival. Survival differences between groups were tested using Breslow statistics.

Results: At the outpatient clinic the number of RA patients treated with etanercept reference drug was 356, the number of patients treated with SB4 with no previous etanercept was 36 and the patients with a non-medical switch from reference etanercept to etanercept SB4 was 84. In the table below baseline demographics and disease measures are shown for the etanercept reference group, the non-medical SB4 switch group and the SB4 naïve to etanercept group. Data in table are presented as percentage for group variables and as mean with standard deviation (SD) for continuous variables.

	Etanercept reference (n=356)	SB4 non-medical switch (n=84)	SB4 etanercept naïve (n=36)
Age, years	63.7 (15.4)	62.2 (11.6)	58.1 (15.3)
Females	71.1%	69.0%	77.8%
Disease duration, years	12.6 (10.3)	18.3 (11.2)	8.5 (8.4)
Anti-CCP positive	75.4%	75.0%	73.7%
DAS28	4.9 (1.4)	2.8 (1.3)	4.0 (1.4)
ESR mm/hr	29.5 (21.5)	17.6 (13.7)	29.2 (26.3)
CRP mg/l	20.3 (23.1)	5.0 (6.5)	13.7 (16.7)
Pain (VAS 0-100)	53.1 (27.0)	30.2 (25.3)	46.5 (20.5)
Fatigue (VAS 0-100)	53.4 (30.6)	34.4 (33.4)	44.7 (27.6)
MHAQ	0.78 (0.56)	0.51 (0.61)	0.71 (0.44)

Mean (95%CI) drug survival for the non-medical SB4 switch group was 1.53 (1.38-1.68) years, for the SB4 group with no previous etanercept 1.23 (0.95-1.51) years and for etanercept reference group 1.38 (1.31-1.46) years. A statistically significant difference (p<0.02) was found between the groups except between etanercept reference group and the etanercept SB4 group without prior etanercept (p=0.23). The percentage of RA patients starting with etanercept as first biologic drug was for etanercept reference 64.6% and for biosimilar etanercept SB4 36.1%. In the figure below Kaplan-Meier drug survival curves are shown.

Conclusion: To the best of our knowledge this is the first data showing that drug survival of an etanercept biosimilar drug after a non-medical