Table 1

DISEASE	STOPPED CAUSE	BACK TO Etanercept original	CONTINUE Etanercept original	TIME UNTIL SWITCH (meses)
AS	Reaction at the injection site	Yes	Yes	28
AS	Headache	Yes	Yes	54
AS	Inefficacy	Yes	Yes	126
RA	Inefficacy	Yes	No	25
AS	Diarrhea	Yes	Yes	87
RA	Inefficacy	Yes	Yes	37
PsA	Inefficacy	No	No	43
RA	Inefficacy	Yes	Yes	54
PsA	Inefficacy	Yes	No	93
PsA	Inefficacy	No	No	132
PsA	Inefficacy	Yes	Yes	62
RA	Inefficacy	Yes	Yes	142
RA	Reaction at the injection site	Yes	Yes	51
RA	Inefficacy	Yes	No	56
PsA	Inefficacy	Yes	No	40
AS	Inefficacy	Yes	Yes	26
AS	Diarrhea	Yes	Yes	48

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AB0273

PREDICTORS OF DRUG SURVIVAL OF bDMARDs IN BIO-NAIVE PATIENTS WITH RHEUMATOID ARTHRITIS (RA) DURING THE FIRST YEAR OF THERAPY.

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Objectives: To investigate predictors of drug survival of bDMARDs in previously bio-naive patients (pts) with RA during the first year of therapy.

Methods: 204 adult bio-naive pts (173 women, 84.8%), with active RA, despite the concomitant DMARD therapy, were included into retrospective study. All of them initiated bDMARDs: infliximab (INF) - 65 pts (31.9%), rituximab (RTM) - 39 (19.1%), adalimumab (ADA) - 30 (14.7%), etanercept (ETA) - 28 (13.7%), abatacept (ABA) - 23 (11.3%), tocilizumab (TZ) - 15 (7.4%), certolizumab pegol - 4 (1.9%). The following indicators were used as survival predictors: sex, age and clinical form of RA. Pts were divided by age according to the classification adopted by the World Health Organization: 18-44 years (74 pts), 45-59 years (68 pts), 60-74 years (57 pts), 75 years or more (5 pts). Clinical forms of RA were presented: RA, seropositive by rheumatoid factor (RF), RA, seronegative by RF, RA with extra-articular manifestations, adult-onset Still's disease, juvenile RA. Predictors of therapy inefficiency or AE were investigated in Cox proportional risk model. Survival on drug was estimated using the Kaplan-Meier method and evaluation of difference significance using log-rank criterion.

Results: A year later, 92 pts (45%) remained on bDMARDs and 112 pts had their treatment discontinued. The reasons of bDMARDs discontinuation during the first year of treatment were: lack of effectiveness (including primary inefficiency) - 50%, adverse events (AE) - 25%, administrative causes - 17%, remission - 6.25%, death due to reasons unrelated to the therapy - 1.75%. By the end of the observation period, the best survival was shown by RTM therapy (69.23% of patients continued treatment for a year), ETA (44.4% of patients) and ABA (43.48% of patients). Discontinuation of bDMARDs due to remission was achieved in 7 patients and proved to be significantly higher in the RTM group (10.26%, $p < 0.05$) compared to the ABA group (8.7%) and ADA group (3.45%). Although the number of women continued after a year was significantly higher than that of men (84.8% and 15.2% respectively), female sex was not a reliable predictor of drug survival. At the same time, the rate of discontinuation due to AE in women was higher (96.55%, $p = 0.03$). After a year, the number of pts continuing treatment in all age groups remained comparable, and the difference between them - statistically not significant: 1 group (18-44 years old, 29 pts) - 31.52% of pts, 2 group (45-59 years old, 36 pts) - 39.13%, 3 group (60-74 years old, 26 pts) - 28.26%, 4 group (75-90 years old, 1 pts). Discontinuation of bDMARDs due

to inefficiency was noted in 1 group more often (46.43%, 26 pts, $p = 0.03$), in other groups this indicator was 33.93% (19 pts) in the 2nd group, 19.64% (11 pts) in the 3rd group and 0% in the 4th group. Discontinuation therapy due to AE was also prevalent in 1 group (50%, 14 pts) than in 2 (14.3%, 4 pts), 3 (32.1%, 9 pts) and 4 (3.6%, 1 pts). Discontinuation of therapy due to inefficiency was more common in the group of seronegative RA - 59.1% ($p < 0.05$). In the seropositive RA group 24.8% of pts had interrupted bDMARDs for this reason, in the RA with extra-articular manifestations group it was 18.1%, in the adult-onset Still's disease group - 30% and in the juvenile RA group - 30%. Discontinuation of therapy due to remission was overwhelmingly observed in seropositive RA group (6 pts, 4%) and was significantly higher than in other groups (1 patient in RA with extra-articular manifestations group, 4.5%).

Conclusion: Female sex, young age (18-44 years), RA, seronegative by RF were associated with less survival of bDMARDs due to lack of effectiveness and/or AE, and RTM and seropositive RA - with more frequency of discontinuation of therapy due to remission.

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AB0274

USE OF TNF-INHIBITORS BIOSIMILARS IN CHRONIC INFLAMMATORY ARTHRITIDES: A THREE-YEAR EXPERIENCE IN A LARGE MONOCENTRIC COHORT OF PATIENTS FROM THE NORTH-EAST ITALY

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Background: In recent years several biosimilars (BS) of tumour necrosis factor inhibitors (TNF-i) were introduced. At the Padova University Hospital the first BS of etanercept (bsETN) was available in October 2016 and the BS of adalimumab (bsADA) was available in November 2018.

Objectives: The objectives of the study were to evaluate the rate of bioriginator-biosimilar (BO-BS) switch in all patients with rheumatoid arthritis (RA), psoriatic arthritis (PSA) and axial spondyloarthritis (axSpA) in the cohort of the Padova University Hospital and to examine factors favouring BO-BS switch. Secondly, we investigated survival of BO-BS switch and BO treatment and factors associated with longer treatment survival.

Methods: We considered all patients on ETN originator (boETN) treatment when the first bsETN was available (1st October 2016) and all patients on ADA originator (boADA) when bsADA was available (1st November 2018). Patients were followed until 30 August 2019 and were classified as BO-BS switchers if they underwent a switch from either boETN or boADA to BS during the follow-up, otherwise they were considered as continuing BO treatment. Factors associated with BO-BS switch were tested with a multivariable regression analysis. To test the survival of the BO-BS switch and of the BO treatment, Cox regression analysis was used including all variables achieving a $p < 0.10$ in univariate analysis tested with Log-rank test and Kaplan-Meier curves.

Results: Among 1208 patients (553 RA, 433 PSA, 215 axSpA), 560 (46.3%) patients switched to bsETN (391) or bsADA (169). Mean disease duration was 16 (14.2) years and mean duration of the bDMARD treatment was 96.3 (56.8) months. After adjustment for potential confounders, factors associated with BO-BS switch were a longer disease duration, a shorter duration of previous bDMARD treatments and diagnosis (Tab.1) RA patients had almost a 3 fold increased likelihood of being switched to BS compared to PSA and axSpA, while difference between PSA and axSpA was not significant.

Following Cox regression analysis we observed a longer drug survival in BO-BS switchers compared to those continuing with BO (HR 1.38; 95% C.I. 1.2-1.58; $p < 0.001$) (Fig. 1). A longer drug survival was also associated with a longer disease duration (≥ 15 years: HR 1.75; 95% C.I. 1.5-2; $p < 0.001$), longer mean duration of previous bDMARDs (≥ 5 years: HR 4.1; 95% C.I. 3.5-4.7; $p < 0.001$), and diagnosis (RA vs PSA: HR 1.22; 95% C.I. 1.02-1.47; $p = 0.030$; RA vs axSpA: HR 0.89 95% C.I. 0.067-0.97; $p = 0.023$; PSA vs axSpA: HR 0.66; 95% C.I. 0.57-0.77; $p < 0.001$) (Fig 2).

Conclusion: BO-BS switch was undertaken in almost half of the patients. Patients with longer disease duration and longer bDMARD duration, were the most likely to be switched successfully to BS. BO-BS switching does not affect the survival of the treatment, indeed, it provides sustained effectiveness particularly if undertaken in patients with stable disease activity.

Table 1. Factors associated with BO-BS switch, multivariate regression analysis.

		OR (95% C.I.)	p value
Age	per 10 years increase	1.11 (0.98-1.25)	0.102
Disease duration	per 5 years increase	1.19 (1.08-1.32)	0.01
Mean time on bDMARD	per 1 year increase	0.71 (0.66-0.77)	< 0.001
HAQ* per 1 unit increase		1 (1-1)	0.68
Gender (male)		1.07 (0.74-1.56)	0.71
Disease diagnosis			<0.001
RA vs PSA		2.70 (1.79-4.07)	<0.001
RA vs axSPA		2.77 (1.62-4.72)	<0.001
PSA vs axSPA		1.03 (1.62-4.72)	0.925
csDMARD combination		0.77 (0.54-1.11)	0.167
Model Constant			<0.04

OR odds ratio, C.I. confidence interval, * at the time the biosimilar of the ongoing originator was available.

Figure 1. Kaplan-Meier curves for treatment survival, Log-rank test.

Figure 2. Kaplan-Meier curves for treatment survival in all patients, Log-rank test

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AB0275

COMPARATIVE EFFICACY (DAS 28) OF TOCILIZUMAB AND OTHER TARGETED IMMUNE MODULATORS (TIMs) FOR RHEUMATOID ARTHRITIS: A NETWORK META-ANALYSIS (NMA)

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Background: With a ‘treat to target’ approach in RA, guidelines recommend tailored monitoring of disease activity using validated composite instruments, such as the disease activity score (DAS) 28. While response assessment at 24 weeks is the standard in clinical trials, assessment as early as 12 weeks is

recommended. There is limited evidence assessing the relative efficacy of TIMs following a ‘treat to target’ strategy.

Objectives: To evaluate the relative efficacy of intravenous (IV) and subcutaneous (SC) tocilizumab plus a conventional disease modifying antirheumatic drug (cDMARD) to other TIMs plus a cDMARD in TIM-naïve or mixed (<20% TIM-experienced) adults with moderate to severe RA. Efficacy was defined as achieving remission according to a DAS28 score <2.6 at 12 and 24 weeks.

Methods: Randomized controlled trials (RCTs) were selected from a recent systematic literature review conducted by the Institute for Clinical and Economic Review (ICER), as well as from trials for upadacitinib (SELECT-NEXT, SELECT-COMPARE), which were not included in the ICER 2017 report. RCTs that compared TIMs to each other or placebo were included. Treatments included Janus kinase (JAK) inhibitors (upadacitinib, baricitinib, and tofacitinib), tumor necrosis factor alpha inhibitors (TNFi; adalimumab, certolizumab pegol, golimumab, and infliximab), and other non-TNFi (rituximab, sarilumab, tocilizumab, and abatacept). A Bayesian NMA was performed in OpenBUGS and R using a fixed effects model. Model selection was based on deviance information criterion. Forest plots of odds ratios (OR) are presented.

Results: In the 12-week analysis, 15 trials were included with a pooled study population of 9,154 patients. Populations were similar across trials and predominantly female (mean 78%, range 39-87%), with a baseline mean age of 52 years (range 47-56), mean disease duration of 8 years (range 2-11), and mean DAS28 score of 6 (range 5-7). In the 12-week analysis, compared to cDMARD, all TIMs were more likely to achieve remission (statistically significant), but tocilizumab IV showed a substantially greater magnitude of effect (OR=19.3, 95% CrI=10.99, 37.22) which was consistent with raw trial results (Figure 1). In pair-wise comparison, tocilizumab IV was associated with a greater likelihood of achieving remission compared to abatacept IV (OR=7.47, CrI=2.53, 20.89), abatacept SC (OR=4.29, CrI=1.96, 9.94), baricitinib (OR=3.39, CrI=1.74, 7.09), adalimumab (OR=5.10, CrI=2.68, 10.42), tofacitinib (OR=5.44, CrI=1.26, 20.57), upadacitinib 15mg (OR=3.23, CrI=1.72, 6.54), and upadacitinib 30mg (OR=4.05, CrI=1.97, 8.85).

In the 24-week analysis, 21 trials were included in the analysis with a pooled study population of 12,180 patients. Patient characteristics were the same as the 12 week analysis. Compared to cDMARD, all TIMs were more likely to achieve remission (statistically significant), with tocilizumab IV and SC showing a greater magnitude of effect (OR=12.08, CrI=8.09-18.30 and OR=11.98, CrI=5.17-35.86, respectively) (Figure 2). In pair-wise comparison, tocilizumab IV and SC were associated with a greater likelihood of achieving remission compared to abatacept IV, adalimumab, baricitinib, infliximab, upadacitinib 15 mg, and sarilumab.

Conclusion: Results of this NMA demonstrate that tocilizumab is associated with a greater likelihood of remission (DAS28 <2.6) at 12 and 24 weeks compared to most other TIMs including new JAK inhibitors, when used in combination with a cDMARD among TIM-naïve/mixed patient populations.

Figure 1. DAS28 at 12 weeks—All TIMs were more likely to achieve remission compared to cDMARD, but tocilizumab IV showed a substantially greater magnitude of effect that was consistent with raw trial data*

Abbreviations- ABT: Abatacept, ADA: Adalimumab, BAR: Baricitinib, cDMARD: Conventional Disease-modifying Antirheumatic Drugs, CrI: credible interval, GOL: Golimumab, IFX: Infliximab, iv: intravenous, sc: subcutaneous, TOF: Tofacitinib, TCZ: Tocilizumab, UPA: Upadacitinib (15 or 30 mg)
* 95% CrIs that do not overlap with 1 are statistically significant
cDMARDs are defined as systemic agents with broad immunomodulatory effects like methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine.