SAT0204 ABATACEPT SURVIVAL IN RHEUMATOID ARTHRITIS PATIENTS AT 2 YEARS IS 59%; ITS USE AS A 2ND LINE BIOLOGIC AGENT AND LOWER BASELINE HAQ PREDICT BETTER SURVIVAL IN CLINICAL PRACTICE: A PROSPECTIVE, OBSERVATIONAL SINGLE CENTER STUDY

I.D. Flouri[1,1], A. Repa[1], N. Avgoustidis[1], N. Kougas[1], A. Fanouriakis[1], I. Papalopoulos[1], C. Adamichou[1], P. Kyfonidou[1], E. Kampouraki[1], M. Terizaki[1], D.T. Boumpas[2], G. Bertsias[1], P. Sidiropoulos[1]. *[1]Rheumatology, Clinical Immunology and Allergy, Faculty of Medicine-University of Crete, Heraklion-Crete; [2]4th Internal Medicine Department, Attikon University Hospital, Athens, Greece*

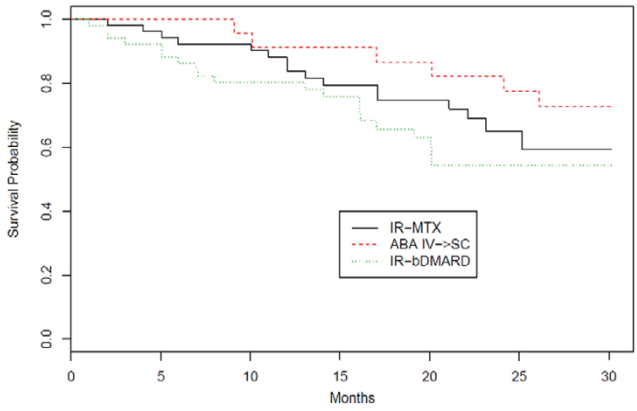
Background: Long-term prospective observational studies are complementary to controlled clinical trials to explore effectiveness and safety of biological therapies in clinical practice.
Objectives: To study abatacept survival, reasons of discontinuation and clinical responses in everyday clinical practice of patients with rheumatoid arthritis (RA).
Methods: Prospective, observational single center study at the Rheumatology Clinic, University Hospital of Heraklion, Crete. At baseline, patient demographics, co-morbidities and disease characteristics are being recorded, while during follow-up, discontinuations, disease activity and adverse events are collected. For this analysis, all patients who received Abatacept intravenously from 6/2007 till 6/2016 were included. Kaplan-Meier curves and Cox regression analysis were used to determine drug survival and predictors thereof. Linear regression was used to compare DAS difference at 12 months between different lines of bDMARD therapy.
Results: A total of 224 patients (women: 87%, seropositive: 34%) were included. Median (IQR) age was 63 (56–70) years, disease duration 7.4 (4–13.4) years and baseline DAS28 5.9 (5.2–6.5). Abatacept was the 1st bDMARD in 59 (26%), 2nd in 71 (32%) and ≥3rd in 94 (42%) patients. During follow-up [total: 508 patient-years, median (IQR): 1.7 (0.7–3.3) years], 54% patients discontinued therapy (87% for treatment failure, 10% for adverse events). Two-year treatment persistence was 59%. In multivariable regression analysis, predictors of longer Abatacept survival were lower baseline HAQ [HR (95% CI) for unit increase =2.29 (1.5–3.48), p<0.001], longer disease duration [HR (95% CI) for ≥8 vs.<8 years=0.51 (0.30–0.88), p=0.016], Abatacept as 2nd vs 1st or ≥3rd bDMARD [HR =0.52 (0.30–0.91), p=0.022] and a more recent year of therapy start [HR=0.39 (0.16–0.95), p=0.022].
DAS28<3.2 and remission at 6 (12) months were achieved by 12% (18%) and 5% (7%) of patients respectively. DAS28 difference at 12 months was greater in patients who received Abatacept as the ≤2nd than those on ≥3rd bDMARD (p=0.009).
A total of 312 adverse events were registered, of which 65 were serious (SAE). Incidence of total (serious) adverse events was 61 (13) /100 patients/year. SAE included 5 cases of cancer, 10 cardiovascular events and 24 infections, mainly of the respiratory tract.
Conclusions: In the present study, Abatacept survival at 2 years was 59%. The majority of patients discontinued therapy due to inadequate response. Use as a 2nd line biologic agent and lower baseline HAQ predicted better survival. Improvement in DAS was higher when Abatacept was used as the ≤2nd bDMARD. Rates of remission or low disease activity in clinical practice are rather low, while the safety profile was excellent.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6931

SAT0205 LONG-TERM DRUG SURVIVAL AND CAUSES OF DISCONTINUATION OF SUBCUTANEOUS ABATACEPT IN RHEUMATOID ARTHRITIS: 32-MONTH RESULTS FROM A PROSPECTIVE COHORT STUDY

J.C. Sarmiento-Monroy[1,2], N. Molano-Gonzàlez[2], M. Rodríguez-Jiménez[2], R.D. Mantilla[1,2]. *[1]Rheumatology, Center of Dermatology and Rheumatology (FUNINDERMA); [2]Center for Autoimmune Diseases Research (CREA), Universidad del Rosario, Bogotá D.C., Colombia*

Background: Survival time or time to discontinuation of medication is a surrogate of the long-term impact on the course of disease in real life. It reflects clinical effectiveness in the absence of significant adverse events [1]. Treatment discontinuation can result from loss of efficacy or safety concerns, but prognostic factors for patient retention have not been explored thoroughly despite data for abatacept and other biologics being available from national registries [2].
Objectives: To assess drug survival of subcutaneous (SC) abatacept among patients with rheumatoid arthritis (RA) according to treatment background.
Methods: This was a prospective study in which well-characterized patients with RA (by 1987 ACR criteria) were assessed from April 2014 to December 2016. Each patient was evaluated by a rheumatologist in a single rheumatology outpatient private center in Bogotá, Colombia. Patients were stratified by treatment background: (n=54) biologic-naïve, (n=24) switched from IV to SC abatacept administration, and (n=51) inadequate response to at least 1 biologic disease-modifying antirheumatic drug. The Mantel-Haenszel test was used to test if there were any differences in the survival curves among groups. The test was performed by the survdiff function of the "survival" R package [3].
Results: A total of 129 patients were included. Baseline characteristics of patients were as follows: female gender 86%, mean age 52±13 years, median disease duration 10 (IQR 11) years, Rheumatoid Factor positive 94%, Anti-Cyclic Citrullinated Peptide Antibodies 89%, and erosive phenotype 35%. At baseline, mean DAS28 and RAPID3 were 5.4±1.3 and 16.6±6.8, respectively. SC abatacept monotherapy was reported in 27%. Demographics and disease characteristics were similar in all groups, except for baseline DAS28 and RAPID3 in switch group (p<0.0001). According to the Mantel-Haenszel test (Fig.1), there were not significant differences between survival curves (p=0.158). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy in 25%, insurance-related problems (i.e., access to medication/specialist) and adverse drug reactions in 16%. Other causes include lack of efficacy, surgeries (i.e., articular replacement), patient preference, and pregnancy.

Figure 1. Subcutaneous abatacept survival by treatment background.



IR-MTX: inadequate response to methotrexate (biologic-naïve); ABA IV→SC: switched from intravenous to subcutaneous abatacept administration (125mg-wk); IR-bDMARD: inadequate response to biologic Disease-Modifying AntiRheumatic Drugs.

Conclusions: Our results disclose a similar drug survival of SC abatacept regardless of treatment background. Patients switching from IV to SC formulation of abatacept had lower activity and functional impairment at baseline, and survival tends to be higher through follow-up. The insurance-related limitations is a reality in Latin American countries, and could have a negatively impact on survival time of several drugs.
References:
[1] Nüßlein HG, et al. BMC Musculoskelet Disord. 2015;16:176.
[2] Souto A, et al. Rheumatology (Oxford). 2016;55(3):523–34.
[3] Therneau, T. and Grambsch, P.M. 2000.
Acknowledgements: The authors are grateful to all the members of the Center of Dermatology and Rheumatology (FUNINDERMA) for their contribution to this work.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4348

SAT0206 RETENTION OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS WITH CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS: A STUDY FROM THE TOCERRA COLLABORATION

K. Lauper[1,2], D.C. Nordström[3], K. Pavelka[4], V. Hernandez[5], M.J. Santos[6], Z. Rotar[7], F. Iannone[8], C. Codreanu[9], G. Lukina[10], S.L. Gale[11], K. Sarsour[11], A. Pethoe-Schramm[12], D.S. Courvoisier[1], C. Gabay[1,2]. *[1]Univ Hosp of Geneva, Geneva; [2]SCQM Registry, Zurich, Switzerland; [3]ROB-FIN Helsinki Univ Central Hosp, Helsinki, Finland; [4]Charles Univ, Prague, Czech Republic; [5]Rheumatology Department, Hospital Clinic Barcelona, Barcelona, Spain; [6]Rheumatology Unit, Hospital Garcia de Orta, Almada, Portugal; [7]BioRx.si, Univ Med Center, Ljubljana, Slovenia; [8]GISEA, Univ Hospital of Bari, Bari, Italy; [9]Univ of Medicine and Pharmacy, Bucharest, Romania; [10]ARBITER, Inst of Rheumatology, Moscow, Russian Federation; [11]Genentech, South San Francisco, CA, United States; [12]F. Hoffmann-La Roche, Basel, Switzerland*

Background: Tocilizumab (TCZ) as monotherapy has been shown to be more efficacious than the TNF inhibitor (TNFi) adalimumab as monotherapy in patients with rheumatoid arthritis (RA). However, effectiveness data comparing TCZ as monotherapy versus TNF inhibitors in combination with csDMARDs are limited.
Objectives: To examine retention of TCZ administered alone (TCZ mono) versus TNFi in combination with csDMARDs (TNFi combo) in patients with RA who had an inadequate response to ≥1 TNFi (TNFi-IR).
Methods: Patients with RA who were TNFi-IR and treated with TCZ mono or TNFi combo with baseline (BL) data, not immediately lost to follow-up and started treatment after TCZ was available across 9 European registries in TOCERRA from 2009 to 2016 were included. The hazard for TCZ discontinuation was modeled using a country-stratified Cox proportional hazards model, adjusting for

age, gender, disease duration, seropositivity, HAQ and CDAI at BL, number of previous csDMARD and biologic DMARD (bDMARD), glucocorticosteroid and calendar year of treatment initiation. Missing data on covariates were imputed using multiple imputation with chained equations.
Results: A total of 4748 patients were eligible, including 585 who received TCZ mono and 4163 who received TNFi combo. Patients who received TCZ mono were older with a longer disease duration, more previous bDMARDs and less glucocorticosteroids at baseline (Table 1) compared with patients who received TNFi combo. The crude median retention for TCZ mono was 1.82 years (95% CI: 1.59–2.09) and 1.54 years (95% CI: 1.43–1.64) for TNFi combo, (P=0.65). Causes of discontinuation differed between TCZ mono and TNFi combo (P<0.001): TCZ mono stopped more frequently for ineffectiveness (25.7% vs. 13.8%) and TNFi combo stopped more frequently for safety issues (18.3% vs. 12.8%). In a country-stratified, covariate-adjusted analysis, we found that hazards of discontinuation were significantly lower among patients who received TCZ mono (HR: 0.71, P<0.001). More previous treatment with bDMARDs and a greater HAQ and CDAI at BL were significantly associated with greater risk of discontinuation.

Table 1. Baseline characteristics.

	TCZ mono (N = 585)	TNFi combo (N = 4163)	*P*
Age, yr, median [IQR]	57.8 [44.2-65.5], n = 585	54.3 [44.2-61.7], n = 4161	< 0.001
Female gender, N (%)	485 (82.9%), n = 585	3333 (80.1%), n = 4161	0.12
Disease duration, yr, median [IQR]	9.7 [4.5-16.7], n = 569	7.8 [3.3-14.3], n = 3575	< 0.001
Seropositivity (RF and/or ACPA), N (%)	445 (83.6%), n = 532	2573 (81.0%), n = 3175	0.17
N previous bDMARDs, N (%)			< 0.001
1	250 (42.7%)	2882 (69.2%)	
2	206 (35.2%)	526 (12.6%)	
≥ 3	129 (22.1%)	755 (18.1%)	
Glucocorticosteroids, N (%)	193 (33.0%), n = 585	2487 (59.7%), n = 4163	< 0.001
Concomitant csDMARD, N (%)			--
MTX	--	1766 (42.4%)	
MTX + other	--	1291 (31.0%)	
Other	--	1106 (26.6%)	
CDAI, mean (SD)	23.2 (16.1), n = 322	21.9 (14.7), n = 3021	0.25
HAQ, mean (SD)	1.4 (0.7), n = 226	1.1 (0.7), n = 2429	< 0.001

Conclusions: In routine care across 9 European countries, TCZ mono retention is better than TNFi combo in patients with RA who were TNFi-IR.
Acknowledgements: Funding by F. Hoffmann-La Roche/Genentech.
Disclosure of Interest: K. Lauper: None declared, D. Nordström Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB, Consultant for: AbbVie, BMS, MSD, Roche, UCB and Pfizer, K. Pavelka Grant/research support from: AbbVie, Roche, Medis, MSD and Pfizer, Consultant for: AbbVie, Roche, Amgen, MSD, BMS, UCB and Egis, V. Hernandez: None declared, M. J. Santos: None declared, Z. Rotar: None declared, F. Iannone: None declared, C. Codreanu: None declared, G. Lukina Consultant for: BMS, Roche, MSD, AbbVie and Pfizer, S. Gale Employee of: Genentech, K. Sarsour Employee of: Genentech, A. Pethoe-Schramm Employee of: F. Hoffmann-La Roche, D. Courvoisier: None declared, C. Gabay Grant/research support from: AB2 Bio, AbbVie, Actelion, BMS, Debiopharm, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB, Consultant for: AB2 Bio, AbbVie, Actelion, BMS, Debiopharm, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB
DOI: 10.1136/annrheumdis-2017-eular.6503

SAT0207 LONG-TERM EFFECT OF BIOLOGICAL THERAPIES ON BONE MINERAL DENSITY (BMD) FOR RA PATIENTS COMPARED TO PATIENTS TREATED BY SYNTHETIC DMARD OVER AN 8-YEAR FOLLOW-UP

L. Bustamente[1], V. Breuil[2], R. Fabre[3], L. Euller-Ziegler[2], C. Pradier[3], C. Roux[1]. *[1]Rheumatology, University Nice, Sofia Antipolis, Nice; [2]Rheumatology; [3]Santé publique, University Nice, Sofia Antipolis, Nice Cedex 1, France*

Background: Secondary osteoporosis is a comorbidity of Rheumatoid Arthritis (RA). Previous studies have suggested that biological therapies may reduce the rate of generalized bone loss in RA. Most of them focus on the short-term effect of Tumor Necrosis factor alpha (TNFα) inhibitors while the long-term effect of biological therapies is rarely studied.
Objectives: Our primary aim was to analyze the long-term effect of biological therapies on bone mineral density (BMD) for RA patients compared to patients treated by synthetic DMARD over an 8-year follow-up.
Methods: Patients were selected from a prospective, observational cohort of RA patients meeting the ACR/EULAR 2010 settings in Nice University Hospital between 2001 and 2016. BMD was assessed before the introduction of the biological therapy and during the follow-up. Two groups were studied: patients treated by biological therapies (TNFα inhibitors, Tocilizumab, Abatacept, Rituximab or Anakinra) and patients treated by synthetic DMARD only. Demographic, disease and treatment data were collected at each visit and BMD of the lumbar spine, femoral neck and total hip were assessed using dual energy X-ray absorptiometry (DXA) at baseline and after 1, 2, 3, 5 and 8 years.
Results: A total of 181 patients with active RA starting a biological therapy were included versus 131 patients treated by synthetic DMARD. In both groups, the BMD of the lumbar spine, femoral neck and total hip remained stable after a 2-year follow-up (respectively -0.37%, p=0.66 versus +0.02%, p=0.83, -3.70%, p=0.77 versus -5.35%, p=0.74 and -3.31%, p=0.45 versus -4.84%, p=0.16), while a significant bone loss was found between initial measurement and 3, 5 and 8 -year-follow-up at femoral neck and total hip level. There was no significant difference between patients whether treated by biological or non-biological DMARD neither over the 0–1-year period nor over the 0–2, 0–3, 0–5 and 0–8-periods. Bone loss in patients treated by Tocilizumab were statistically lower at femoral neck level compared with TNFα inhibitors (p=0.02), Abatacept (p=0.02) and Rituximab (p=0.02), but also at total hip level, in comparison with TNF α inhibitors (p=0.05) and Abatacept (p=0.05).
Conclusions: This study is the first to assess the effects of biological RA therapies as compared to synthetic DMARD ones. It highlights the protective effect of both biological and non-biological DMARD on bone loss during the first two years of treatment with no significant difference between them. Our results suggest that the effects of RA treatments depend on the inflammatory and disease activity which must be monitored clearly. Tocilizumab seems to be more effective than the other biological therapies, but further studies are necessary to confirm or infirm this tendency.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2851

SAT0208 CYCLING VERSUS SWAPPING IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO AT LEAST ONE TUMOR NECROSIS FACTOR ALPHA INHIBITOR: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

M.A. Lopez-Olivo[1], A. Matusevich[2], M.E. Suarez-Almazor[1]. *[1]General Internal Medicine, The University of Texas, MD Anderson Cancer Center; [2]School of Public Health, The University of Texas, Health Science Center at Houston, Houston, United States*

Background: In patients with rheumatoid arthritis (RA) who do not respond or lose response, opinions are divided on whether it is better to try an alternative TNFi (cycling) or switch to a therapy with a different mode of action (swapping).
Objectives: To compare the efficacy and safety of the cycling versus the swapping strategies.
Methods: We searched 4 electronic databases, sources of gray literature, and bibliographic references of relevant articles for observational studies evaluating the efficacy and safety of targeted therapies in adult RA patients who failed to respond to at least one TNFi. Studies were excluded if they were single-arm or had insufficient data to evaluate the outcomes of interest. Two independent reviewers selected studies, extracted data and evaluated study quality using the Newcastle-Ottawa Scale (NOS). Our primary outcome measure was change in Disease Activity Score of 28 joints (DAS28). We also evaluated the modified American College of Rheumatology 20%, 50% and 70% response criteria (mACR which excludes acute phase reactants) and total serious adverse events. All analyses were based on the random-effects model.
Results: Of 33,716 citations, 24 observational studies (n=10,074 patients) representing 14 countries, met the inclusion criteria. Eight were conference abstracts. Most publications (13 of 24) were based on registries. Most studies had a NOS score equal to or greater than 7 (out of 9) with comparability being the weakest domain. The mean age of patients was 48.7–62.8 years, the majority were females (78%) with a disease duration of 6–17.3 years and a baseline disability score 0.6–2.0. Sixteen studies evaluated cycling versus swapping directly of which 13 were suitable for analysis. Most compared TNFi to rituximab (10 of 13) with two studies investigating tocilizumab or abatacept and one comparing non-TNFi as a group. Other comparisons reported were: (i) cycling vs. conventional disease modifying antirheumatic drugs (cDMARDs), (ii) swapping vs. cDMARDs, (iii) cycling vs. another cycling alternative, (iv) swapping vs. another swapping alternative, (v) swapping monotherapy vs. swapping combined with cDMARDs, and (vi) combination of TNFi and non-TNFi vs. TNFi alone. At 12 and 24 weeks, DAS28 score improved significantly in those swapping compared to those cycling (mean difference (MD) 0.89, 95% confidence interval (CI) 0.05 to 1.74 and MD 0.34 95% CI: 0.2, 0.48; respectively). Similar results were observed for the mACR50 favoring the swapping strategy at 24 weeks (OR =1.45 95% CI: 1.06, 1.98). At 52 weeks no difference was observed. No statistically significant differences were observed between groups in the odds of achieving DAS28 remission, mACR20 or mACR70, or experiencing a serious adverse event.
Conclusions: Current evidence from observational studies shows greater improvements with the swapping strategy compared with the cycling strategy in terms of efficacy for RA patients failing their first TNFi. No differences were observed regarding safety. Data were not available for anakinra, certolizumab pegol, golimumab, or tofacitinib.
Acknowledgements: Funding for this project was provided by the Rheumatology Research Foundation Investigator Award.
Disclosure of Interest: None declared