with methotrexate (MTX) was observed in 48% and with others classic DMARDs in 30%, while 22,3% received rituximab monotherapy. First-line rituximab option was justified by lung involvement in 21%, past malignancy in 13%, recurrent infections in 5%, congestive cardiac failure in 3%, vascular involvement in 3% and untreated latent tuberculosis in 3%. In the group previously exposed to biologics, 13% switched therapy due to ineffectiveness and 87% due to adverse events. No significant differences were found between the 2 groups in terms of age, gender, concomitant use of MTX and baseline DAS28. The group previously exposed to biologics had a longer disease duration (mean 23 vs 15 years, p=0.001) and fewer patients with ACPA seropositivity (79% vs 97%, p=0.035). There was a significant reduction of DAS28 at 6, 12 and 18 months ($p<0.001$ for all). Fifty six percent of the patients achieved a EULAR response at 6 months, 46% at 12 months and 59% at 18 months. DAS28 variation at 6 months differed significantly between groups, with a better clinical response in naive biological patients comparing to those previously exposed to biologics (median 1.173 vs 0.477; p=0.038). There were no differences in terms of DAS28 variation at 12 and 18 months (p=0.642 and p=0.135, respectively) and in EULAR responses at 6, 12 and 18 months between the groups (p=0.289, p=0.523 and p=1.000, respectively).

Conclusions: Our study confirms the effectiveness of rituximab in RA patients and suggests a higher magnitude of response in naive biological patients at 6 months of RTX therapy. These findings put in perspective an extension of rituximab as a first-line biologic for RA treatment.

Disclosure of Interest: None declared

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SAT0212 SARILUMAB DOSE REDUCTION IN AN OPEN-LABEL EXTENSION STUDY IN RA PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS

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Background: Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg SC q2w) + csDMARDs demonstrated efficacy in adults with active, moderate-to-severe RA and inadequate response or intolerance to ≥1 TNFi. Infections, neutropenia, injection site reactions, increased lipids, and increased transaminases were among the most common TEAEs. EXTEND (NCT01146652) is an open-label extension study evaluating long-term safety and efficacy of sarilumab in patients from the sarilumab clinical development program.

Objectives: To examine the effects of dose reduction of sarilumab 200 mg q2w to 150 mg q2w in patients from TARGET that occurred in EXTEND primarily for protocol-specified laboratory abnormalities.

Methods: Patients were switched to or initiated on sarilumab 200 mg q2w after enrolling in EXTEND. Per protocol, investigators could reduce the sarilumab dose from 200 mg q2w to 150 mg q2w for ANC ≥0.5 to 1.0 Giga/L, platelet count ≥50 to 100 Giga/L, or ALT ≥3 to 5×ULN. Dose reductions were also performed at the investigator's discretion. Efficacy data from EXTEND were analyzed before and 24 weeks after dose reduction.

Results: As of the July 2016 interim analysis (N=452), dose reduction from sarilumab 200 mg q2w to 150 mg q2w had occurred in 14.6% of patients (n=66) from TARGET. The most common reasons for dose reduction were decreased ANC (8.8%; n=40) and increased ALT (3.3%; n=15). At the time of analysis, 80.3% of patients (n=53) whose dose was reduced were continuing treatment, with a median treatment duration of 1.6 years after dose reduction. Improvements in ANC and ALT were observed over the 6 months after dose reduction (Table 1). Efficacy was maintained 24 weeks after dose reduction (Table 2).

Table 1. ANC and ALT After Dose Reduction[a]

	Before dose reduction n (%)	6 months after dose reduction n (%)
ANC		
≥0.5 to <1.0 Giga/L	25/40 (62.5)	5/39 (12.8)
<0.5 Giga/L	0	0
ALT		
>3 to ≤5×ULN	13/15 (86.7)	1/13 (7.7)
>5 to ≤10×ULN	1/15 (6.7)	0

[a]Denominator represents patients who dose reduced because of decreased ANC or increased ALT who had ANC/ALT measured within specified time point.

Table 2. Efficacy After Dose Reduction

	Before dose reduction (N=60)	6 months after dose reduction (N=53)
ACR20 response rate, n (%)	49 (81.7)	43 (81.1)
ΔHAQ-DI, mean (SD)	-0.7 (0.6)	-0.8 (0.7)
ΔDAS28-CRP, mean (SD)	-3.0 (1.2)	-3.0 (1.3)
ΔCDAI, mean (SD)	-28.4 (12.5)	-28.6 (14.6)

Conclusions: In patients from TARGET whose sarilumab dose was reduced from 200 mg q2w to 150 mg q2w during EXTEND, there was an improvement in laboratory abnormalities and continuation of treatment for the majority of patients. Improvements in signs and symptoms of RA and physical function were maintained after dose reduction.

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SAT0213 LOW DOSE IL-2 RESTORES DECREASED ABSOLUTE NUMBER OF REGULATORY T CELLS AND IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: A therapeutic revolution in the past decade is still a considerable unmet need in the treatment of rheumatoid arthritis (RA). On the other hand, dysfunction of regulatory T cells (Tregs) has been considered to be a pivotal cause of RA and correction of this dysfunction to be a potential RA therapy[1]. However, abnormalities of Tregs in patients with RA were reported controversially in previous studies[2], in which only proportion was measured and Tregs were defined using different protein markers.

Objectives: In this study, we measured both absolute numbers and proportions of CD4+CD25+Foxp3+ Tregs in peripheral blood of RA patients and investigated the effects of low-dose recombinant human IL-2 (rhIL-2) on Tregs and CD4+ effector T cell subsets in patients with RA.

Methods: Both absolute numbers and proportions of Treg and Th17 cells in peripheral blood, defined as the CD4+CD25+FOXp3+T or CD4+IL-17 + T cell population, were examined by flow cytometry in 342 patients with RA with different 28-joint Disease Activities (DAS28), including 75 who had never received disease-modifying antirheumatic drugs (DMARD) and 151 who were receiving or had received DMARD. Among these patients, 112 consented at enrollment to receive rhIL-2 treatment. Before and after treatment, the Th17 and Treg cells in peripheral blood were analyzed by flow cytometry.

Results: The absolute count of Treg cells in patients with RA was significantly low compared with that of healthy controls ($P<0.05$), but the absolute count of Th17 cell was no different between RA and healthy controls. After the course of rhIL-2 treatment, there was a significant increase in the absolute count of Th17 and Treg cells in the CD4+ T cell population ($P<0.01$), but Th17/Treg was significantly low after the treatment.

Conclusions: The data suggest that, besides propotion, the decrease of Treg cell number, defined as the CD4+CD25+FOXp3+population, may contribute to the pathogenesis of RA. Over the treatment of rhIL-2, there was a more significant increase in the absolute count of Treg cells than that of Th17, and consequently restore the balance of Th17/Treg.

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SAT0214 AN ANALYSIS OF INCREASING SPACING TIME FOR THE INTRAVENOUS ADMINISTRATION OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Although the biological disease-modifying antirheumatic drugs (bDMARDs) are the most effective treatment for rheumatoid arthritis (RA), the costs are much higher than those of conventional synthetic DMARDs. A number

of studies on discontinuation, dose reduction and/or spacing of bDMARDs have been performed, but there have been few reports on increased spacing time between tocilizumab (TCZ) administrations so far.
Objectives: To analyze the efficacy of spacing of the intravenous (IV) administration of TCZ in patients with RA.
Methods: 63 patients (11 M, 52 F) who were administered IV TCZ for more than 1 year were enrolled. Eleven patients had shifted to subcutaneous injection and the data at the last IV infusion were analyzed.
Results: Mean age was 57.4 years old (30–78), mean body weight was 55.5kg (37–85.5), mean duration of illness was 10.7yrs (0–32), The number of the bDMARDs previously administered were 0.9 (0–3), and duration of TCZ treatment was 46.9 months (13–83). The intervals between administrations were 4 weeks: 28.6%, 5 weeks: 38.1%, 6 weeks: 17.5%, 7 weeks: 6.0%, 8 weeks: 7.9%, and 10 weeks: 1.6%. Tender joint count, swollen joint count, erythrocyte sedimentation rate (ESR), C-reactive protein, matrix metalloproteinase-3 (MMP-3), patient's visual analogue scale (VAS), doctor's VAS, disease activity score (DAS) 28-ESR, simplified disease activity index (SDAI), clinical DAI (CDAI) were significantly improved. All of patients remission rates were 90.5% for DAS28-ESR, 44.4% for CDAI, and 42.9% for SDAI. Patients with prednisolone (PSL) decreased from 50 to 38 (p=0.031), at doses of 5.3 (2–10) to 2.7 (0.5–5) mg/day (p<0.0001). Patients with methotrexate (MTX) decreased from 46 to 32 patients (p=0.017), at doses of 8.1 (2–18) to 6.6 (2–14) mg/weeks (p<0.0001). There were no changes in the usage of other csDMARDs. The remission rates of the patients with increased spacing (n=45) were 75.6% for DAS28-ESR, 28.9% for CDAI, and 35.6% for SDAI. In 45 patients with increased spacing, both PSL and MTX were significantly reduced even after spacing (2.9: 0.5–5.5 to 2.6: 1–7.0) mg/day, and (6.45: 2–10 to 5.2: 2 -12) mg/ weeks, respectively (p=0.0013, p=0.0085). At the introduction of TCZ, there was no difference in the serum levels of MMP-3 in patients with increased spacing and without spacing 274.8 (24–1310) ng/ml vs 283.3 (32–626) ng/ml p=0.692). Serum revels of MMP-3 at the first time of increased spacing were significantly lower in the patients with increased spacing than those at the final point of patients without spacing 72.0 (22.2–236.0) ng/ml vs 165.8 (35.8 -619.0) ng/ml, p=0.000752. The number of patients with normal levels of MMP-3 among the patients with increased spacing were 25/45 (55.6%) with significantly higher levels for those patients who had no spacing 3 /18 (16.7%, p=0.00567).
Conclusions: TCZ treatment was associated with significantly reduced disease activity and reduced use of PSL and MTX. Increased spacing between administrations was used in 71.4% of the patients. TCZ was able to reduce PSL and MTX even after spacing. MMP-3 might be a useful marker to decide the spacing period. TCZ is the most inexpensive bDMARD in Japan, but with increased spacing, it is possible to reduce the cost even further with acceptable control of RA symptoms.
Disclosure of Interest: None declared
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SAT0215 CHARACTERISTICS OF PATIENTS WITH ANKYLOSING SPONDYLITIS, RHEUMATOID AND PSORIATIC ARTHRITIS IN TREATMENT WITH BIOLOGICS IN VERONA'S COHORT: RESULTS FROM VENETO'S REGION BIOLOGICS REGISTER

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Background: Since 2013, in Veneto's Region, data registration is mandatory for all patients affected by Rheumatoid arthritis (RA), Psoriatic Arthritis (PA), Ankylosing Spondylitis (AS) in treatment with biologic agents. The biologic DMARDs currently marketed in Italy are: anti-TNF (originator and biosimilar infliximab, etanercept, adalimumab, certolizumab and golimumab), anti-IL6 (tocilizumab), anti-CD20 (rituximab), CTLA-4 like (abatacept) and anti IL-12/23 (ustekinumab).
Objectives: The aim of this study was first to describe the characteristics of patients with RA, PA, AS under biologics and then, to extract and analyze real-life data regarding rheumatic treatments in Verona's cohort.
Methods: The study has been carried out on behalf of Regione del Veneto, Giunta regionale- Ricerca Sanitaria Finalizzata-Venezia-Italy. Data used for analysis were retrieved from Veneto's Region Biologics Register (VRBR). VRBR provides that core variables such as onset and type of disease, anthropometric characteristics (age, sex, body weight, height) are registered at the beginning. Furthermore, prior and concomitant rheumatic treatment (conventional and biologic DMARDs, corticosteroids, NSAIDs), disease activity indicators (DAS 28-PCR, ASDAS-PCR, pain-NRS), prognostic factors (positivity for rheumatoid factor and/ or anti-citrulline antibodies in AR, presence of radiological erosions) were assembled at baseline, every 6 months and at the time of biologic's switch or swap.
Results: A total of 983 patients under biologics were examined; 543 (55,2%) with AR, 272 (27,7%) with AP and 168 (17,1%). Between these, 262 (27,2%) patients were naïve to biologics, 128 with AR, 84 with AP, 50 with SA. Mean duration of disease was of 15,3, 10,7 and 12,6 years respectively for RA, PA and AS. Radiological erosions were present in 73% of RA-patients and the percentage was higher in those with positivity for rheumatoid factor and/ or anti-citrulline antibodies (84,4% versus 56,2%). More than half of the patients in this cohort were treated at least with one biologic agent; anti-TNFs were the main biologic used (RA:54,8%, PA:92,7%, AS: 100%) followed by Abatacept (25,4%), tocilizumab (12,3%) and rituximab (5,9%) in patients with RA. Methotrexate (MTX) was the prevalent associated c-DMARDs (41,8% in RA and 34,2% in PA) with mean dose of 11,9 mg/week in RA and 12,1 mg/week in PA. The optimal dose of methotrexate was not achieved prevalently because of drug intolerance.
Conclusions: Profile of both conventional and biological DMARDs looks very different according to the type of rheumatic disease. The first data show an underuse of MTX in patients with RA and PA under biologics with a low mean dosage due to intolerance. Next step is to evaluate long-term outcomes in clinical practice.
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SAT0216 ABATACEPT EXPERIENCE IN BIOLOGIC NAIVE RHEUMATOID ARTHRITIS PATIENTS: HUR-BIO REAL LIFE RESULTS

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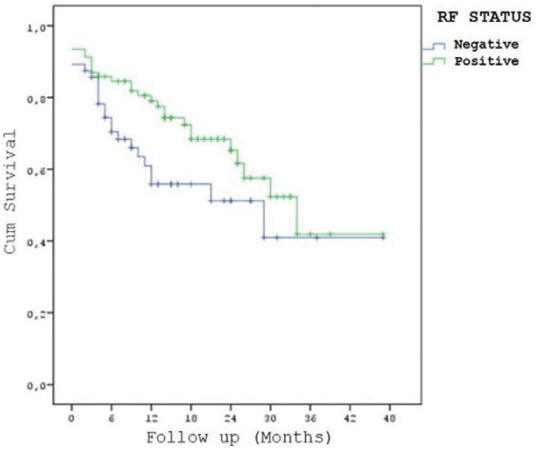
Background: Abatacept (ABA), a T lymphocyte blocker, is one of the treatment options in rheumatoid arthritis (RA) patients who are resistant to initial therapy with non-biologic disease modifying drugs (DMARDs).
Objectives: Aim of this study was to evaluate the effectiveness, safety and drug survival rates of ABA in RA patients registered in HUR-BIO (Hacettepe University Rheumatology Biologic Registry) database.
Methods: HUR-BIO is a prospective,single center database of biological treatments including 1229 RA patients by August 2016. In total, 247 of patients had received ABA and in 175 (71%) of them ABA was the first biological agent. In this analysis, 158 patients were evaluated due to lack of first follow-up visit in 17 patients. Demographics, clinical and serological data were evaluated. DAS-28 and HAQ-DI scores before ABA and last follow-up visit were also assesed. Kaplan-Meier analysis was used to estimate drug survival rates.
Results: Among 175 (82% female) patients, mean age was 53.6±11.3 and mean disease duration was 10.3±7.3. Seropositivity for RF and/or ACPA was present in 74.8% of patients. Table 1 represents DAS-28 scores of patients before ABA and last follow-up visit. Mean duration from ABA initation to first and last follow-up visit was 4.5±3.1 and 15.1±10.2 months, respectively. Female gender was found as a risk factor in terms of remaining of DAS-28 above 3.2 at first control [OR 5,63 (%95 CI 1,72–18,41)]. In first follow-up visit, improvement in DAS-28 score of ≥1,2 from baseline was more frequent in ACPA positive patients (48/62 (77.4%) vs 17/33 (51.5%), p=0.01). HAQ score of >1.0 was observed in 57.8%, 36.3%and 26.1% of patients at baseline, first follow-up visit and last follow-up visit, respectively. ABA had been cessated in 60 (38.0%) patients during follow-up. The reason for ABA withdrawal was primary unresponsiveness in 22 (36.6%) patients and infection in 2 (3.3%) patients. Drug survival for ABA was shown in Figure 1. Log-rank between RF positive and negative patients was found as 0.067.

Table 1. DAS-28 scores at first and last follow-up visits

	First control visit (n=136)	Last control visit (n=136)
Follow up duration, mean (SD)	4.5 (3.1)	12,3 (10.9)
DAS-28 >5.1,n (%)	11 (8.2)	16 (11.8)
DAS-28=3.2–5.1,n (%)	56 (41.8)	46 (33.8)
DAS-28=2.6–3.2,n (%)	23 (17.2)	23 (16.9)
DAS-28 <2.6,n (%)	44 (32.8)	51 (37.5)
Remission or low disease activity among patients with at least one follow-up visit, n (%)	67 (50.0)	74 (54.4)
Remission or low disease activity among all patients, n (%) (The worst scenario)	67/158 (42.4)	74/158 (46.8)

Figure 1. ABA survival rates in RF positive and negative patients



Conclusions: In our database, 70% of RA patients received ABA were biologic naive. Remission or low-disease activity was achieved approximately 50% of patients in first follow-up visit with an average of 4.5 months after begining of the treatment. Functional improvement was observed in two thirds of patients.