Results: Sample: 2055 RA patients, female=85.1%, median disease duration=6.02 yrs; mean (SD) age=50.3 (12.1) yrs; mean (SD) DAS28=5.3 (3.1); seronegative RA=14.1%; median follow-up duration=3.9 yrs. In total, 565 patients received 664 courses of the MTX-LEF combination (median duration, 2.5 years/course; 2209 person-years). The incidence of SAE was 4.75/100 patient-years in the entire sample. There was no significant increase in the risk of any of the outcomes with the use of combined therapy (table 1) comparing with methotrexate (without leflunomide). The use of antimalarials was associated with reduced risk of SAE (adjusted HR=0.62, 95% CI 0.48 to 0.79, $P<0.001$), while sulfasalazine (adj. HR=1.78, 1.18 to 2.68, $P=0.006$) and biologic DMARDs/tofacitinib (adj. HR=1.67, 1.31 to 2.12, $P<0.001$) increased the risk of SAE.

Table 1

Outcome(number of SAE)	HR (95% CI), p Value	HR (95% CI), p Value
SAE (457)	1.00(0.78-1.26), p=0.970	1.06(0.83-1.35), p=0.629
SAE infections (228)	1.1(0.79-1.55),p=0.538	1.24(0.89-1.75), p=0.207
SAE non-mycobacterial lung infections (78)	0.90(0.50-1.62), p=0.733	0.97(0.53-1.74), p=0.908
SAE hepatic AE(14)	1.12(0.28-4.48), p=0.873	NA
SAE hematologic (10)	2.09(0.52-8.36), p=0.299	NA
SAE CV (61)	1.22(0.65-2.30), p=0.529	1.11(0.58-2.12), p=0.755

*Comparing with MTX (without leflunomide) and adjusted for the use of LEF (without MTX) and a category representing absence of MTX and LEF. †Adjusted also for time-fixed covariates (age, gender, smoking, history of malignancy, diabetes, hypertension, renal failure, ischemic cardiomyopathy, bronchopulmonary obstructive disease) and time-varying covariates (use of sulfasalazine, antimalarials, biologic DMARDs/tofacitinib, and corticosteroids). SAE: serious adverse events, MTX: methotrexate, LEF: leflunomide, NA: not applicable due to reduced number of events, CV: cardiovascular.

Conclusion: BIOBADABRASIL results suggest that the combination of methotrexate and leflunomide is safe in the treatment of RA.

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FRI0143

IS PATIENT – PHYSICIAN DISCORDANCE IN ASSESSMENTS OF BURDEN OF RHEUMATOID ARTHRITIS A DETERMINANT OF METHOTREXATE ADHERENCE?

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Background: Accurate assessments of disease activity in rheumatoid arthritis (RA) have a crucial role in establishing disease severity and monitoring response to treatment. There is no objective, numerical

measures to estimate RA severity and treatment response. A frequently used means of quantifying the overall perception of disease activity is through an subjective assessment of global disease activity on a visual analogue scale (VAS), both by the patient, and by the physician, as well. The common direction of the discrepancy usually points toward better rating by the physicians than by the patients themselves, leading to potential medication adherence.

Objectives: The aims of the study were to explore the presence of disagreement between patients' and physicians' assessment of global disease severity, as well as to investigate the possible correlation between patient – physician discordance in assessments of RA burden and methotrexate adherence.

Methods: In the period between May 1 and September 15, 2019, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic "Merkur Nera" randomly chosen Montenegrin clinics were enrolled in this multi-centric cross-sectional study. The inclusion criteria were as follows: age ≥ 18 years, diagnosis of RA of at least 6 months, current methotrexate (MTX) use for at least 1 month (with or without concomitant usage of another RA drugs), and written informed consent. Non-adherence to MTX was defined as ≥ 1 dose missed against medical advice. The global disease activity is estimated by VAS (using a 0–10 ordinal scale), both by the patient, and by the physician. The differences between groups are assessed using the Mann-Whitney U-test. The correlation between the patient – physician discordance and MTX adherence is evaluated using the Spearman rank correlation.

Results: The most of the participants (87.8%) were female with median current age of 57.5 years (range 21-83 years). The median duration of RA was 8 years (range 0-34 years), while the median duration of MTX treatment was 6 years (range 0-26 years). The median value of VAS score estimated both, by the patients and their physician was 5, with no statistically significant difference between these two groups ($Z = 1.447$; $p = 0.748$). The analysis of patient – physician discordance in VAS assessment showed that full agreement is achieved in 76 (77.6%) cases, while in 21 (21.4%) RA patients their doctors underestimated their self-perception of disease burden. In only one participant, the physician overestimated patient's perception of RA severity. In total sample the self-estimated prevalence of MTX non-adherence was 32.7%. However, the analyses of the frequency of MTX non-adherence in sub-cohorts stratified by the presence of patient – physician discordance in VAS assessment showed that in "concordance group" the prevalence was 26.3% (20 out of 76 RA patients), while in "discordance group" the prevalence was 54.5% (12 out of 22 RA patients), with statistically significant difference between these two groups ($Z = -5.745$; $p < 0.001$). Statistically significant correlation has been observed between presence of patient – physician discordance in VAS assessment and MTX non-adherence ($\rho = 0.427$; $p < 0.001$).

Conclusion: The results of our study have shown that the presence of patient – physician discordance in assessment of global RA activity could deeply influence the MTX adherence in a Montenegrin sample of patients with RA. This finding emphasizes the need to focus on patients' preferences and values to deliver individualized patient-centered care that could potentially enhance adherence and consequently achieved optimally control of disease activity.

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FRI0144

JOINT-SPECIFIC RESPONSES TO TOFACITINIB AND ADALIMUMAB IN RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM ORAL STANDARD AND ORAL STRATEGY

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Background: Inflammatory arthritides affect joints variably despite systemic inflammatory cues. Anatomical site-specific differences have been seen in the transcriptome and function of synovial fibroblasts from different joints,¹ including evidence that some joints in rheumatoid arthritis (RA) show differential methylation of genes encoding biological pathways, such as interleukin 6 signalling via the JAK-STAT pathway.² Whether such site-specific JAK-STAT sensitivity translates into joint-specific responses to therapeutic JAK inhibition is unknown. Tofacitinib is an oral JAK inhibitor for the treatment of RA.

Objectives: To explore joint-specific responses to tofacitinib and adalimumab (ADA) in RA clinical trials.

Methods: This was a post hoc analysis of 3-, 6- and 12-month data from the active treatment arms of Phase (P)3 study, ORAL Standard (NCT00853385; n=609) and P3b/4 study, ORAL Strategy (NCT02187055; n=1152) in patients with active RA refractory to methotrexate (MTX). Both studies included tofacitinib 5 mg BID + MTX and ADA (40 mg SC q2w) + MTX treatment arms. ORAL Standard also included a tofacitinib 10 mg BID + MTX treatment arm and ORAL Strategy, a tofacitinib 5 mg BID treatment arm. A paired joint pathology score (PJPS), a combination of bilateral tender/swollen joint counts ranging from 0 (neither side swollen/tender) to 4 (both sides swollen/tender) was calculated. Data for 33 (ORAL Standard) and 14 (ORAL Strategy) joint pairs were available. The percentage change from baseline (%Δ) in PJPS for each joint was presented in a heat map to visualise responses. To show tofacitinib-specific effects at each joint, difference in mean PJPS for each tofacitinib regimen at 3 months minus the respective ADA + MTX group was calculated.

Results: Across all treatment arms of both studies, baseline joint involvement ranged from 15.7% (5th distal interphalangeal joint of the hand) to 93.3% (wrist). All joints showed a treatment response, with Δ PJPS ranging from -36 to -94% (Figure). The heat map showed lower response rates in the wrist and knee vs most other joints in both studies persisting to 12 months, regardless of treatment arm. Similarly, in ORAL Standard, the ankle (not assessed in ORAL Strategy) showed a lower response vs most other joints. Tofacitinib-specific responses vs ADA + MTX (not shown) were seen (mean differences in PJPS ranged from -0.4 to 0.2) with no clear pattern in the combination therapy groups. In the tofacitinib 5 mg BID arm of ORAL Strategy, a pattern was observed in the metacarpophalangeal (MCP) joints, with tofacitinib responsiveness vs ADA + MTX increasing progressively (mean difference in PJPS increased from 0.16 in MCP1 to -0.08 in MCP5).

Conclusion: There is variation in the responsiveness of RA joints to tofacitinib $\pm$ MTX and ADA + MTX, with the wrist, knee and ankle responding less well vs other joints, irrespective of treatment mode of action. Concomitant MTX use in most treatment arms may mask joint-specific actions of tofacitinib and ADA. Observed responsiveness to tofacitinib monotherapy vs ADA + MTX increased from MCP1–5, which may be tentative evidence of differential sensitivity to JAK inhibition across embryologically imprinted functional genetic gradients. Further analyses of the monotherapy arms of randomised trials may yield additional evidence of joint-specific responsiveness, and provide a basis for personalised RA treatment.

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FRI0145

FACTORS ASSOCIATED WITH NEAR REMISSION DIFFER BETWEEN AUTOANTIBODY-POSITIVE AND -NEGATIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Disease remission is recommended as the treatment target in patients with early rheumatoid arthritis (RA). According to the criterion, the proportion of patients classified as in remission considerably varies, with the Boolean-based definition being the most restrictive [1]. A considerable proportion of patients with established RA misses Boolean remission solely because of one of the 4 criteria (near remission) [2]. The frequency and the limiting variables to Boolean remission in real-life cohorts of patients with early RA are however unknown.

Objectives: To assess the frequency and the limiting factors for fulfilling Boolean remission in early RA patients treated with csDMARDs according to a treat-to-target strategy.

Methods: The study population consisted of 578 early RA patients (<12 months of symptoms) consecutively recruited at our Early Arthritis Clinic. treatment-naïve at inclusion and prospectively followed-up upon initiation of therapy with methotrexate (MTX) aimed at the achievement of low disease activity (28-joints disease activity score [DAS28] ≤ 3.2). After 6 months of treatment, patients were classified as in remission or near remission according to the Boolean criterion as follows: (i) remission – swollen joint count (SJC28), tender joint count (TJC28), C-reactive protein (CRP) and patient global assessment of disease activity (PGA) all ≤ 1 ; (ii) near remission – just 3 of the 4 core items. Patients characteristics between remission and near remission were compared, and reasons for missing Boolean remission were analysed in relation to disease variables.

Results: Complete follow-up data after 6 months of treatment were available for 89.3% of the patients. Disease remission was achieved in 25.6% of the cases according to the DAS28, 16.7% according to the simplified disease activity index (SDAI) and 11.6% according to the Boolean criterion. One-hundred and thirty-three patients (25.8%) failed to reach Boolean remission solely because of one of the 4 criteria. Of these, 45.9% were in DAS28 remission and 22.6% in SDAI remission. No differences in baseline demographic and clinical characteristics were found between patients in Boolean remission and patients in near remission. Use of prednisone co-medication and MTX starting dose were also comparable. Patients negative for both rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) were more frequently in near remission rather than in Boolean remission compared to autoantibody-positive patients (**Fig. 1A**). The missing criterion in near remission was SJC28 >1 in 49% of the cases, PGA >1 in 41%, and TJC28 >1 or CRP >1 mg/dl in the remaining 10%. Collectively, failure to achieve Boolean remission because of SJC28 >1 was more common in RF and/or ACPA positive patients. Rather, autoantibody-negative patients more frequently missed remission due to PGA (**Fig. 1B**).

Conclusion: In patients with early RA treated with csDMARDs, near remission is up to two times more frequent than Boolean remission. Collectively, autoantibody-negative patients more commonly miss complete remission solely because of one criterion compared to autoantibody-