age, and DAS28, and their correlation coefficients (CC) were 0.00004174, 0.01943, and 0.02941, respectively.

At FU, the R-value of the equation in MLR was 0.6309. Factors that demonstrated significant correlation with the HAQ score were age, Com, PS, and SvdHS, and their CCs were 0.00007042, 0.0004365, and 0.002886, 0.02354, respectively.

The R-value of the change of the HAQ score correlation equation demonstrated 0.4755. Factors that demonstrated significant correlation with change of the HAQ score were changes of DAS28-CRP, PS, age, and Com, and their CCs were 0.002703, 0.003750, 0.003480, and 0.009886.

Correlation procedure needed elimination of the case whose average DAS28 exceeded 2.6, SvdHS exceeded 100, and PS exceeded 20 mm. After correction, patients have been limited to 158. However, age demonstrated significant correlation with the HAQ score, and its CC was 0.00004439, and the constant of age was 0.01132. After correction, Com demonstrated no significant correlation with the HAQ score.

Com demonstrated significant correlation with age with 0.01253 for CC. However, the R-value of the equation was 0.1982.

Conclusions: These results suggested that age have deep influence on the HAQ score. Com also affects on the HAQ score, however, Com and ageing is independent factor for each other. Therefore effect of ageing on the HAQ score is concluded independent. The HAQ score increases its standard value for approximately 0.01 as age increase one.

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AB0232 DISEASE ACTIVITY STATE IN PATIENTS WITH RHEUMATOID ARTHRITIS INCLUDED IN THE BIOBADABRASIL REGISTRY

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Objectives: to analyse disease activity of RA patients at the start of treatment with a biologic agent (adalimumab, infliximab, certolizumab, etanercept, golimumab, abatacept, rituximab and tocilizumab -bDMARDs), target (tofacitinib-tsDMARDs) therapy or conventional DMARDs (comparison cohort of RA patients – csDMARDs).

Methods: BiobadaBrasil is a prospective observational cohort study, part of an international initiative (biobadaAmerica) in collaboration with BiobadaSeR; established in 2009, is an ongoing study supported by the Brazilian Society of Rheumatology (29 public centres located at academic institutions and 2 in private practice) focused on the study of adverse events in patients on biologic therapy. Additionally, by decision of its investigators, disease activity scores were also recorded at the beginning of each treatment. Sex, age, disease duration, RA -DAS-28, concomitant treatments at baseline were collected. Results expressed in mean $\pm$ SD, % (n).

Results: -Data from 1984 RA patients (67% on ts/bDMARDs) were analysed: 86% of the patients were women; mean age=56.6 $\pm$ 14.95 years; disease duration=14.4 $\pm$ 9.42; 87% RF positive. There were 3802 treatment courses, 67% with aTNF (Adalimumab-ADA, Certolizumab-CTZ, Etanercept-ETA, Golimumab-GOL, Infliximab-INFL), 33% non-aTNF (Abatacept-ABA, Rituximab-RIT, Tocilizumab-TCL) including Tofacitinib-TOF. The table 1 below depicted the medications prescribed at the initiation of a new treatment course:

Abstract AB0232 – Table 1

n courses	ADA (855)	CTZ (85)	ETA (708)	GOL (113)	INFL (772)	ABA (163)	RIT (184)	TCL (192)	TOF (70)	csDMARDs (660)
DAS28	5.1	4.9	5.1	4.9	5.3	5.3	5.3	5.4	5.3	5.2 $\pm$ 2.8
	$\pm$ 1.6	$\pm$ 1.5	$\pm$ 1.6	$\pm$ 1.7*	$\pm$ 1.6	$\pm$ 1.4	$\pm$ 1.6	$\pm$ 1.4*	$\pm$ 1.3	
CE (%)	58	76	60	61	58	68	74	71	83	78
MTX (%)	55	57	53	56	59	54	51	62	49	83
LFN (%)	27	42	27	31	23	31	25	18	27	45
Chlor (%)	14	15	11	10	15	11	19	17	11	30

Considering the more recent medications patients beginning TCL have more active disease than the ones beginning GOL and CTZ ($p<0.006$); anti-TNF are prescribed in association with MTX in less than 60% of the treatments. Extensive use of corticosteroids was identified besides consistent use of leflunomide and of hydroxychloroquine. Starting of new treatments was related to moderate/high levels of disease activity.

Conclusions: patterns of bDMARDs, csDMARDs and corticosteroid use clearly surfaced. Possibilities of improvement can be addressed.

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AB0233 CLINICAL AND FUNCTIONAL EFFICIENCY OF LARGE JOINTS REPLACEMENT IN PATIENTS WITH HIGH ACTIVITY OF RHEUMATOID ARTHRITIS

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Background: The synovium in rheumatoid arthritis (RA) produces a variety of cytokines that cause the destruction of articular cartilage, determining, in some cases, the need for replacement of the joint. Inflammatory substrate within the joint can be a source of high activity of RA. At the same time usually patients are taken to surgery only in the period of minimal activity of the disease.

Objectives: To evaluate the results of knee and hip joints replacement in patients with high RA activity and the quality of life of patients during the first year after the operation.

Methods: Replacement of knee and hip joints was performed in 36 patients (mean age 55.8 $\pm$ 9.4 years) with high RA activity DAS28 (mean 5.53 $\pm$ 0.67). At the time of surgery, the duration of the disease was 11.86 $\pm$ 4.92 years, RF positive in 27 (75%) pts. At baseline, 30 (83.3%) patients were treated with DMARDs (methotrexate-25 (69.4%), leflunomide-3 (8.3%), sulfasalazine 2 (5.6%)), steroids (prednisolone in an average dose of 4.2 $\pm$ 4.3 mg per day) –16 (44.4%) people, of whom, in combination with DMARDs – 8 (22.2%). The volume of therapy did not change after the operation. Biologics (infliximab, adalimumab, rituximab, etanercept) before surgery were given to 7 (19.4%) patients. Before the operation, after it, after 6 and 12 months, pain in the joints (VAS), activity of the disease – DAS28, functional capacity by the HAQ index was estimated.

Results: Reduction of VAS was observed already in the first month after surgery (47.3 $\pm$ 18.6 mm), initially it was 72.6 $\pm$ 14.2 mm, after 6 months it decreased 1.5 times to 48.7 $\pm$ 11, 2 mm ($p<0.05$), after 12 months – up to 29.8 $\pm$ 10.3 mm ($p<0.05$). After 6 months after surgery, the activity of the disease decreased reliably ($p<0.05$) with DAS28 from 5.53 $\pm$ 0.67 to 3.84 $\pm$ 0.56; to 12 months DAS28-3.24 $\pm$ 0.61. Positive dynamics of functional ability was recorded according to the HAQ index: 1.74 $\pm$ 0.25 before the operation, 1.64 $\pm$ 0.28 in a month after, and 1.22 $\pm$ 0.28 after 6 months ($p<0.05$), after 1 year – 1.03 $\pm$ 0.18 ($p<0.05$).

Complications after operations were not recorded.

Conclusions: Joints replacement in patients with high RA activity can be justified and effective in improving the functional ability and pain relief. Removal of pathologically altered joint tissues helps to reduce the activity of RA as a whole.

Disclosure of Interest: None declared

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AB0234 PATIENT'S EXPECTATIONS ABOUT SURGERY FOR THE RHEUMATOID FOREFOOT DEFORMITY

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Background: Forefoot deformity has been a common problem in rheumatoid patients, often demanding surgery. Typical deformities include hallux valgus and deformity of lesser metatarsophalangeal joints (MTPJ) and toes. Patient's satisfaction has not been well dealt in the literature as most studies have focused on radiological and clinical parameters following surgical treatment.

Objectives: to assess preoperative patient's expectations and postoperative satisfaction, and also factors (e.g. fulfilment of expectations, radiological parameters, and clinical outcomes) that could affect on postoperative satisfaction following first MTPJ arthrodesis and lesser toe resection arthroplasty in patients with rheumatoid forefoot deformity

Methods: 40 patients who underwent first MTPJ arthrodesis on great toe and resection arthroplasty for all less toes were enrolled. Clinical and radiological outcomes were investigated retrospectively. Preoperative primary expectations for surgery were questioned and fulfilment of expectation was assessed by 5-point

ordinal scale. Overall subjective satisfaction, radiological improvements, AOFAS forefoot score, and subjective Foot function index were also assessed. Correlation between overall satisfaction after surgery and above other factors was performed. Statistical analysis was done using SPSS and Spearman's rho rank correlation test was performed to analyse the correlation between factors.

Results: Mean follow-up was 38 months (range; 24–54). For preoperative expectations, 30 (75%) patients considered improvement in pain as the most important parameter and improvements in shoe wearable and gross appearance were expected in 7 (17.5%) and 3 (7.5%) patients, respectively. Fulfilment of expectations assessed showed very satisfied in 14 (35%), satisfied in 20 (50%), average in 5 (12.5%) and disappointed in 1 (2.5%) for great toe, and those regarding lesser toe showed very satisfied in 15 (37.5%), satisfied in 18 (45%), average in 6 (15%) and disappointed in 1 (2.5%), respectively. For overall postoperative satisfaction assessment, 16 patients (40%) were excellent while 16 (40%) were good, 6 (15%) fair, and 2 (5%) poor. AOFAS hallux and lesser toe score were 69.7 ± 11.71 and 70.7 ± 12.26 , respectively. Foot function index was 20.5 ± 12.07 at final follow-up. Preoperative and postoperative hallux valgus angle were $45.6^\circ \pm 10.55$ and $17.4^\circ \pm 5.13$, respectively. Those of 1–2 intermetatarsal angle were $14.2^\circ \pm 3.84$ and $8.4^\circ \pm 3.72$, respectively. Correlation analysis showed that significant factors that affected on overall satisfaction were fulfilment of expectation on the great toe (Spearman's $\rho = 0.842$, $p < 0.001$) and that of lesser toe, and AOFAS score. Radiological degree and improvement in HVA and IMA were not significantly associated with patient's satisfaction.

Conclusions: Expectations from surgery on rheumatoid forefoot deformity were improvement in pain as the most common parameter, improvements in shoe wearable and gross appearance. Fulfilment of patients' expectations on the great toe as well as on the lesser toe significantly affected on postoperative satisfaction. Careful counselling for patients' expectations and corresponding fulfilment should be performed before performing reconstructive surgery for rheumatoid forefoot deformity.

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AB0235 POLYMORPHISMS OF HLA-DRB1 AND TNF-308 G/A ARE ASSOCIATED WITH RADIOGRAPHIC JOINT DESTRUCTION IN PATIENTS WITH VERY EARLY RHEUMATOID ARTHRITIS

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Objectives: To clarify the association between HLA-DRB1 and TNF α (–308G>A) genes polymorphism and joint destruction/further progression during 12 months of the follow-up period (FUP) in patients with early (<6 months), active, predominantly ACPA and RF-positive RA treated according to "Treat to target" strategy.

Methods: The study included 85 patients with early RA and duration of symptoms <6 months. RA diagnosis was established according to ACR/EULAR 2010 criteria. All patients were initially assigned to subcutaneous methotrexate (MTX) with rapid dose escalation to 20–25 mg/week. Combination MTX+biological therapy, mainly adalimumab, was used when MTX was ineffective. Joint destruction was assessed by Sharp-Van der Heijde modification scoring method at baseline and after 12 months FUP. Real time polymerase chain reaction (PCR-RT) was used for TNF α gene polymorphism (–308G>A) genotyping. Low resolution PCR-RT with subsequent sequence-based typing of *04 were performed to study HLA-DRB1 gene polymorphism. The HLA-DRB1*01, *04:01, *04:04, *04:05, *04:08, *10 alleles were categorised as SE+ (Shared Epitope) alleles.

Results: It was revealed that the number of erosions and joint space narrowings as well as the total Sharpe score were not associated with the presence and the dose of the SE alleles, either at baseline or after 12 months FUP. However, the progression of joint destruction, assessed as the change (Δ) in the number of erosions, joint space narrowings and the total score, was statistically significantly associated with HLA-DRB1*(SE) genotypes: the carriers of SE (SE+/SE+) double-dose had more advanced progression as compared to (SE+/SE-)/(SE-/SE-) carriers ($p < 0.028$, $p < 0.019$, $p < 0.035$, respectively). As for TNF α gene polymorphism, it was demonstrated that the number of narrowings and total Sharpe score values were almost twice as high at baseline in GG genotype carriers as

compared to GA genotype carriers ($69.0^{49.5; 98.0}$ and $37.0^{29.0; 63.0}$ respectively, $p < 0.005$) and ($72.0^{49.5; 98.5}$ and $37.0^{29.0; 63.0}$ respectively, $p < 0.004$). Similar association was found after 12mo FUP, however, it should be mentioned that further progression of joint space narrowing and total Sharpe score was minimal ($p > 0.05$).

Conclusions: Our data suggest that HLA-DRB1 (SE+) gene polymorphism is associated with the progression of radiographic joint destruction at 12mo FUP in treated pts. Meanwhile TNF α (–308G>A) polymorphism is associated with more pronounced joint destruction at baseline in terms of joint space narrowing and total Sharpe score, but without further progression of joint destruction at 12mo in early and active RA pts managed according to "Treat to target" strategy.

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AB0236 DEVELOPMENT AND VALIDATION OF A SENSITIVE LC-MS/MS-BASED METHOD FOR ANALYSIS OF ENZYMATIC ACTIVITY OF FOLYLPOLYGLUTAMATE SYNTHETASE AND METHOTREXATE POLYGLUTAMATES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Methotrexate (MTX) is a widely applied anti-rheumatic and anti-leukemic drug. For its intracellular retention and pharmacologic activity, MTX relies on the enzymatic activity of folypolyglutamate synthetase (FPGS) to convert MTX into its polyglutamate forms (MTX-PG₂₋₆). Loss of FPGS activity is associated with reduced MTX activity and although red blood cell (RBC) MTX-PG_n levels correlate with disease activity in RA patients,¹ it is anticipated to be more relevant to measure MTX-PG_n in peripheral blood mononuclear cells (PBMCs). Thus, the aim of our study was to develop a LC-MS/MS method to 1) measure FPGS activity replacing laborious radioactive assays, and 2) to measure MTX-PG_n in PBMCs.²

Objectives: To validate a rapid, sensitive and non-radioactive assay to measure FPGS activity and MTX-PG_n in PBMCs based on LC-MS/MS technology.

Methods: Protein extracts (n=5) of PBMCs of MTX-treated RA patients were incubated for 2 hours at 37°C in FPGS assay buffer (pH8.8) containing 250 μ M MTX and 4 mM L-glutamic acid as substrates. Next, MTX-PG₂ formation was analysed with AB Sciex 4000 Q Trap tandem mass spectrometer coupled to an Acquity Ultra Performance LC system. Measurement of PBMC-MTX-PG_n (n=5) was performed by extraction of MTX-PG_n from PBMCs by perchloric acid precipitation. Quantification was performed with ¹³C₅-¹⁵N-labelled MTX-PG₁₋₅ internal standards. In FPGS activity and MTX-PG validation studies, human CCRF-CEM leukaemia cells, CEM/R30dm (a FPGS-deficient, MTX-resistant subline of CCRF-CEM), and human acute lymphoblastic leukemia (ALL) cells served as reference.

Results: In CCRF-CEM, the FPGS enzymatic assay showed linearity with protein input (10–250 μ g) and incubation time (0.5–3 hours). Substrate affinity parameters (Km) for MTX (65 μ M) and L-glutamic acid (2.2 mM) were consistent with earlier reports.³ FPGS activity in CEM/R30dm was <1% of CCRF-CEM. FPGS activity in ALL blasts was similar to CCRF-CEM while FPGS activity in RA patient PBMCs was 1%–5% of CCRF-CEM, and was non-detectable in RBCs. Average individual fractions of total MTX-PG_n in RA patient PBMCs were 22.1% (range: 8.2%–36.2%) for MTX-PG₂, 32.8% (27.1%–43.6%) for MTX-PG₃, 34.4% (30.4%–41.3%) for MTX-PG₄ and 10.6% (0.0%–28.4%) for MTX-PG₅. Average total MTX-PG_n levels per number of RA patient PBMCs were 30–50 fold higher than matched numbers of erythrocytes, and 6–9 fold lower than ALL blasts incubated for 24 hours with 1 μ M MTX.

Conclusions: A sensitive LC-MS/MS based method was developed for the measurement of FPGS activity and MTX-PG_n levels in PBMCs of RA patients. This method holds promise to guide future MTX-therapy response evaluations.

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