Results: The melatonin serum levels in RA patients were in 2 and 3 times higher in the morning and evening time than those of healthy individuals in the control group ($p=0.001$). We noticed significant correlations between melatonin level and disease duration ($r_s = -0.5$, $p < 0.01$). Significant differences in melatonin levels were revealed in RA patients in 1st and 3rd groups ($p=0.049$), in 1st and 4th groups ($p=0.012$), in 2nd and 3rd groups ($p=0.001$), in 2nd and 4th groups ($p=0.001$). Also we determined significant differences in melatonin levels between 1st and 2nd radiological stages ($p=0.001$) of RA patients. However, melatonin levels were not related to physical activity (HAQ).

Conclusion: We found a close relationship between serum melatonin levels, duration of the disease and radiological progression in RA patients. The most significant changes in melatonin metabolism occur in patients with the duration of the disease up to 5 years and with lower radiological stages. Our data indicate the important role of neurotransmitter in the pathogenesis of RA, especially at the initial stage of the disease.

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POS0499

WORK ABSENCE DUE TO MUSCULOSKELETAL SYMPTOMS IN PATIENTS AT-RISK OF RHEUMATOID ARTHRITIS IS COMPARABLE TO THOSE WITH ESTABLISHED DISEASE

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Background: Rheumatoid arthritis (RA) is an established cause of disability and work absence; however, little is known about the impact of musculoskeletal (MSK) symptoms on sick leave in patients at-risk of developing the disease.

Objectives: To describe the sick leave of individuals at-risk of RA, compared to patients who had recently been diagnosed with RA, over a 12-month period. Additionally, to investigate baseline predictors for sick leave within the first 12 months.

Methods: A prospective observational cohort for individuals at-risk of RA was conducted. A total of 591 consecutive anti-citrullinated protein antibody positive (ACPA+) individuals, with no clinical synovitis were recruited. A MSK ultrasound scan and a blood test were performed at baseline, and information about employment regime (retired, not in a paid job, part time and full time), days of sick leave and reasons for absences within the previous months were collected every 3 months and analysed at baseline, 6 months, 12 months and at the moment of diagnosis of an inflammatory arthritis (IA) (if the patient had progressed). Subjects who had retired ($n=80$) were excluded from the analysis.

A comparison was made with 114 RA patients from an observational study. Employment information was collected at pre-treatment, 6 months and 1 year after diagnosis. Univariable and logistic regression analyses were performed to assess predictors of work absence due to MSK reasons in the next 12 months from baseline for at-risk individuals.

Results: Even though the reasons for unemployment were not available, there were no statistically significant differences between employment rates across the timepoints of the study for the at-risk individuals' group ($p=0.778$). A similar pattern was observed in the RA patient group; which also maintained the same employment rates throughout the study ($p=0.311$) and these were comparable to the at-risk individuals' ($p=0.480$).

Over 35% of at-risk individuals in paid employment had work absences in the 3 months prior to the baseline visit. Of these 65.5% were due to MSK related issues, meaning 23.2% of the total absences were MSK related. The other reasons for work absence can be seen in table 1. This fell to 12.9% of the total absences at 6 months (which probably reflects clinical intervention) and increased to 38% if the patient progressed to an IA (graph 1).

Table 1. REASONS FOR SICK LEAVE AT BASELINE IN INDIVIDUALS AT-RISK OF RA (%)

MSK related issues	65.5
Flu-like symptoms	20.1
Gastrointestinal issues	19.4
Stress/anxiety	14.4
Headaches	11.5
Infection	3.6
Fatigue	1.4
Other	3.6

The percentage of individuals who took absence from work due to MSK related issues, was similar in both the at risk and RA group, including an initial reduction possibly due to drug intervention (graph 1). However, the median number of days off work 3 months prior baseline, 6 months and 1 year in RA patients tended to be higher than those in the at-risk group (10, 2 and 6 versus 5, 4 and 3 respectively).

Several factors were assessed to predict sick leave within 12 months in at-risk individuals: age, gender, smoking status, ACPA, rheumatoid factor (RF), anti-nuclear antibodies (ANA), C-reactive protein (CRP), early morning stiffness, shared epitope, joint pain, joint tenderness and abnormal findings in the ultrasound scan (erosions or power doppler); however, only RF [OR 0.18; $p=0.018$; 95% CI (0.04-0.84)] and CRP [OR 1.3; $p=0.021$; 95% CI (1.04-1.60)] were statistically significant in the multivariable analysis.

Conclusion: Even though being at-risk of RA is not considered a potential cause of disability, results show that the burden on the workplace, due to MSK related absences, was comparable to subjects diagnosed with RA. Although further investigation is required, initial data suggests that clinical intervention may reduce this burden; which tends to be higher in at-risk individuals with a negative RF and a high CRP.

Graph 1. Percentage of individuals who had work absences related to MSK issues 3 months prior to each timepoint.

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POS0500

NUMBER AND CO-EXPRESSION OF TNF RECEPTORS TYPE 1 AND 2 ON IMMUNOCOMPETENT CELLS ARE ASSOCIATED WITH STABILITY OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: The balance of TNF α receptors expression on cells which are actively involved in immunopathological processes affects both the density of distribution of receptors on cells and co-expression in subsets. Previously it was shown that basic effective RA therapy with methotrexate and glucocorticoids leads to equalization of the expression profile either in the percentage of cells or in the number of receptors, approaching those of healthy donors, but not simultaneously. However, questions about the relationship between the effectiveness of biological therapy and receptors co-expression remain unknown.

Objectives: To assess the differences in co-expression and quantitative expression of TNF receptors type 1 and 2 in subsets of cells associated with the severity of the disease, depending on the response to rituximab therapy.

Methods: Subanalysis of patients with high disease activity level successfully treated with rituximab (alone or in combination treatment scheme) during

hospitalization was performed ($n = 14$). The first group included 6 patients who retained low disease activity during 1 month follow-up (RA, stabilization). The second group consisted of 8 patients who had exacerbation during follow-up period. As a control group, we used data from 43 comparable healthy donors. Subsets of T regulatory cells and monocytes were studied. A comparison was made among the indicators of receptors number and proportion of cells expressing the corresponding receptor.

Results: For T regulatory cells, the key differences for patients who did not retain low disease activity were significantly higher number of TNF type 1 and type 2 receptors on double-positive cells with a lower percentage of these cells compared to stable patients. At the same time, higher differences between proportions of double-positive cells in comparison with control values of healthy donors were associated with higher probability of maintaining in remission.

For monocytes, the key differences in stable patients were the very high quantitative expression of type 1 receptors on double-positive cells, with a lower percentage of these cells compared to patients with exacerbation. At the same time, lower differences between proportions of double-positive cells in comparison with control values of healthy donors were associated with higher probability of maintaining in remission.

Conclusion: Obtained data confirm the previously proposed hypothesis about the essential role of balance in quantitative expression of TNF receptors type 1 and 2 on double-positive cells to determine the intensity and type of cell response to the mediator and its association with the level of disease activity and response to therapy.

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POS0501

SUSTAINED 2-YEAR REMISSION OF THE DISEASE IN A CLINIC OF EXCELLENCE IN RHEUMATOID ARTHRITIS. EXPERIENCE OF THE CLINICAL REGISTRY IN COLOMBIA

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with no cure, characterized by episodes of exacerbation and remission, which requires permanent use of medications. Clinics of excellence are multidisciplinary and

centralized programs that improve adherence to treatments. Information on the benefits of these models of care has been published but is not definitive. In Colombia, the clinical registry of patients with RA is kept in the Cuenta de Alto Costo (CAC).

Objectives: To demonstrate the difference in the percentages of sustained remission at 2 years, between an institution with non-centralized management or standard of care (Hospital Militar Central-HMC) compared to another institution with centralized management or clinic of excellence (BIOMAB-IPS) and determine if the results are determined by any of the intervention variables or by the program.

Methods: The 2-year clinical records for the CAC were compared between an institution with non-centralized management (HMC) in comparison with another institution with centralized management (BIOMAB-IPS), performing a socio-demographic description, measuring control of the disease DAS28 clinimetry, Fisher's test non-parametric bivariate analysis, multiple regression model, and population matching with Propensity score Matching (PSM).

Results: Complete information was obtained from 2 years of follow-up, in centralized management 3457 patients and for the non-centralized unit 114 patients. Most of them corresponded to 2962 women (82%), with time of illness of 9.5 years and 10.2 years, respectively, without statistically significant differences. A difference was observed in the 2 programs to maintain remission at 2 years, in favor of the centralized program 54.7% vs 28.6.2% ($p < 0.00$). With the binomial generalized linear regression model, it was confirmed that this difference was not explained by variables such as the use of biological therapy ($RR = 0.77$; 95% CI 0.69-0.86), use of DMARDs ($RR = 0.71$; 95% CI 0.62-0.82) and number of rheumatology consultations ($RR = 0.97$; 95% CI 0.92-1.02) in comparison with the centralized care model ($RR = 2.32$; 95% CI 1.58-3.35). Due to the biases between the groups due to the non-probability sampling, a PSM was performed, with a 1:1 match, caliper of 0.065, obtaining a pseudo population with well-balanced covariates (see table 1). In the common support area, statistically significant differences were documented in sustained remission over 2 years, in favor of the centralized care group 45 vs 17.9% ($p = 0.001$).

Conclusion: With the information from the clinical records, statistical strategies can be used to evaluate important differences in centralized care programs, observing favorable results of these types of care that are not related to isolated elements of the program, but to the overall effect of the program.

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POS0502

WHAT IS THE ROLE OF VITAMIN D STATUS IN DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH bDMARDs? – DATA FROM A RHEUMATOLOGY CENTER

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Background: Vitamin D is a fat-soluble vitamin, mainly involved in the regulation of calcium metabolism, and it has gained increasing interest in recent years because of its potential role in immunomodulatory activity. Recent data suggest that it is negatively associated with disease activity in rheumatoid arthritis (RA), however this is not yet fully understood.

Objectives: This study's aim was to investigate if there is any correlation between vitamin D serum levels at baseline, before taking the first biological disease-modifying antirheumatic drug (bDMARD), and at 6 months after, with disease activity in a cohort of RA patients.

Methods: This is a cross-sectional study, including all the rheumatoid arthritis patients taking the first bDMARD with evaluation of the vitamin D status at baseline and 6 months after biologic therapy at our Rheumatology Department and registered in the national database (Reuma.pt).

Demographic, clinical and laboratorial characteristics and disease activity measures were collected from the baseline visit and the visit after 6 months of treatment with the first biologic. For the statistical analysis, two groups were defined, based on the serum levels of 25(OH) vitamin D, considering the most common cut-off of 30 ng/mL. For comparison analyses between groups, chi-square test was used for categorical variables and Mann-Whitney U and T-tests were applied for continuous variables.