Conclusions: Pts with CDAI ≤ 35 –36 at BL achieved sustained LDA more frequently and more rapidly than pts in the higher disease category at BL. In pts with higher disease activity at BL a more robust response was observed with bari 4 mg treatment.

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- Disclosure of Interest:** J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, A. Kavanaugh Consultant for: Eli Lilly and Company, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, Astra-Zeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv, D. Muram Employee of: Eli Lilly and Company, J. Alam Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB
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AB0236 ASSOCIATION OF LYVE-1 PROTEIN IN EXOSOME WITH DISEASE ACTIVITY AS A NEW CANDIDATE BIOMARKER FOR RHEUMATOID ARTHRITIS

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Background: Exosomes, membrane-bound vesicles of 40–100 nm in diameter, have protein and lipid composition that depends on the cell origin, the state of activation, infection and/or transformation of the parent cells. Those proteins and lipid have a role in mediating inflammatory and autoimmune disease as well. Discovery of inflammatory marker to evaluate appropriate response of treatment could give effective timing to adjust treatment for rheumatoid arthritis patients.

Objectives: The aim of the study was to identify protein candidates in exosome being related with other inflammatory parameters.

Methods: The study population consisted of 60 RA patients, in which there were 30 patients of clinical remission (CR) group with DAS28-ESR ≤ 2.6 and 30 patients of non-clinical remission (non-CR) group with DAS28-ESR > 2.6 . By exosome preparation with ExoQuick™ kit and protein identification with tandem mass tags labeling/mass spectrometry between the groups, potent protein markers were selected. Level of the proteins was measured by ELISA.

Results: We identified 6 proteins by proteomics approach. Amyloid A (AA) and lymphatic vessel endothelial hyaluronan receptor-1 (LYVE-1) was identified with different levels in exosome between CR group and non-CR group. AA levels of both serum and exosome were higher in non-CR group than CR group (p value=0.001). Significant positive correlations were found between exosome AA level and CRP as well as between serum AA level and CRP ($p=0.614$, p value=0.001 and $p=0.624$, p value=0.001). Though LYVE-1 level of serum was not different between non-CR group and CR group, LYVE-1 level of exosome was lower in non-CR group than CR group (p value=0.01). We found positive correlations between serum/exosome of LYVE-1 and CRP in only non-CR group (serum $p=0.376$, p value=0.04; exosome $p=0.545$, p value=0.002).

Conclusions: We suggest that LYVE-1 in exosome can be used as an additional marker of disease activity in RA patients and this study provides the evidence about the role of exosome for RA as the carrier of useful marker.

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AB0237 PREVALENCE AND CLINICAL CHARACTERISTICS OF MALIGNANCY IN SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients with rheumatoid arthritis (RA) are at an increased risk of malignancies compared with the general population.

Objectives: The aim of this study was to evaluate the prevalence and risk factors

of malignancy in National Health Insurance Service Ilsan hospital patients with seropositive RA.

Methods: We found patients with seropositive RA who fulfilled the American College of Rheumatology criteria and American College of Rheumatology criteria/European League Against Rheumatism criteria, from May 2008 to September 2015. Occurrence of malignancy was originally collected by electronic medical record reports and diagnostic code. We consecutively enrolled patients with newly diagnosed malignancy. Control group was selected as five times the number of patients randomized.

Results: Total 12 malignancies in 647 patients were newly identified during the retrospective observation period of 2051 person-years. Malignancy types were 3 lung cancers, 2 colon cancers, gastric cancer, breast cancer, thyroid cancer, cervix cancer, cholangiocarcinoma, lymphoma and parotid gland cancer. In multivariate logistic regression, the variables with independent predictive value were older age (age: odds ratio =1.11, 95% CI =1.01–1.22, p-value =0.02), rheumatoid factor (RF) negativity (RF positivity: odds ratio =0.06, 95% CI =0.01–1.27, p-value 0.07) In cox regression, the variables with independent predictive value were older age (age: hazard ratio =1.12, 95% CI =1.01–1.24, p-value =0.02), negative RF (RF positivity: hazard ratio =0.12, 95% CI =0.02–0.78, p-value 0.02), lower anti-cyclic citrullinated peptide (CCP) antibody titer (anti-CCP antibody titer: hazard ratio =0.98, 95% CI =0.96–0.99, p-value 0.03) and positive antinuclear-antibody (ANA) (ANA positivity: hazard ratio =14.97, 95% CI =0.87–255.05, p-value 0.06).

Table 1. Associations between variables and malignancy event in subjects: longitudinal data

Variables	Univariable			Multivariable		
	Hazard ratio	95% CI	p-value	Hazard ratio	95% CI	p-value
Etiology						
Age	1.14	1.05–1.24	<0.01	1.12	1.01–1.24	0.02
Gender	3.71	0.47–29.08	0.21			
Laboratory results						
RF positivity	0.33	0.09–1.13	0.07	0.12	0.02–0.78	0.02
Anti-CCP Ab titer	0.99	0.98–1.00	0.10	0.98	0.96–0.99	0.03
ANA positivity	5.56	0.69–44.64	0.10	14.97	0.87–255.05	0.06

Conclusions: Age, RF positivity, anti-CCP antibody titer, ANA positivity may be associated with malignancy risk in seropositive rheumatoid arthritis. So, continued vigilance and regular cancer screening are recommended for case of older age, RF negativity, lower anti-CCP antibody titer and ANA positivity.

Disclosure of Interest: None declared

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AB0238 THE INFLUENCE OF FATIGUE IN THE DEFINITION OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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Background: Achieving disease remission or low disease activity is the therapeutic goal in rheumatoid arthritis (RA) treatment. Disease activity is defined through established criteria most of them requiring the evaluation of patient global assessment (PGA). PGA is considered a limiting factor for achieving remission definition, as it can be influenced by many factors not RA-related, namely fatigue which is commonly reported in RA and has been correlated with increased levels of interleukin-6 (IL-6).

Objectives: To evaluate the relation between PGA and fatigue, and whether fatigue influences disease remission definition in RA patients treated with tocilizumab (TCZ), an anti-IL-6 receptor monoclonal antibody.

Methods: We prospectively recruited 18 consecutive patients with RA (ACR/EULAR 2010 criteria), on TCZ treatment (≥ 3 months), from a single referral centre. Disease activity was evaluated by disease activity score for 28-joints (DAS28), and the ACR/EULAR Boolean-based criteria for remission were calculated. Visual Analog Scale for Fatigue (VASF) and Multidimensional Assessment of Fatigue scale (MAF) were used to measure fatigue.

Results: 89% of the patients were female and mean age was 55.5 $\pm$ 13.8 years (yrs). Mean disease duration was 8.8 $\pm$ 6.8yrs and mean duration of TCZ treatment was 2.3 $\pm$ 1.3yrs (50% 1st line). Mean PGA score was 3.3 $\pm$ 2.0 (0-best health) and mean DAS28 C-reactive protein (CRP) was 2.27. According to DAS28-CRP 44% of the patients were in remission, 22% had low disease activity and 33% had moderate activity. 3 patients (17%) fulfilled the ACR/EULAR Boolean criteria for remission. Considering all the composites of the Boolean criteria, PGA was the only reason for not achieving remission in 10 patients (56%). The mean fatigue scores were: VASF 6.6 $\pm$ 2.3 (0-best health), Global Fatigue Index (GFI), calculated through MAF scale, 24.3 $\pm$ 14.9 (1-best health). Amongst the 18 patients, PGA correlated with higher fatigue scores on VASF ($r=0.50$, $p=0.00951$) and on GFI ($r=0.49$, $p=0.037$). In the group of patients not fulfilling Boolean remission, a similar correlation between PGA and higher fatigue scores was found (VASF: $r=0.54$, $p=0.036$; GFI: $r=0.79$, $p=0.00041$). In the sub-group of patients in which PGA was the only factor for not achieving Boolean remission, there was a significant correlation between PGA and fatigue scores (GFI: $r=0.79$, $p=0.009$), that was not present in the other patients (GFI: $r=0.24$; $p=0.49$).

Conclusions: We found a positive correlation between higher PGA and fatigue

scores in RA patients treated with TCZ. PGA was the major limiting factor for not achieving ACR/EULAR Boolean remission criteria, and in this sub-group of patients the same positive correlation between higher PGA and fatigue scores was found, not present in the rest of the cohort. These results enhance the influence of fatigue in patients' perspectives of disease and reinforce the limitations of using PGA to define RA activity and remission. Furthermore, considering the influence of TCZ in fatigue mechanisms, by blocking IL-6 receptor, we still found high fatigue scores in this cohort, which can enhance the complex physiopathology of fatigue in chronic inflammatory diseases, and the role of several other cytokines (IL-1, TNF- α). This effect and comparison with RA patients treated with anti-TNF- α can be explored further in larger prospective studies.

Disclosure of Interest: None declared

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AB0239 DKK1 IS NOT ASSOCIATED WITH INFLAMMATORY ACTIVITY INDEXES IN RHEUMATOID ARTHRITIS, BUT WITH FUNCTIONAL DISABILITY RELATED TO THE LONG EVOLUTION OF THE DISEASE

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Background: Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease characterized by joint destruction, deformity, lower functional status and decrease in life expectancy. Wnt signaling pathway recently it has been implicated in bone homeostasis. Studies suggest that overexpression of inhibitors of the way, like the Dickkopf 1 protein (DKK1) has been implicated in bone destruction

Objectives: To compare circulating levels of DKK1 in patients with RA to their disease activity and functional status

Methods: 379 consecutive patients with early and established RA were evaluated at the Hospital Militar Central in Bogotá-Colombia, between March 2015 and November 2016. A complete medical history related to RA was obtained. Disease activity was evaluated by DAS28-CRP, CDAI, SDAI and RAPID3. functional status was measurement using MDHAQ and the Steinbrocker functional classification. DKK1 levels measured by ELISA using an Abcam[®] kit

Results: The mean age was 60,7 $\pm$ 13,1 years, disease duration 13,1 $\pm$ 10,9 years, 80,4% were female. Higher levels of DKK1 were not associated with higher disease activity by CDAI (p=0,70), SDAI (p=0,84), DAS28 with CRP (p=0,80) or RAPID3 (p=0,70). Interestingly Higher levels of DKK1 were significantly associated to greater disability and lower functional status according to the Steinbrocker functional grading (p=0.013) and with severe disability by MDHAQ (p=0.004), Table 1.

Other variables associated with joint destruction were osteoporosis, elevated rheumatoid factor, smoking, and hospitalization

Steinbrocker functional grading	n (%)	DKK1 (pg/mL) M $\pm$ ds	P
Class I-II	286 (75,2)	4930,9 $\pm$ 8061,5	0,013
Class III-IV	93 (24,5)	7930,6 $\pm$ 10811,3	
MDHAQ			
Without or low disability	334 (88,0)	3192,0 $\pm$ 2729,4	0,004
Moderate or severe disability	45 (12,0)	4445,67 $\pm$ 2821,0	

Conclusions: Higher levels of DKK1 were found in patients with lower functional status. This association was not found in patients with greater disease activity according to CDAI, SDAI, DAS28 and RAPID3. This could be explaining by greater structural damage though more studies would be needed to explore this possibility

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AB0240 ASSOCIATION BETWEEN LEPTIN CONCENTRATIONS AND CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It has been observed that leptin plays a role in the development of cardiovascular risk, independently associated with the development of atherosclerosis, as well as with traditional risk factors such as obesity and arterial hypertension, on the other hand, its participation in carbohydrate and lipid metabolism and in coagulation, makes leptin a promoter of the complications of obesity and therefore increase cardiovascular risk.

Objectives: Identify whether there is a relationship between serum leptin concentrations and cardiovascular risk assessed using the Framingham scale.

Methods: We studied patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria; the leptin determination was through an enzyme immunoassay (ELISA) with the TECO[®] Test Kit. Cardiovascular risk was calculated using the modified Framingham score, as reported by EULAR, the result obtained was multiplied by 1.5. Were considered as risk values of <1% as low; 1–5% moderate and >5% high. Statistical analysis was performed using the SPSS 22.0 package. A p $\leq$ 0.05 was considered a significant result. Categorical variables were compared with Chi square test. Continuous variables were compared with either the Student's T test or the Mann-Whitney non-parametric test, according the case.

Results: We studied 77 patients. The traditional CVR factors that presented the highest prevalence were age, hypoalbuminemia and obesity; With regard to the prevalence of non-traditional factors, hyperleptinemia, glucocorticoid use and positive RF were predominant. More than ¾ parts of the study population consumed methotrexate and hydroxychloroquine, which have been considered as CVR protective factors. Serum leptin concentrations and CVR factors were compared and found that there was a significant difference between higher leptin values and disease activity (p=0.047), obesity (p=0.038), positive rheumatoid factor (p=0.009), Tobacco (0.009) and metabolic syndrome (p=0.001). Likewise, a significant relationship was found between lower leptin concentrations and hydroxychloroquine consumption (p=0.023). Framingham CVR was calculated and the result obtained was multiplied by 1.5. The 35.2% of the population studied had a low Framingham RCV, 38.9% moderate and 25.9% presented a high risk. We compared the level of CVR and serum leptin concentrations, finding that the highest CVR were the leptin values.

Conclusions: There is a positive association between CVR and serum leptin concentrations. It is also significantly associated with traditional and non-traditional risk factors

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AB0241 RELATIONSHIP BETWEEN LEPTIN AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Increased concentrations of leptin have been observed during infectious processes and inflammation, in such a way that it plays a role in the inflammatory and the immune response

Objectives: Determine the association between serum leptin and disease activity measured through DAS-28 PCR.

Methods: Patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria were studied. Leptin was determined by enzyme immunoassay (ELISA) with the TECO[®] Test Kit, the values higher than 17ng/mL were considered as hyperleptinemia. Disease activity was assessed by the DAS-28 PCR, classifying as remission <2.3, low activity $\geq$ 2.3 to <3.8, moderate activity as $\geq$ 3.8 to <4.9 and high activity $\geq$ 4.9. Statistical analysis was performed using the SPSS 22.0 package. A p $\leq$ 0.05 was considered a significant result. A multivariate logistic regression model was used to determine the association between significant variables and leptin concentrations.

Results: 77 patients were studied, 93.5% were female. The activity of the disease was determined, finding that 40,3% of patients were in remission, 41,6% had low activity, 11,7% had moderate activity and 6,5% had high activity. The 46,8% had obesity, 32,5% were overweight, 18,2% had normal weight and 2,5% were underweight. The 37,7% of the patients studied had metabolic syndrome, being the main factor the presence of an altered abdominal perimeter. The 63,6% had positive rheumatoid factor. The 71,4% had leptin levels $\geq$ 17 ng/mL. A multivariate logistic regression was performed with leptin as dependent variable. The results show an independent association between higher concentrations of leptin and disease activity (OR 1,9; 95% CI 1,3–3,8; p=0,045), obesity (OR 3,63; 95% CI 1,1–11,9; p=0,033), the presence of metabolic syndrome (OR 2,74; 95% CI 1,7–10,4; p=0,038), and positive rheumatoid factor (OR 3,5; 95% IC 1,2–11,3; p=0,033). It was also found that at higher disease activity, there were higher concentrations of serum leptin. Patients with severe activity had higher leptin media than patients in remission

Conclusions: There is a positive relationship between the activity of the disease and the serum leptin concentration, likewise this hormone is related to other inflammatory processes such as metabolic syndrome and rheumatoid factor.

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