the triple positivity was significantly associated with male gender (OR=3.5; $p=0.02$), the presence of rheumatoid nodules (OR=5.3; $p=0.015$) and pulmonary involvement (OR=2.6; $p=0.007$). Anti-IF116 auto-Abs were associated to male gender independently of the presence of the other two auto-Abs.

Conclusions: Our study demonstrated that anti-CEP-1 auto-Abs may participate to the development of RA-associated pulmonary manifestation together with anti-CCP and that the assessment of multiple auto-Abs in daily practice may help clinician to stratify RA patients at identify those at higher risk to develop extra-articular manifestations.

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AB0192 SERUM MEASURES OF TYPE I COLLAGEN DEGRADATION ARE SURROGATE MARKERS OF JOINT DESTRUCTION AND PROGRESSION; FIRST STEPS TOWARDS A PROGNOSTIC SCORE

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Background: Monitoring of patients with rheumatoid arthritis (RA) requires assessment of biomarkers reflecting disease activity and its progression. There is a need for non-invasive markers for frequent monitoring of disease severity and progression as well as response to therapy.

Objectives: Serological markers together with clinical parameters was tested in a multi-marker model to assess its ability to objectively predict progression of RA.

Methods: Current post-hoc analysis included RA patients from the biomarker substudy of the phase III clinical study LITHE investigating the safety and efficacy of tocilizumab^{1–4}. Patients had moderate/severe, active RA. In addition, only patients of the placebo arm and with total sharp score (SHP) recorded at baseline (BL), week 24 (W24) and W52 were included. Progressors were defined as the delta from BL to W24 and W24 to W52. Biochemical markers reflecting tissue turnover (table) were assessed at BL and W16. Associations with structural progression (deltaSHP) were investigated by spearman's r , least squared multivariate and logistic regression. Covariates were CRP, sex, BMI, age, disease duration, DAS-ESR, no. prior DMARDs/aTNF use and SHP/BL. The data were divided into a training and confirmation set; 1) association between markers/W16 and deltaSHP/W52 ($n=31$ prog./42 non-prog.), 2) association between markers/BL and deltaSHP/W24 ($n=33/48$).

Results: The training set. Eight markers were correlated ($R>0.2$) with deltaSHP/W52. Of these C1M, PINP, ICTP and MMP3 were predictive for progression (deltaSHP/W52 >0) with ORs of 3.2 [1.3–8.0], 4.0 [1.4–12], 8.5 [2.4–31], and 2.5 [1.3–5.1]; all $p<0.01$, respectively. A logistic model for prediction of disease progression incorporating C1M, ICTP, disease duration and BMI demonstrated an AUC of 0.77 [0.66–0.86], $p<0.01$. The model correctly identified 72% of the progressors. The confirmation set: The results were confirmed in the second dataset with an AUC of 0.75 [0.64–0.81], $p<0.01$. The model correctly identified 65% of the progressors.

Biochemical marker	Description	Biomarker of	Spearman correlation between DeltaSHP/W52 and baseline biochemical marker $R>0.2$
C1M	MMP-mediated type I collagen degradation	Connective tissue destruction	0.377
C2M	MMP-mediated type II collagen degradation	Cartilage degradation	0.088
C3M	MMP-mediated type III collagen degradation	Connective tissue destruction	0.277
C4M	MMP-mediated type IV collagen degradation	Basement membrane destruction	0.157
C6M	MMP-mediated type VI collagen degradation	Connective tissue destruction	0.175
CRP	C-reactive protein	Acute reactant	0.354
CRPM	C-reactive degradation	Tissue inflammation	0.290
CTX-I/OC	Ratio between cathepsin K-mediated type I collagen degradation and osteocalcin	Bone turnover balance (Bone resorption/formation)	0.063
Gender	-	-	0.090
HAQ	Health assessment questionnaire	-	-0.032
ICTP	MMP-mediated type I collagen degradation	Connective tissue destruction /bone degradation	0.334
MMP3	Matrix metalloproteinase 3	Joint inflammation	0.226
Pain (VAS)	-	-	0.073
Patient global score (VAS)	-	-	0.110
Physician global score (VAS)	-	-	0.051
P1IAMP	Propeptide of type II collagen	Cartilage formation	-0.077
P1INP	Propeptide of type I collagen	Connective tissue and bone formation	0.217
VCAM	MMP-mediated Versican degradation	Epithelial turnover	-0.054
VICM	MMP-mediated degradation of citrullinated vimentin	Macrophage activity	0.232

Conclusions: We demonstrated that a multi-marker model was able to point-out, which patients were more likely to be structural progressors. Such first steps to build a progression model, rather than a score reflecting disease activity only, may

enrich clinical studies with structurally active disease. Importantly, the markers with strongest influence were those associated with MMP-driven bone (ICTP) and connective tissue (C1M) remodelling.

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AB0193 MEDICAL ADHERENCE IN PATIENTS WITH TIGHTLY CONTROLLED RHEUMATOID ARTHRITIS

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Background: Medication adherence is very important in the treatment of rheumatoid arthritis (RA). However, medication adherence of the patients with RA was not optimal in many of the studies (1–2).

Objectives: The purpose of this study was to investigate the medication adherence in tightly controlled RA patients and reasons of non-adherence.

Methods: A total of 82 RA patients (65 women and 17 men) who followed regularly in our outpatient clinic were included. Socio-demographic features and medical history were collected. The eight-item Morisky scale (MMAS-8) was used to evaluate adherence to medication. Disease activity score (DAS28), health assessment questionnaire (HAQ), mini mental state examination (MMSE) test and Beck depression inventory (BDI) were evaluated.

Results: According to Morisky scale, 34.1%, 15.9% and 50% of our patients were categorized as low, moderate and high adherence, respectively. The most prevalent noticed barriers for adherence were forgetting medication, inadequate information about using instructions, side effects of medications (Table 1). Socio-demographic features, duration of disease, type and number of drugs used per day, the route of drug administration, co-morbid diseases, body mass index, smoking and alcohol consumption were not found to be associated with medication adherence, whereas low MMSE and high BDI score were associated with low medication adherence ($p=0.009$ and $p=0.011$, respectively). We found that the disease activity was significantly higher in non-adherent cases ($p=0.00$) (Table 2).

Table 1. Barriers to medication adherence

Barriers	%
Forgetfulness	41.4%
Inadequate information	22%
Side effects of medications	17%
Fears about drug benefit	12.2%
Anxiety about side effects	4.8%
Cost of medications	2.6%

Table 2. Medication adherence and disease activity

DAS 28	Low adherence (Morisky <6)	Moderate adherence (Morisky 6–7)	High adherence (Morisky = 8)	Total
Remission (<2.6)	2 (5.6%)	5 (13.9%)	29 (80.6%)	36
Low disease activity (2.6–<3.2)	7 (36.8%)	3 (15.8%)	9 (47.4%)	19
Moderate disease activity (3.2–<5.1)	17 (68.0%)	5 (20%)	3 (12%)	25
High disease activity (≥ 5.1)	2 (100%)	0 (0%)	0 (0%)	2
Total	28	13	41	82

DAS: Disease activity score.

Conclusions: Our RA patients who were closely followed had 50% high medication adherence. This rate is quite high compared to other studies using MMAS-8. It should be kept in mind that tight control and adequate communication increase medication adherence but different parameters may also be effective. Assessing cognitive disorders and emotional problems of the patient will be beneficial for improving adherence and controlling disease activity.

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AB0194 JOURNEY OF A PATIENT WITH RHEUMATOID ARTHRITIS: DELAY IN DIAGNOSIS AND TREATMENT

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Background: It has been shown that there is a window of opportunity for treatment in Rheumatoid Arthritis (RA). Several Argentinean studies showed an average of 8 months to arrive to a rheumatology visit and 12 months to receive DMARDs. There aren't recent studies.

Objectives: To establish delay time from onset of rheumatoid arthritis (RA) symptoms to the first rheumatology visit, to diagnosis of the disease and to the beginning of treatment with DMARDs; and to assess impact of such delay on structural damage, in a cohort of RA patients.

Methods: A retrospective study was performed including all patients with RA (fulfilling ACR/EULAR 2010 criteria) seen at a Prepaid Medical Health Plan between 2002–2015. Diagnosis delay and its impact on functional capacity measured by HAQ-A and structural damage by Sharp van der Heide score (SvdH) was estimated. Demographic and clinical data, and dates of diagnosis, onset of symptoms and HAQ-A were extracted from electronic medical records. SvdH score was performed by an experienced rheumatologist.

Results: 246 patients (mean age at diagnosis 67.25±14 years, 199 (81%) female) were included. Clinical presentation was polyarticular in 49% of the cases, oligoarticular in 47% and monoarticular in 3%. 79% had high titers of anti-cyclic citrullinated peptide antibodies, 12% low titers, and 9% were negative. Rheumatoid factor was positive in 82.5%. Mean time of follow up was 7 years (SD: 3.8). At the end of the follow-up, median HAQ-A (n=145) was 0.125 (IQR: 0–0.87). Hands and feet lastxray available were analyzed in 171 patients. Median SvdH score was 15 (IQR: 6–33). 242 patients (98.4%) received DMARDs as initial treatment: methotrexate monotherapy (76%) was the most frequent one. 41 patients (17%) received biological agents at some point of their disease. Table 1 shows different delay times in accessing rheumatology consultation, diagnosis and beginning of treatment.

At the end of follow up, 21 patients (12.28%) had noradiological damage (SvdH score =0). In the ROC curve (AUC 0.57, 95% CI: 0.45 - 0.69), 5.6 months of diagnosis delay was the best cut off value to discriminate the presence of erosions (SvdH erosions score >0), with a sensitivity and specificity of 54.17% and 61.90%, respectively. Delay in diagnosis greater than 12 months (n=70) was associated with significantly radiological damage: SvdH mean 30.91 (IC 95% 21.99–39.79) vs 21.32 (IC 95% 16.93–25.72); p=0.0325.

Table 1. different delay times

Variable	Mean (SD)	Median (IQR)
Time from first symptoms to first rheumatology visit (months)	9.21 (20.50)	3 (1–7)
Time from first symptoms to diagnosis (months)	14.2 (24)	4.8 (2.4–13)
Time from first symptoms to DMARDs indication (months)	16.9 (25.4)	7 (3–17)
Time from first symptoms to biological indication (years)	6.2 (4.8)	5.7 (2.4–7.2)

Conclusions: In a Prepaid Medical Health Plan with ease of referral, there is still a significant delay in diagnosis and treatment of RA patients. Delay in diagnosis greater than 12 months was associated with more radiological damage.

Disclosure of Interest: None declared

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AB0195 IS THERE AN ASSOCIATION BETWEEN PERIODONTITIS AND LEVELS OF ANTI-CITRULLINATED PEPTIDES ANTIBODIES IN RHEUMATOID ARTHRITIS?

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Background: Positivity of anti-citrullinated peptides antibodies (ACPA) indicates severity in Rheumatoid Arthritis (RA). There is evidence for chronic periodontitis (PD) in RA autoimmune response by periodontopathogenic bacteria such as *P.gingivalis*, through citrullination of L-arginine.

Objectives: 1. To determine whether there is an association between PD and its severity with ACPA(+). 2. To assess relationship between PD and ACPA titres. 3. To identify association between certain periodontal parameters and ACPA titres and their possible cutoff points.

Methods: Observational, cross-sectional study RA patients ≥18 with ≥4 teeth, no tooth cleaning, antibiotic intake 6 months before. Socio-demographic and anthropometric variables, annual dental prophylaxis and comorbidities. Serum

ACPA detection: Ab IgG against CCP2 (ELISA) Eurodiagnostica: positive ≥25; ACPA titres stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), bleeding on probing (BoP), probing pocket depth, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti): T level 0 (absence), T1 (mild), T2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi-squared tests by Stata program 13.1.

Results: 187 RA patients included (table 1), ACPA determined in 168 patients: 67.86% (+) with similar titres distribution: low 18%, moderate 26%, high 23%. PD: 182 patients (97.3%): T1 52.4%, T2 44.9%. Although prevalence of severe PD/ACPA(+) was higher compared to PD/ACPA(-) (69.2% vs 30.7%), there was no association between PD and ACPA positivity/titres. Regarding the association with periodontal parameters, there was tendency of association between ACPA(+) and number of periodontal pockets ≥5mm (NPP), OR 1.02 (95% CI 0.9–1.04) adjusted. There was a gradient effect, where NPP increased as ACPA titres increased, which was significant for high ACPA titres (p≤0.05, OR 1.03 95% CI 1.0–1.05). When ACPA(+) was related to %PI and BoP, a strong association was observed for PI, OR 10.32 (p<0.026), and only a tendency for BoP (p<0.062). With cutoff points of 8% PI and 65% BoP, a risk for ACPA(+) was detected with an OR 2.19 and OR 2.45, respectively.

Table 1

	RA (N)	RA (%)
Female sex	147	78.6
Mean age (SD)	54.4 (10.8)	
Follow up time, median (SD), years	8.88 (7.32)	
Early RA	35	18.7
Rheumatoid factor, seropositive	138	74.2
Disease Activity Ranges		
Remission	39	20.9
Low	45	24.1
Moderate	85	45.4
High	18	9.6
Medication RA		
Without Treatment	10	5.3
DMARDs	99	52.9
≥2 DMARDs	22	11.8
Biologic Drugs	56	29.9

Conclusions: 1. Despite higher prevalence of severe PD in ACPA(+) patients, we found no association between the presence of PD and ACPA positivity nor with serum titres. 2. On analysis of ACPA titres in relation to the severity of the periodontal parameters, there was a “gradient” risk, where NPP increased as ACPA titres increased, which was significant for high ACPA titres. 3. Risk cutoff points for ACPA(+) were 8% for PI and 65% for BoP.

Disclosure of Interest: None declared

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AB0196 VASCULAR ENDOTHELIAL GROWTH FACTOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The level of vascular endothelial growth factor (VEGF) may reflect the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatoid arthritis (RA).

Objectives: to study features of VEGF level changes in the blood of RA patients, depending on the duration of the disease, the degree of activity, the level of antibodies to cyclic citrullinated peptide (anti-CCP)

Methods: 194 patients were examined with a diagnosis of RA (verified according to criteria ACR/EULAR 2010), without concomitant pathology. Among the examined patients with RA women predominated 168 (86.6%), and there were 26 men (13.4%). The age of patients was 22 to 65 years (mean age 47.7±10.22 years), mean duration of the disease was 3.82±3.43 years. Assessment of RA activity was done by DAS 28 index, using blood CRP in the formula. 152 patients were positive for the presence of anti-CCP (≥20 U/ml) (78%) and 42 (22%) - negative. Serum CRP concentrations (Vector-Best, Russia), anti-CCP (Orgentec, Germany), VEGF (BCM Diagnostic, Canada) were determined by ELISA. Statistical processing of the data was performed using non-parametric methods, univariate (ANOVA) variance analysis on a personal computer using a licensed software packages (“Microsoft-Excel” and “Statistica-Stat-Soft”, USA)

Results: Analysis of VEGF level changes in the blood depending on the duration of RA revealed that the measure was high in patients with small diseases duration 0–23 months (472.96 (341.1; 582.1) pg/ml) compared with the group 5 years (324.1 (199.2; 556.2) pg/ml) (p<0.04). Analysis of VEGF level in blood depending on the degree of RA activity showed that the VEGF concentration in blood increased with increasing degree of RA activity and it was the greatest - 564.4 (340.1; 758.4) pg/ml in the group with a high degree (DAS28 >5.2) compared to the minimum (DAS28 ≤3.2) - 230.5 (178.1; 385.3) pg/ml, and moderate (DAS28 3.3–5.2) - 356.4 (278.9; 553.1) pg/ml, (p<0.001; p=0.005, respectively). Using ANOVA variance analysis, it was found that the degree of RA activity influenced the VEGF levels in the blood (KW =17.37; p<0.001).

Analysis of the VEGF levels in the blood depending on the level of anti-CCP