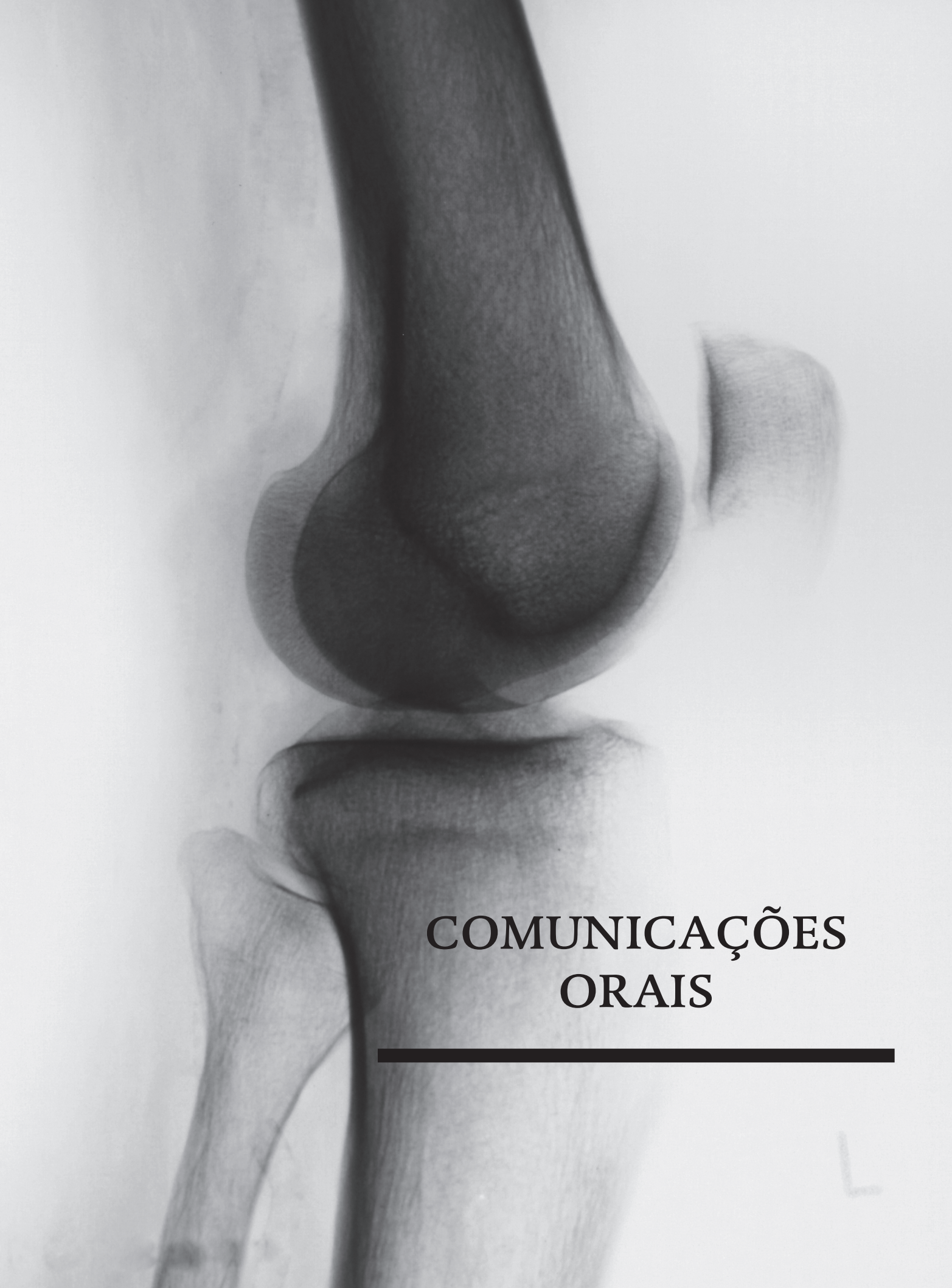

COMUNICAÇÕES ORAIS

Comunicações orais

ACTA REUMATOL PORT. 2019:44:18-40 (SUP)

C0009 - SAFETY AND EFFECTIVENESS OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Elderly population with rheumatoid arthritis (RA) is increasing. However, these patients are frequently excluded from clinical trials and data on effectiveness and safety of biologic Disease-Modifying Antirheumatic Drug (bDMARD) is scarce.

Objectives: To assess the persistence of 1st bDMARD among elderly (≥65 years old) RA patients and to compare effectiveness and safety of bDMARD between adults (<65 years-old) and elderly.

Methods: Prospective multicenter cohort-study of RA patients starting a 1st bDMARD registered at Reuma.pt. Demographic and disease characteristics, comorbidities, medications, disease activity at baseline and follow up (3, 6 and 12 months) and adverse events (AE) were compared between elderly and adult patients. Treatment persistence was estimated using Kaplan-Meier analysis. Effectiveness was measured as good plus moderate EULAR crude response rates, LUNDEX corrected, and adjusted for baseline characteristics.

Results: In total, 2400 patients were included, of which 486 aged ≥65 years (table). Crude median persistence in bDMARD was 19.7 months (95%CI 14-25) in adults and 14.5 (95%CI 3-26) in elderly patients (log rank test, p=0.46, figure). EULAR response (crude and LUNDEX corrected) was similar in the two groups at 3 and 6 months (table). After adjustment for baseline cha-

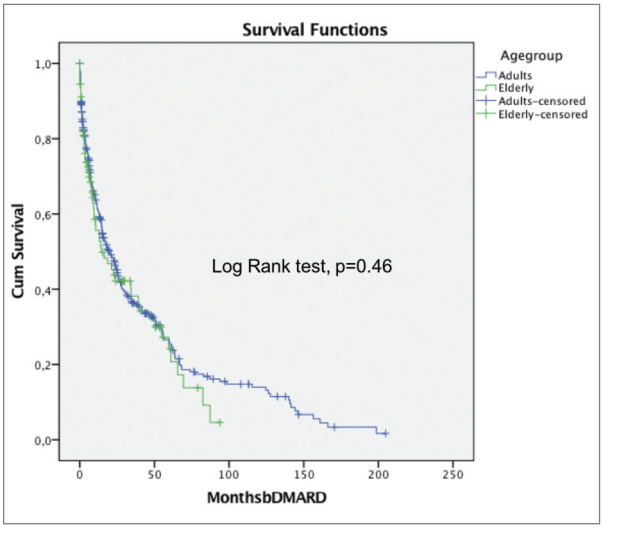

FIGURE 1. Persistence in 1st bDMARD (months) for elderly and adults

TABLE. BASELINE CHARACTERISTICS AND EFICACY AND SAFETY

Baseline characteristics	Total	Adults	Eldery	P value
Female - N (%) N=2400	2038 (85)	1630 (85.2)	408 (84)	-
Disease duration till 1st bDMARD in years - N (%) N=2074	10.3 (3.7-14.5)	7.4 (4-14)	9.6 (4-18)	**<0.01**
RF and/or anti-CCP positive - N (%) N=2400	1693 (70.5)	1350 (70.5)	343 (71)	-
Erosive disease - N (%) N= 1639	1213 (74)	947 (73)	266 (79)	-
Extraarticular manifestations - N (%) N=2400	482 (20)	383 (20)	99 (20.4)	-
Hypertension - N (%) N=1769	530 (30)	381 (27)	149 (43)	**<0.01**
Dyslipidemia - N (%) N= 1769	141 (8)	107 (7,5)	34 (10)	-
BMI - median ± IQR N=1210	27 (24-30)	26 (24-30)	27 (23-30)	-
Diabetes - N (%) N= 1769	148 (8.4)	98 (7)	50 (14.3)	**<0.01**
Cardiovascular disease – N (%) N=1769	134 (8)	107 (7.5)	24 (10)	**<0.01**
DAS 28-ESR - mean ± SD N=1295	5.6 ± 1,3	5.5 ± 1.3	5.7 ± 1.3	**0.02**
CDAI - mean ± SD N=1069	29 ± 13	28 ± 13	31 ± 15	**0.03**
SDAI - mean ± SD N=1023	31 ± 14	30 ± 13	33 ± 16	**0.01**
HAQ-DI - mean ± SD N=1090	1.5± 0.6	1.4 ± 0.6	1 ± 0.7	**<0.01**
Efficacy and safety	Total	Adults	Eldery	P value
EULAR response at 3 month (Lundex corrected) %	77.8 (51)	78.4 (51)	75 (51)	-
EULAR response at 6 month (Lundex corrected) %	80.6 (50)	81.7 (52)	76 (45.2)	-
EULAR response at 12 month (Lundex corrected) %	81.5 (35.6)	83.8 (37)	71.5 (29.3)	**0.01**
N patients with AE during 1st bDMARD	409	319	90	-
AE infection –N (%) N=407	237 (58,2)	176 (55,3)	61 (68,5)	**0.03**
AE opportunist infection – N (%) N=408	30 (7,4)	21 (6,6)	9 (10)	-
AE allergic reaction – N (%) N=407	71 (17,4)	59 (18,6)	12 (13,5)	-
Severe AEs– N (%) N=391	82 (21)	64 (21)	18 (20,9)	-
Hospitalization– N(%) N=407	56 (13,8)	42 (13,2)	14 (15,7)	-
bDMARD suspention due to AE – N (%) N=407	171 (42)	130 (40,9)	41 (46,1)	-
bDMARD reintrodution after AE– N (%) N=211	61 (28,8)	48 (30)	13 (25,5)	-

N: number; IQR: interquartile range; SD: standard deviation; RF: Rheumatoid factor; CCP: Cyclic Citrullinated Peptide; BMI: Body Mass Index DAS: disease activity score, CDAI -clinical disease activity Index, SDAI – simple disease activity index, HAQ-DI health assessment questionnaire-disability index, AE: adverse event. When p value>0,05 no value is presented.

racteristics, response rate was inferior in elderly at 12 months (p=0.01). There were 697 AE reported. Except for infections, more common in elderly patients (p=0.03), the rates of severe AE, opportunistic infection, allergic reactions, cancer or hospitalizations were similar in the two groups, as well as the time to 1st AE occurrence (table).

Conclusion: Our findings showed that persistence of 1st bDMARD was similar in adults and elderly RA patients. Though elderly had more severe disease and comorbidities at baseline, bDMARD treatment was equally effective and safe in the short term. However, it is necessary to consider the greater risk of infection in elderly when prescribing a biologic.

C0028 – RITUXIMAB IN CONNECTIVE TISSUE DISEASE – ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a major cause of morbi-mortality in patients (pts) with connective tissue diseases (CTD). Small studies have recently demonstrated a promising role for rituximab (RTX) in the treatment of CTD-ILD.

Methods: We conducted a retrospective multicenter study including CTD-ILD pts treated with RTX. ILD was based on high resolution CT (HRCT) and/or lung biopsy. Results of HRCT, pulmonary function tests (PFTs) and 6-minute walking test (6MWT) before and after RTX were collected and compared using Wilcoxon matched pair test.

Results: Forty-nine pts were included (79.6% female, mean age at first RTX administration 58.6±12.9 years (yrs)). Five pts were current smokers (median 37.8 pack-yrs) and 13 were previous smokers. Thirty (61.2%) pts had rheumatoid arthritis, 4 (8.2%) primary Sjögren's syndrome (SS), 4 (8.2%) systemic lupus erythematous (SLE), 3 (6.1%) systemic sclerosis (SSc), 2 (4.1%) overlap SSc/polymyositis (PM), 2 (4.1%) PM, 2 (4.1%) antisynthetase syndrome (ASS), 1 (2%) dermatomyositis (DM) and 1 (2%) overlap SLE/SS.

ILD was diagnosed after 4 yrs [IQR 1-9.5; minimum -1; maximum 22] of CTD diagnosis. Non-specific interstitial pneumonia (NSIP) was present in 17 (34.7%) pts, usual interstitial pneumonia (UIP) in 20 (40.1%), lymphocytic interstitial pneumonia in 2 (4.1%) and endogenous lipoid pneumonia in 1 (2%); 9pts had unclassifiable ILD pattern in HRCT.

RTX was administered 1g twice, 2 weeks apart, with a median of 2 cycles [IQR 1-4]. Four pts received concomitantly azathioprine (AZA) and 1 mycophenolate mofetil (MMF). Eleven pts were previously treated with cyclophosphamide and/or MMF and/or AZA in association with steroids. Median ILD duration at first RTX administration was 1 yr [IQR 0-4].

After 1 yr on RTX there was a stabilization in gas transfer (DLCO; +5.4%, p=0.12) and in forced vital capacity (FVC; +4.3%, p=0.03) in the whole group. When analysing this evolution according to ILD pattern, patients with NSIP had a mean increase of 8.5% (p=0.08) in DLCO and 4.5% (p=0.04) in FVC, while patients with UIP had a mean increase of 2.5% (p=0.77) in DLCO and 4.2% (p=0.16) in FVC.

At last follow-up (median 2yrs [IQR 1-3.9] after starting RTX), 34/38 pts (89.5%) had stabilized/improved

TABLE. DETAILED RESPONSES TO RITUXIMAB AT DIFFERENT POINTS IN TIME

Revaluation	6-24 months	25-48 months	49-72 months
DLCO (n)	**26**	**12**	**5**
≥ 15% from baseline	23 (88.5%)	9 (75%)	4 (80%)
FVC (n)	**31**	**12**	**5**
≥ 10% from baseline	24 (77.4%)	12 (100%)	4 (80%)
HRCT (n)	**18**	**11**	**8**
Improvement/stabilization from baseline	17 (94.4%)	9 (81.8%)	7 (87.5%)

Legend: DLCO – gas transfer; FVC – forced vital capacity; HRCT - high resolution computed tomography

dyspnea according to modified Medical Research Council scale. 6MWT was performed at baseline and during follow-up in 13 pts, with 3 of them (all NSIP) achieving minimal clinically important improvement in walking distance, according to criteria used for idiopathic pulmonary fibrosis. One pt with primary SS and NSIP performed 6MWT at 5 and 10 years after starting RTX with clinically important improvement in walking distance. Detailed responses to RTX are shown in table 1.

Thirteen (26.5%) pts stopped RTX, with infection being the main cause (4pts; none had hypogammaglobulinemia; 2 receiving concomitant leflunomide and 1 AZA). Two pts suspended RTX due to long-standing stable disease. In our cohort, 5 pts died, 2 related to respiratory infection.

Conclusion: Our results reinforce the promising role of RTX in a wide range of CTD-ILD patients and demonstrate an association with long-standing disease stability, particularly in patients with NSIP pattern, and in monotherapy. Regarding UIP pattern, although it is usually progressive, our data suggest that disease progression might be put on hold with this treatment. Infection was the main reason for RTX discontinuation and led to 2 deaths. Therefore, monitoring these patients closely and adopting prophylactic attitudes, particularly vaccines, is of extreme importance.

C0034 – ATHEROSCLEROSIS AND BONE LOSS IN HUMANS – RESULTS FROM DECEASED DONORS AND PATIENTS SUBMITTED TO CAROTID ENDARTERECTOMY

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Background and aims: Atherosclerosis and osteoporosis are among the most prevalent diseases and share common risk factors, as well as molecular and pathophysiological mechanisms, frequently occurring in the same individual. We hypothesized that there is an association between vessel and bone behavior and our aim was to understand if atherosclerotic lesions are related with disturbances in bone.

Methods: Gene expression of pro-inflammatory cytokines and bone remodeling markers were analyzed in arteries and bones from 45 deceased donors. In 139 patients with advanced atherosclerosis submitted to carotid endarterectomy we explored the associations between gene expression in atherosclerotic plaques and bone mineral density (BMD). Additionally, serum levels of pro-inflammatory cytokines and bone remodeling markers were measured and plaque morphology and immunochemistry evaluated.

Comparisons between groups and correlations were performed using parametric and non-parametric tests, as appropriate. When justified multivariable linear regression analyses with backward selection of covariates was performed.

Results: The donors' group was composed by 23 men (49.6±17.8 years old) and 22 women (61.1±12.9 years old). The aortas were evaluated macroscopically and in 6 of them (about 13%) calcifications were visible. Gene expression of bone remodeling and inflammatory proteins correlated positively in bone and aorta, independently of donors' age and gender. No association between serum and gene expression levels was found.

The carotid endarterectomy patients' group was composed by 95 (68.3%) men, 70.3±8.7 years old and 44 (31.7%) women, 71.5±9.6 years old. 64 patients had low BMD according to WHO definition and among these 3 had a t-score in the range of osteoporosis.

The expression of bone formation genes, specifically CBFA1 and OCL, was higher in atheroma plaques from endarterectomized patients with normal BMD comparing with those with low BMD, but we found no differences in the expression of inflammatory markers neither in the serum levels of pro-inflammatory and

bone remodeling markers. Immunohistochemical analysis revealed higher CD3 and CD68 scores in patients with normal vs low BMD.
Conclusions: We suggest that the relationship between changes observed in bones and vessels in the context of atherosclerotic disease and osteoporosis, may rely on the intrinsic connection between the tissues involved, independently of the progression of the diseases affecting them.

C0044 – IS THERE AN ASSOCIATION BETWEEN METABOLIC SYNDROME AND SEVERITY OF HAND OSTEOARTHRITIS? RESULTS FROM A NATIONWIDE STUDY

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Background: Hand osteoarthritis (HOA) is a highly prevalent rheumatic disease that predominates in females and causes pain, joint deformities and loss of functional capacity. Overweight and metabolic syndrome have been previously suggested to associate with the severity of HOA, but clarity on these associations is yet to be achieved.
Objectives: To test the possible association between body mass index (BMI) and other individual components of the metabolic syndrome and severity of HOA in female patients from a nationwide epidemiological study.
Methods: EpiReumaPt was a three-stage national health survey (2011-2013) where, in the first phase, 10,661 adult participants were randomly selected and interviewed using a structured face-to-face questionnaire that included screening for rheumatic diseases, such as HOA. In the second phase, positive screenings for ≥1 rheumatic complaint plus 20% of the negative screenings were invited for an assessment by rheumatologists. Finally, 3 rheumatologists revised all the information and defined the final diagnosis by consensus. Female patients with a final clinical diagnosis of primary HOA, where included in this analysis. Hand functional status as assed by the Cochin questionnaire was the outcome of interest. The explanatory variables of interest were: BMI evaluated as a categorical variable (Normal: 18-24.99; overweight: 25-29.99; obesity: ≥ 30), diabetes mellitus, hypertension and hypercholesterolemia (all self-reported and as binary variables: yes/no). The possible associations between BMI and the individual components of the metabolic syndrome and the Cochin score were tested in a multivariable linear regression model. Variables were kept in the final model only if significant ($p<0.05$). Potential confounders of the associations of interest and the outcome were defined a priori on clinical grounds and included age and symptoms of depression (HADS score).
Results: Out of the 3,877 participants evaluated by Rheumatologists, 473 women had primary HOA (National prevalence: 6.6%). In this population, 40% were

TABLE. ASSOCIATION BETWEEN INDIVIDUAL COMPONENTS OF THE METABOLIC SYNDROME AND HOA SEVERITY (COCHIN SCORE). MULTIVARIABLE LINEAR REGRESSION MODEL

	HOA severity (Cochin score) *β coefficient (95% CI)* *N= 408*
BMI (categorical)	*0.31 (0.05; 0.57)*
Diabetes (yes vs no)	*3.63 (0.13; 7.13)*
Age (years)	*0.13 (-0.01; 0.27)*
HADS score (continuous)	*0.90 (0.59; 1.22)*

overweight and 29% were obese. Ninety-three (20%) participants had diabetes, 261 (56%) had hypertension and 261 (56%) had hypercholesterolemia. In the multiple regression model, BMI and diabetes were found to significantly associate with HOA severity (Cochin score), whereas hypertension and hypercholesterolemia did not, thus not being selected in the final model (table).

Conclusion: In this study, higher BMI and the presence of diabetes mellitus were associated with a worse functional capacity in women with primary HOA. These data add to the body of evidence suggesting a possible role of metabolic factors in the severity of HOA.

C0047 - TNF INHIBITORS REDUCE SPINAL RADIOGRAPHIC PROGRESSION IN AXIAL SPONDYLOARTHRITIS (PARTIALLY) BY DECREASING DISEASE ACTIVITY

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Background: Recent observational data suggest that TNFi reduce spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) mostly by inhibiting disease activity1. Yet, resolution on the controversial effect of TNFi on structural progression is yet to be achieved.

Objectives: To investigate whether in r-axSpA TNFi have an indirect (through ASDAS) and/or direct effect on spinal radiographic progression.

Methods: Patients (pts) with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The indirect effect of TNFi on mSASSS progression was evaluated by testing the interaction between TNFi and ASDAS at the start of each 2-year interval (t). If significant (p<0.15) the association between ASDAS at t and mSASSS at the end of the interval (t+1) was assessed in 3 groups of exposure to TNFi: i. treatment in all visits; ii. treatment in some visits and iii. Never treated. The direct effect of TNFi on mSASSS progression was evaluated by testing the association between TNFi at t and mSASSS at t+1 (adjusting for ASDAS at t). Multivariable GEE models adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds (Figure). In a sensitivity analysis, the direct effect of TNFi was also tested after adjusting for a propensity score (PS), to take confounding by indication into account.

Results: In total, 314 pts were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. The interaction between ASDAS and TNFi at t was significant (p=0.10). A gradient was seen for the effect of ASDAS at t on mSASSS at t+1, which was more than 2 times higher in patients never treated with TNFi ((95% CI): 0.41 (0.13; 0.68) compared to those always treated [(95% CI): 0.16 (0.00; 0.31)] (Figure), showing that treatment with TNFi diminishes the effect

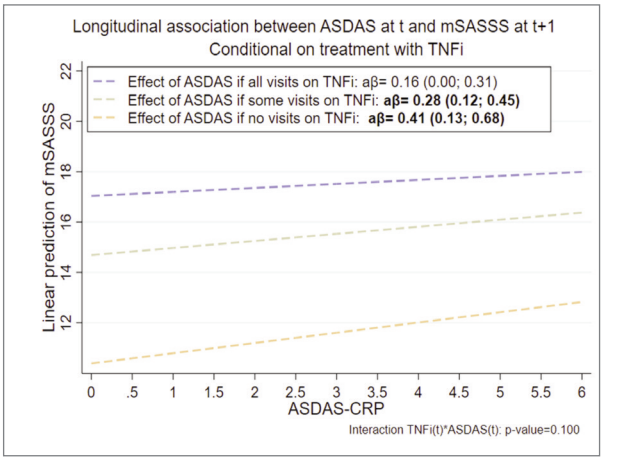

FIGURE 1. Longitudinal effect of ASDAS as the begging of each 2-year interval on mDASSS 2 years later conditional on TNFi treatment group (multivariable linear GEE model with autoregression adjusted for symptom duration, gender, HLA-B27 and number of previous TNFi)

of ASDAS on mSASSS. In addition to the indirect effect, TNFi also directly associated with less mSASSS progression: Pts receiving TNFi at t had on average 0.87 mSASSS-units less on t+1 compared to those not treated [(95% CI): -0.85 (-1.35; -0.35)] and this was noted independently of ASDAS. Importantly, this effect remained significant after PS-adjustment [(95% CI): -0.80 (-1.37; -0.22)].

Conclusion: This data is in in agreement with previous evidence showing that treatment with TNFi limits spinal radiographic progression in pts with r-axSpA by decreasing disease activity. Additionally, a direct effect of TNFi reducing mSASSS progression, and independent of ASDAS inflammation, is also seen suggesting that other mechanisms also contribute to the structural effect of TNFi.

C0049 - ASSOCIATION BETWEEN BONE MARROW EDEMA AND STRUCTURAL PROGRESSION IN THE SAME QUADRANT IN AXIAL SPONDYLOARTHRITIS – 5-YEAR DATA FROM THE DESIR COHORT

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Background: The overall presence of inflammation in the MRI-SIJ is associated with overall 5-year radiographic damage in patients with axSpA1. But we do not know if a bone marrow edema (BME) lesion leads to a structural lesion at the same place (i.e. in the same quadrant).

Objective: To investigate the association between BME and structural progression in the same quadrant of the SIJ, over time.

TABLE. PREVALENCE OF THE DIFFERENT IMAGING LESIONS* PER QUADRANT – AT BASELINE AND 5 YEARS MODEL

Baseline (n=197)					
Left side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	14.2	4.1	23.4	9.6	1.5
Q2	12.7	0	4.1	12.7	1.5
Q3	11.7	0	1.5	7.6	2.2
Q4	14.7	2.5	13.7	10.7	2.2
Right side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	13.7	3.1	19.8	3.6	0.5
Q2	13.7	0	6.1	14.2	0.5
Q3	10.7	0	1.5	8.1	1.5
Q4	16.2	1.0	11.7	7.1	1.5
At 5 years (n=136)					
Left side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	7.9	5.0	28.1	13.7	2.9
Q2	11.5	0	5.8	18.7	2.9
Q3	6.5	0	2.9	18.0	2.9
Q4	10.8	1.4	13.0	13.7	2.9
Right side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	11.8	3.6	25.9	8.6	2.2
Q2	14.0	0	7.2	20.9	2.2
Q3	7.4	0	5.8	15.1	5.0
Q4	11.0	1.4	12.2	10.1	5.0

* Agreement between ≥ 2 out of the 3 readers. Q= quadrant; BME: Bone Marrow Edema

Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with ≥2 consecutive MRI-SIJ (out of baseline, 2 and 5 years), were included. Each image was independently scored by 3 trained central readers blinded to chronological order. BME was considered present in a time point if detected in ≥1/6 slices in each of the 8 quadrants. The prevalence of BME (yes/no) and structural lesions (sclerosis, erosions, fatty lesions and ankylosis; all yes/no) defined, per quadrant, by the agreement of ≥2 out of 3 readers, was described at BL and at 5 years. The longitudinal association between BME and each of the structural lesions in the same quadrant was tested in time-lagged multilevel Generalized Estimating Equation (GEE) models with autoregression, taking individual reader data into account, and adjusting for clinical variables selected a priori on clinical grounds (age, gender, disease activity and treatment).

Results: In total, 197 patients were included (age 34 (SD 9) years, 48% male and 61% HLA-B27 positive). While BME and fatty lesions were evenly distributed across quadrants, erosions and sclerosis occurred preferably in the iliac side (i.e. Q1 and Q4) (Table 1). The prevalence of BME decreased over time (baseline range: 11%-16%; 5-year range: 7%-14%), while erosions (baseline range: 2%-23%; 5-year range: 3%-28%) and especially fatty lesions (baseline range: 4%-14%; 5-year range: 9%-21%) increased. Ankylosis and sclerosis were rare in this early axSpA cohort. In the multivariable models, BME was longitudinally associated with sclerosis (OR:1.7 (95% CI: 1.0;3.2)), erosions (2.0 (1.5;2.5)) and fatty lesions (1.7 (1.1;2.5)). The possible association with ankylosis could not be tested due to too low number of lesions.

Conclusion: We here demonstrate that in early axSpA-patients inflammation in one SIJ quadrant leads to structural damage in the same quadrant. This finding reinforces the pathophysiological implications of inflammation in axSpA.

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C0071 - A PHASE 3, RANDOMIZED CONTROLLED TRIAL COMPARING UPADACITINIB MONOTHERAPY TO MTX MONOTHERAPY IN MTX-NAIVE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background/Purpose: To compare the clinical efficacy, including inhibition of structural damage, and safety of upadacitinib (UPA), a JAK1-selective inhibitor, as monotherapy, vs methotrexate (MTX) monotherapy, in MTX-naïve patients (pts) with moderate to severely active rheumatoid arthritis (RA).

Methods: In SELECT–EARLY, MTX-naïve pts with active RA who were positive for both RF and ACPA and/or had ≥1 joint erosion were randomized 1:1:1 to once-daily (QD) UPA at 15mg or 30mg, or weekly MTX (titrated by Wk8). Separate primary endpoints were ACR50 at Wk12 (FDA), or the proportion of pts achieving DAS28CRP<2.6 at Wk24 (EMA). Secondary endpoints included mean changes from baseline (Δ BL) in modified Total Sharp Score (mTSS) and proportion of pts with no radiographic progression (mTSS≤0) at Wk24.

Results: Of 947 randomized pts, 945 received study drug; 840 (88.7%) completed Wk24. ~50% had an RA diagnosis of <6 months and RA symptoms <2 years. Of the 945 pts, 874 (92.5%) had no prior MTX exposure; 706 (74.7%) had no prior csDMARD exposure. Both primary endpoints were met. Significantly more patients receiving UPA 15 and 30mg vs MTX achieved ACR50 responses at Wk12 (52.1% and 56.4% vs 28.3%) and DAS28CRP<2.6 at Wk24 (48.3% and 50.0% vs 18.5%) (Table 1). All ranked secondary endpoints were met: ACR50 at Wk24, improvements in DAS28CRP, HAQ-DI, SF36-PCS, and the proportion of pts achieving DAS28CRP≤3.2 at Wks12 and 24. At Wk24, mean ΔmTSS were 0.14 and 0.07 vs 0.67 for UPA 15, UPA 30 and MTX, respectively; significantly more pts had no radiographic progression on UPA 15 and 30mg vs MTX. LDA and remission by various criteria at Wks12 and 24 were achieved in more pts on

TABLE I. EFFICACY AT WEEKS 12 AND 24

	WEEK 12			WEEK 24		
	MTX N=314	UPA 15 MG QD N= 317	UPA 30 MG QD N=314	MTX N=314	UPA 15 MG QD N= 317	UPA 30 MG QD N=314
ACR20, %	54.1	75.7***	77.1***	58.6	78.9***	78.0***
ACR50, %	28.3	52.1***	56.4***	33.4	60.3***	65.6***
ACR70 , %	14.0	32.5***	36.9***	18.5	44.5***	49.7***
DAS28CRP<2.6, %	13.7	35.6***	40.8***	18.5	48.3***	50.0***
DAS28CRP≤3.2, %	28.3	53.3***	54.8***	32.2	59.9***	65.0***
ΔDAS28CRP	-1.85	-2.73***	-2.85***	-2.15	-3.07***	-3.34***
ΔHAQ-DI	-0.49	-0.83***	-0.86***	-0.60	-0.87***	-0.91***
ΔSF-36 PCS	5.74	9.99***	10.08***	6.97	10.70***	11.39***
ΔmTSS	NA	NA	NA	0.67	0.14**	0.07***
No radiographic progression, %	NA	NA	NA	77.7	87.5**	89.3***
CDAI≤10 (LDA), %	29.6	46.4***	49.0***	38.2	56.2***	60.5***
CDAI≤2.8 (REM), %	6.4	16.1***	21.3***	10.5	28.4***	29.3***
Boolean REM, %	6.4	12.9**	15.3***	7.0	24.3***	24.8***

Values are LS mean unless otherwise specified. Δ, Change from baseline; QD, once daily; ACR20/50/70, 20/50 or 70% improvement in ACR criteria; CDAI, clinical disease activity index; DAS28CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire disability index; LDA, low disease activity; mTSS, modified total Sharp score; SF-36 PCS, short form 36- physical component score; REM, remission.

Results are based on following analyses: binary endpoints, NRI; DAS28CRP and HAQ-DI, ANCOVA with Multiple Imputation; mTSS, ANCOVA with linear extrapolation.

, p<.01, p<.001 for UPA vs MTX*

TABLE II. TREATMENT-EMERGENT ADVERSE EVENTS SUMMARY THROUGH WEEK 24, N (%)

	MTX N=314	UPA 15 MG QD N= 317	UPA 30 MG QD N=314
Any Adverse Event (AE)	205 (65.3)	203 (64.0)	224 (71.3)
Serious AE	13 (4.1)	15 (4.7)	20 (6.4)
AE Leading To Discontinuation Of Study Drug	16 (5.1)	14 (4.4)	12 (3.8)
Deaths*	1 (0.3)	2 (0.6)	3 (1.0)
Infection	103 (32.8)	104 (32.8)	115 (36.6)
-Serious Infection	4 (1.3)	5 (1.6)	8 (2.5)
-Opportunistic Infection	0	1 (0.3)	1 (0.3)
-Herpes Zoster ¥	1 (0.3)	7 (2.2)	7 (2.2)
+Hepatic disorder	17 (5.4)	19 (6.0)	14 (4.5)
Gastrointestinal perforation ♀	0	0	2 (0.6)
Malignancy (including NMSC) ♈	1 (0.3)	3 (0.9)	0
MACE (adjudicated) §	1 (0.3)	1 (0.3)	2 (0.6)
VTE (adjudicated)	1 (0.3)	0	1 (0.3)
-PE	1 (0.3)	0	0
-DVT	0	0	1 (0.3)

AE, adverse event; NMSC, non-melanoma skin cancer; VTE, venous thromboembolic events; PE, pulmonary embolism. DVT, deep vein thrombosis.

**Deaths: MTX: 1 sudden cardiovascular (CV) death; UPA 15, 1 CV death, 1 death due to metastatic malignant melanoma; UPA 30, 1 CV death, 1 death due to pneumonia and sepsis, 1 death due to peritonitis (also counted under GI perforation)*

+Hepatic disorder: majority were asymptomatic transaminase elevations

¥Herpes zoster: All non-serious, 12 were single dermatome

♀ Gastrointestinal perforation UPA 30, 1 pt with large intestinal perforation, 1 pt with peritonitis

♈ Malignancies: MTX: 1 case of ovarian cancer; UPA 15: 1 metastatic malignant melanoma, 1 squamous cell carcinoma of the lung, 1 uterine carcinoma in situ

§ MACE, major adverse cardiovascular events (adjudicated): MTX, 1 CV death; UPA 15, 1 non-fatal myocardial infarction (MI), CV death due to other CV causes; UPA30, 1 non-fatal MI and 1 CV death (sudden).

UPA vs MTX (nominal p<.001 for all).

Up to Wk24, treatment-emergent adverse events (AEs) and serious AEs were similar in the UPA 15mg and MTX arms, and slightly higher in the UPA 30mg arm (Table 2). AEs leading to discontinuation were similar across arms. A numerically higher proportion of pts on UPA 30mg reported serious infections vs MTX and UPA 15mg, and there were more cases of herpes zoster in the UPA vs MTX arms. Four malignancies, 4 major adverse cardiovascular events (MACE), and 6 deaths were reported (Table 2). Two venous thromboembolic events were reported (1 pulmonary embolism on MTX, 1 deep vein thrombosis on UPA 30mg, none on UPA 15mg). Laboratory abnormalities were consistent with other Phase 2 and 3 studies with UPA. **Conclusion:** In MTX-naïve pts at high risk for disease progression, UPA 15 and 30mg QD monotherapy demonstrated significant and clinically meaningful improvements in RA signs & symptoms vs MTX. Radiographic progression was significantly less with UPA vs MTX. Safety events were consistent with Phase 2 and 3 studies with UPA in RA to date.

C0073 - ECONOMIC IMPACT OF HEALTHCARE RESOURCE UTILIZATION AND WORK DISABILITY IN PORTUGUESE PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS (AREA) STUDY

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Background: Ankylosing spondylitis (AS) has a significant burden upon the individual, family and society. Understanding the economic impact of AS is crucial to substantiate policies that promote early referral, diagnosis and treatment.
Objective. To assess the economic impact of AS in Portugal concerning healthcare utilization and work disability.
Methods. The Assessment of REsults in Ankylosing spondylitis (arEA) study was developed by the NOVA--Information Management School (Lisbon) in collaboration with the Portuguese Society of Rheumatology, the Portuguese Association of Family Physicians, the National Association of Primary Care Units, the National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The arEA aimed at assessing reasons for delayed diagnosis of AS, as well as disease impact in patients' lives, global health and work. A comprehensive online survey was developed and sent to AS patients. Data on demographics, lifestyle habits, daily life activities, working habits, disease indexes and healthcare utilization was retrieved. Costs of the disease for patients resulting from the use of health systems was obtained thorough patient's declaration, the cost for the national health service (SNS) was obtained combining primary data and secondary data related with the average costs of service use. Finally, the impact over the economy was also estimated through the participation of patients in labor market and using as mediator variables the absenteeism and presenteeism. A set of generalized linear models were used to identify the factors with significant effect over health status, SNS costs and impact over economy.
Results: 354 patients responded the survey, 42.1% female, more frequently from the 35-44 year-old age group. In the previous 12 months, 76% reported using the National Healthcare System (SNS) for AS-related reasons (85% outpatient visits; 74% diagnostic exams; 48% ER visits; 8% inpatient admissions). During that period, estimated SNS expenditure with AS patients reached €47 million, excluding costs with medication (ongoing analysis), distributed as: outpatient visits €25 million, diagnostic exams €7 million, ER visits €3 million and inpatient admissions €12 million. Adding to this, patients spent on average €84 million out of their own pocket on AS-related expenses (€1.786 per patient: outpatient visits €245, diagnostic exams €151, ER visits €48, inpatient admissions €415, medication €593, travelling expenses €334). Regarding work disability, working AS patients reported an average of 12 days on leave of absence and 25 days on sick leave per year, with an estimated cost of €28 and €57 million, respectively. Presenteeism led to a loss of 73 working days with a cost of €165 million. Taking also into account patients with prolonged leaves of absence (€72 million), permanent leaves (€18 million), unemployed (€50 million) and family medical leaves (€47 million), the overall costs with work disability in AS reached €437 million in one year.
Conclusions: AS-related work disability and healthcare resource utilization have an enormous economic impact in Portugal. Investment in strategies that encourage early referral, diagnosis and treatment is fundamental to mitigate such burden.

C0081 - CHILDREN WITH EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS HAVE A CYTOKINE PATTERN FAVOURING B CELL ACTIVATION IN CIRCULATION SIMILARLY TO EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS

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Introduction: The majority of polyarticular JIA (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfil classification criteria for rheumatoid arthritis (RA) in adulthood. B cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.
Objectives: The main goal of this study was to determine the concentration of cytokines potentially relevant for B cell activation in serum from children with pJIA and extended oJIA when compared to children with persistent oJIA, adult JIA, early and established RA patients.
Methods: Serum samples were collected from children

with extended oJIA (n=8), persistent oJIA (n=6), pJIA (n=6), adult JIA (n=8), untreated early RA (< 1 year of disease duration, n=12), established RA patients treated with synthetic DMARDs (n=10) and two corresponding groups of age- and sex-matched healthy donors (children, n=6 and adults, n=10). A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), interleukin (IL)-6 and IL-21 serum levels were measured by ELISA.

Results: Children with extended oJIA, early and established RA patients had significantly higher BAFF serum levels when compared to controls, but no significant differences were observed in children with persistent oJIA, pJIA and adult JIA when compared to all groups included. APRIL serum levels were significantly increased in all patient groups when compared to controls, except in adult JIA, who had similar APRIL concentrations in comparison to controls. In addition, children with extended oJIA and pJIA had significantly higher APRIL serum levels when compared to adult JIA. IL-6 serum levels were significantly increased in children with extended oJIA, pJIA, early and established RA when compared to controls, but no significant differences were found in children with persistent oJIA and adult JIA patients. IL-21 serum levels were significantly increased in early RA when compared to controls, but no significant differences were observed between any of the other groups included.

Conclusions: The similarity in B cell cytokine pattern found between extended oJIA, pJIA, early and established RA patients, contrarily to what was observed in persistent oJIA, suggests an early B cell involvement in the pathogenesis of extended oJIA and pJIA as described for RA.

C0107 - EVALUATION OF PATIENT REPORTED OUTCOME MEASURES IN ASSOCIATION WITH ANKYLOSING SPONDYLITIS RESPONSE TO TNFI: PRELIMINARY RESULTS FROM THE BIOEFFICACYSPA CLINICAL TRIAL

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Background: Patients reported outcome measures (PROMs) are routinely applied to patients with Ankylosing Spondylitis (AS) to improve disease management. TNFi have shown to be effective in improving quality of life and function in AS, but which PROMs better correlate with disease activity scores is still a matter of debate. The aim of this study was to analyse differences in PROMs between responders and non-responders to adalimumab treatment in AS patients.

Methods: Data from patients included in the Biomarkers identification of anti-TNF alfa agent's efficacy in AS patients using a transcriptome analysis and mass spectrometry (BioEfficacySpa) study was collected at baseline and week 14 post-treatment with Adalimumab. The PROMs evaluated at both time points were the Hospital Anxiety and Depression Scale (HADS), the AS Quality of Life (ASQoL) Scale, the EuroQol 5 dimensions(EQ-5D) and the Bath AS Functional Index (BASFI). Treatment response was assessed using Ankylosing Spondylitis Disease Activity Score (ASDAS) and Assessment in AS Response Criteria (ASAS) response criteria. For response stratification the clinically important improvement (Δ ASDAS$\geq$1.1), ASDAS major improvement (Δ ASDAS$\geq$2), ASAS-20 and ASAS-40 were used. ASAS-70 was not included in this analysis due to low sample size. The mean differences in PROMs (Δ PROMs) between baseline and week 14 were compared among responders, non-responders and between groups of responders. Statistical analysis was performed using the IBM-SPSS (v.25) software. Differences between means were calculated using Fisher s exact test and student-t test. The Kruskal-Wallis test was used to assess differences in ASAS and ASDAS response categories.

Results: Sixty-nine patients were included in the study. Five patients were excluded due to adverse events and 9 due to non-compliance with the study protocol. Data from 55 patients (37 males; 67.2%), with a mean age of 44(±11) years and a mean disease duration of 14(±10) years, was analysed. There was a total of 42

TABLE. COMPARISON OF PROM SCORES USING DIFFERENT TREATMENT RESPONSE MEASURES

PROMs Mean(±SD)	ASAS-40		ASAS-20		ASDAS		
	Yes N=33	No N=22	Yes N=42	No N=13	Δ≥ 2 N=19	2< Δ≥1.1 N=15	Δ< 1 N=21
HADS Anxiety †	3.9(3.4)*	1.3 (3.4)	3.7 (3.33)*	0.2 (3.2)	3.7 (3.4)	3.5 (3.4)	1.4 (3.6)*
HADS Depression†	3 (3)	2.5 (3.6)	3.1 (3)	2.2 (3.9)	3.8 (2.6)	3.4 (2.4)	1.3 (3.9)
EuroQol-5D‡	0.4 (0.2)**	0.1 (0.2)	0.3 (0.3)*	0.1 (0.2)	0.4 (0.2)	0.3 (0.2)	0.1 (0.2)**
AsQoL¥	7.5 (4.8)**	1.8 (3.6)	6.2 (5.3)**	1.7 (2.6)	9 (4.7)	5.7 (3.2)	1.3 (3.6)**
BASFI	3.5 (2.1)**	1.3 (1.1)	3.1 (2)**	1 (1.1)	3.7 (2.5)	3 (1.3)	1.5 (1.4)**

*p<0.05; **p<0.001; missing data:† N=4; ‡ N=1; ¥ N=5;ASDAS- Ankylosing SpondylitisDisease Activity Score; ASQoL- Ankylosing Spondylitis Quality of Life ;BASFI- Bath Ankylosing Spondylitis Functional Index (BASFI); HADS- Hospital Anxiety and Depression Scale; PROM-Patients reported outcome measures.

ASAS 20 responders and 32 ASAS-40 responders. ASDAS clinically important improvement was observed in 15 patients and major improvement in 19 patients. Comparing with non-responders, patients achieving ASAS-40 and ASAS-20 presented significant improvements in EQ-5D (ASAS-40: 0.4 vs 0.06; ASAS-20: 0.3 vs 0.1; p<0.001), AsQoL (ASAS-40: 7.5 vs 1.8; ASAS-20: 6.2 vs 1.7; p<0.001), BASFI (ASAS-40: 3.5 vs 1.2; ASAS-20: 3.1 vs 1; p<0.01) and HADS anxiety (ASAS-40: 3.9 vs 1.3; ASAS-20: 3.7 vs 0.2; p<0.05) but there were no statistically significant improvements in HADS depression (ASAS-40: 2.69 vs 2.5; ASAS-20: 3.1 vs 2.2; p>0.05). The same results were found when non-responders were compared with ASDAS responders (Table). Comparing ASAS-40 responders with responders not achieving ASAS-40 (N=9), significant differences were found for EQ-5D (0.4 vs 0.04; p<0.001), ASQoL (7.5 vs 2; p<0.05) and BASFI (3.5 vs 1.7; p<0.05). Also, patients with ASDAS major improvement presented greater positive impact in ASQoL than patients with ASDAS clinically important improvement (5.7 vs 9; p<0.05).

Conclusions: Except for HADS depression, PROMs seem to correlate well with ASAS-20, ASAS-40 and ASDAS clinical response to adalimumab therapy. Our results suggest that ASQoL, a disease-specific PROM assessing quality of life, is more sensitive in detecting changes in disease activity.

C0147 - SLE DISEASE ACTIVITY SCORE (SLE-DAS): A NEW SLE CONTINUOUS SCORE WITH HIGH SENSITIVITY FOR CHANGES IN DISEASE ACTIVITY AND THAT ENABLES AN ACCURATE DEFINITION OF SLE REMISSION

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Background: Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is a widely used instrument. However, it lacks sensitivity to discriminate improvement/worsening as it only scores items categorically and does not include several potentially severe lupus features, such as hemolytic anemia.

Objectives: To derive and validate a new SLE disease activity measure, the SLE Disease Activity Score (SLE-DAS), with improved sensitivity to change as compared to SLE Disease Activity Index (SLEDAI), while maintaining high specificity and easiness of use.

Methods: We studied 520 patients fulfilling ACR'97 and/or SLICC'12 classification criteria for SLE from 2 tertiary care centers (derivation and validation cohorts). At each visit, disease activity was scored using the Physician Global Assessment (PGA) and SLEDAI-2K. To construct the SLE-DAS, we applied multivariate linear regression analysis in the derivation cohort, with PGA as dependent variable. Independent variables tested in the models included items from SLEDAI-2K and continuous variables for swollen joint count, proteinuria, platelet and white blood cells counts. Some features absent from SLEDAI, such as hemolytic anemia, gastrointestinal and cardiopulmonary involvement were added to the model. The formula was validated in a different cohort through the study of: (i) correlations between SLE-DAS, PGA and SLEDAI-2K; (ii) performance of SLEDAI-2K and SLE-DAS in identifying a clinically meaningful change in disease activity (variation in PGA≥0.3); (iii) accuracy of SLEDAI-2K and SLE-DAS time-adjusted means in predicting damage accrual. The best cut-off values of SLE-DAS to define different SLE disease activity categories (remission, low

disease activity, mild disease activity and moderate/severe disease activity) were estimated using Receiver Operating Characteristic (ROC) curve analysis and accuracy, precision, sensitivity and specificity values for these cut-off values were then calculated.

Results: The final SLE-DAS instrument included 17 items. SLE-DAS was highly correlated with PGA (rho=0.875, p<0.0005) and SLEDAI-2K (rho=0.943, p<0.0005) in the validation cohort. The optimal discriminative variation of SLE-DAS cut-off to detect a clinically meaningful change was 1.72 points. In the validation cohort, SLE-DAS showed a higher sensitivity than SLEDAI-2K (change ≥4) to detect a clinically meaningful improvement (89.5% vs 47.4%, p=0.008) or worsening (95.5% vs 59.1%, p=0.008), while maintaining similar specificities. Furthermore, SLE-DAS performed better in predicting damage accrual than SLEDAI-2K. The proposed cut-off values of SLE-DAS to define each disease activity category were: remission SLE-DAS ≤2.08, low disease activity 2.08< SLE-DAS ≤3.77, mild disease activity 3.77< SLE-DAS ≤7.64, and moderate/severe disease activity SLE-DAS >7.64. The overall accuracy of these SLE-DAS cut--off values to identify each disease activity state was 96.4%.

Conclusion: SLE-DAS has a good construct validity and has better performance than SLEDAI-2K in identifying clinically significant changes in disease activity and in predicting damage accrual. Furthermore, SLE-DAS has a high precision in identifying remission, low disease activity, and other disease activity states, suggesting that it is an accurate tool in defining achievable targets in SLE management.

CO154 - BODY MASS INDEX AND DISEASE ACTIVITY IN PORTUGUESE AND BRAZILIAN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: RESULTS FROM RHEUMATIC DISEASES PORTUGUESE REGISTER

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Background: The influence of body mass index (BMI) on Juvenile Idiopathic Arthritis (JIA) disease activity is poorly understood. In adults with Rheumatoid Arthritis, obesity has been associated with higher disease activity, while in patients with JIA, a previous study has failed to find any association.

Objectives: To investigate the relationship between BMI and JIA disease activity.

Methods: This is an international, multicenter, observational, cross-sectional study. JIA patients (according to ILAR criteria) aged ≤ 18 years, registered at the Rheumatic Diseases Portuguese Register (Reuma.pt) in Portugal and Brazil were included. Data was analyzed upon records from the first registered visit. Age- and sex-specific BMI percentiles (P) were calculated based on WHO growth standard charts and categorized into underweight (P<3), normal weight (3≤ P≤ 85), overweight (85< P≤ 97) and obesity (P>97). Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS-27). Univariate linear regression was used to examine the association of JADAS-27 with BMI categories. Two multivariate regression models were then performed a) adjusting for age, gender, race, country, disease duration and JIA category (model 1); b) adjusting for those covariates plus use of DMARDs (model 2).

Results: A total of 255 patients were included. Mean age was 10.1±4.7 years and mean disease duration was 6.3±4.9 years; 62% were female; 85% were caucasian; 88% were part of Portugal's database. Thirty-two percent were persistent oligoarticular, 9% extended oligoarticular, 34% polyarticular RF+, 6% systemic, 13% enthesitis-related arthritis, 5% psoriatic arthritis

TABLE. RELATIONSHIP BETWEEN JADAS-27 (DEPENDENT VARIABLE) AND DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF JIA PATIENTS.

	Univariate analysis			Multivariate analysis					
				Model 1			Model 2		
	B	95% CI	*p*-value	B	95% CI	*p*-value	B	95% CI	*p*-value
Age, years	-0.299	[-0.532 – (-0.066)]	**0.012**	-0.378	[-0.613-(-0.143)]	**0.002**			
Disease duration, years	-0.396	[-0.625-(-0.167)]	**0.001**	-0.245	[-0.465-(-0.024)]	**0.030**			
Gender (female)	0.104	[-2.173 – 2.382]	0.928						
Country (Portugal)	-5.357	[-8.675- (-2.038)]	**0.002**				-4.728	[-8.427-(-1.030)]	**0.013**
Ethnicity									
White european*									
White non-european	-0.620	[-8.549- 7.308]	0.878						
Black	6.852	[0.545 – 13.159]	**0.033**	5.967	[0.225-11.708]	**0.042**			
Biracial	-5.985	[-14.831-2.860]	0.184						
Romani	8.240	[-9.340-25.819]	0.357						
Asiatic	-0.860	[-11.053-9.332]	0.868						
JIA subtype									
Persistent oligoarthritis*									
Extending oligoarthritis	-1.408	[-5.365 – (2.548)]	0.484						
RF-positive polyarthritis	7.101	[4.557-9.644]	**<0.001**	5.471	[3.303-7.640]	**<0.001**	4.447	[1.968-6.925]	**0.001**
Systemic-onset	2.853	[-1.785- 7.490]	0.227						
Enthesitis-related arthritis	2.226	[-1.199 – 5.651]	0.202						
Psoriatic arthritis	2.856	[-2.078-7.789]	0.255						
Undifferentiated arthritis	8.833	[-3.049-20.714]	0.144						
BMI									
Underweight*									
Normal weight	-9.563	[-13.664 – (-5.462)]	**<0.001**	-9.706	[13.678-(-5.735)]	**<0.001**	-9.964	[-14.364 – (-5.565)]	**<0.001**
Overweight	-10.661	[-15.382 – (-5.940)]	**<0.001**	-10.382	[-14.949-(-5.816)]	**<0.001**	-10.316	[-15.540- (-5.902)]	**<0.001**
Obesity	-7.422	[-12.458 – (-2.386)]	**0.004**	-7.819	[-12.660-(-2.978)]	**0.002**	-9.502	[-14.912-(-4.092)]	**0.001**
cDMARD use	-3.414	[-6.055-(-0.773)]	**0.012**					-	
bDMARD use	-2.660	[-6.227-0.906]	0.143					-	
Any DMARD use	-4.831	[2.168-7.493]	**<0.001**				-4.858	[-7.319- (-2.396)]	**<0.001**

*Reference group

and 1% undifferentiated arthritis. The prevalence of underweight, normal weight, overweight and obesity was 7.5%, 65.9%, 15.7% and 11%, respectively. In the univariate linear regression, underweight was significantly associated with higher JADAS-27 scores, compared to normal weight (B=-9.563, p<0.001), overweight (B=-10.661, p<0.001) and obesity (B=-7.422, p=0.004). Lower age (B=-0.299, p=0.012), shorter disease duration (B=-0.396, p=0.001), black race (B=6.852, p=0.033), RF+ polyarthritis (B=7.101, p<0.001), living in Brazil (B=5.357, p=0.002) and the absence of DMARD therapy (B=4.831, p<0.001) were also associated with higher JADAS-27.

In the model 1 of the multivariate analysis (R2=0.256), the same variables, except the country, remained significantly associated with higher disease activity. When DMARD therapy was added to the model (model 2, R2=0.285), RF+ polyarthritis (B=4.447, p=0.001) and living in Brazil (B=4.728, p=0.013) were significantly associated with higher disease activity. Patients with normal weight (B=-9.964, p<0.001), overweight (B=-10.316, p<0.001) and obesity (B=-9.502, p=0.001) had significantly lower activity disease, compared to underweight patients, as well as those under DMARD therapy (B=-4.858, p<0.001) (Table 1).

Conclusion: Despite the lack of adjustment for corticosteroids use, there seems to be an independent association between underweight and higher disease activity in JIA patients. Importantly, these results suggest that active disease can impair child's weight gain. Further studies are needed to confirm these findings and understand the underlying mechanisms of this association.

C0156 - GENDER DIFFERENCES IN PSORIATIC ARTHRITIS – IMPACT ON TUMOR NECROSIS FACTOR INHIBITORS PERSISTENCE AND RESPONSE

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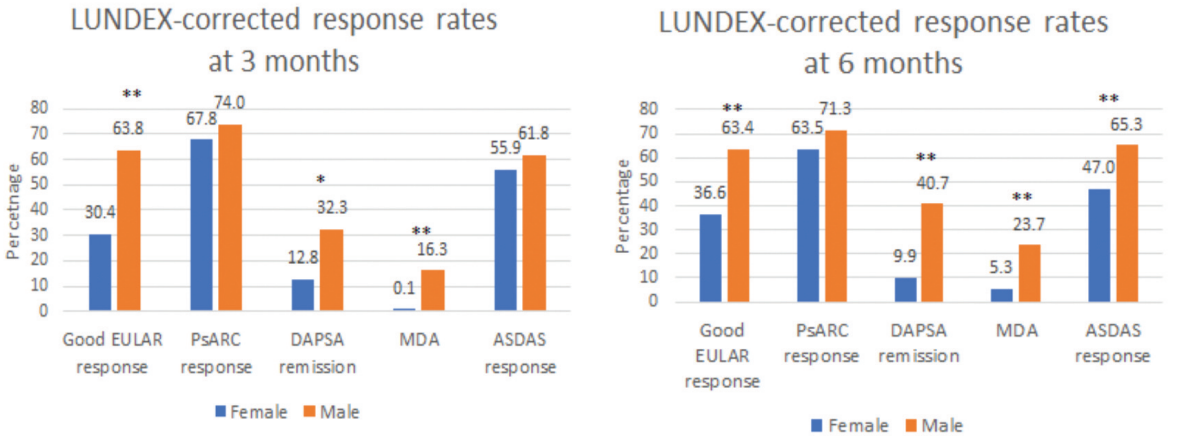
Background: The impact of gender on tumor necrosis factor inhibitors (TNFi) effectiveness has been poorly studied in Psoriatic Arthritis (PsA) patients.

TABLE I. BASELINE DEMOGRAPHIC AND DISEASE CHARACTERISTICS OF PSORIATIC ARTHRITIS PATIENTS FROM REUMA.PT, TREATED WITH A 1ST TUMOR NECROSIS FACTOR INHIBITOR, ACCORDING TO GENDER

Characteristics		Population (n=750)	Female (n=377)	Male (n=373)	p-value
Age at 1st TNFi, years (mean ± sd)		47.6 ± 11.6	48.5 ± 11.7	46.7 ± 11.5	0.030†
Obese (BMI>30Kg/m^2), n (%)		104 (25.2%)	64 (30.9%)	40 (19.5%)	0.008†
Clinical Subtype, n (%),	Symmetric polyarthritis	401 (60.6%)	228 (68.9%)	173 (52.3%)	<0.001†
	Arthritis distal interphalangeal joins	29 (4.4%)	9 (2.7%)	20 (6.0%)	
	Asymmetric oligoarthritis	95 (14.3%)	49 (14.8%)	46 (13.9%)	
	Mutilating arthritis	9 (1.4%)	3 (0.9%)	6 (1.8%)	
	Predominant axial	128 (19.3%)	42 (12.7%)	86 (26.0%)	
Years since diagnoses until 1st TNFi (mean ± sd)		6.6 ± 6.8	7.1 ± 7.0	6.0 ± 6.6	0.033†
Swollen joints (mean ± sd)		5.3 ± 5.5	6.2 ± 6.3	4.4 ± 4.4	<0.001†
Tender joints (mean ± sd)		9.7 ± 9.6	11.9 ± 10.4	7.3 ± 8.1	<0.001†
ESR mm/1st h (mean ± sd)		31.8 ± 25.3	35.8 ± 26.0	27.1 ± 23.8	<0.001†
Patient's global VAS (0-100mm) (mean ± sd)		61.5 ± 23.9	64.0 ± 23.0	58.7 ± 24.7	0.020†
Patient's pain VAS (0-100mm) (mean ± sd)		61.2 ± 23.4	64.2 ± 23.6	57.8 ± 22.9	0.011†
MASES (mean + sd)		2.0 ±3.2	3.0 ± 3.9	1.1 ± 2.1	<0.001†
DAS28 (mean + sd)		4.9 ± 1.4	5.2 ± 1.3	4.5 ± 1.4	<0.001†
DAPSA (mean ± sd)		29.9 ± 15.4	32.5 ± 16.5	26.7 ± 13.3	0.001†
HAQ-DI (mean ± sd)		1.13 ± 0.68	1.34 ± 0.66	0.90 ± 0.63	<0.001†
Concomitant csDMARDs, n (%)		505 (67.6%)	276 (73.6%)	229 (61.6%)	<0.001†
Concomitant corticosteroids, n (%)		253 (33.9%)	157 (41.9%)	96 (25.8%)	<0.001†

TNFi:tumor necrosis factor inhibitor; BMI: body mass index; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale.; DAS28 4v: Disease Activity Score 28 4 variables; DAPSA: Disease Activity Psoriatic Arthritis Score; HAQ-DI: Health Assessment Questionnaire Disability Index; csDMARDs: conventional synthetic disease modifying anti-rheumatic drugs.
Sample size according to groups and variables:
Study population –BMI (n=412); Clinical Subtype (n=662); Swollen joints (n=495); Tender joints (n=501); ESR (n=505); Patient's global VAS (n=453); Patient's pain VAS (n=342); Physician's global VAS (n=390); MASES (n=159); SPARCC (n=131); DAS28 (n=370); DAPSA (n=299); HAQ-DI (n=320); Concomitant csDMARDs (n=747); Concomitant corticosteroids (n=747).
Discontinuers – BMI (n=171); Clinical Subtype (n=251); Swollen joints (n=163); Tender joints (n=166); ESR (n=176); Patient's global VAS (n=155); Physician's global VAS (n=121); MASES (n=44); SPARCC (n=31); DAS28 (n=123); DAPSA (n=90); HAQ-DI (n=110); ASDAS (n=59); BASFI (n=63); Concomitant csDMARDs (n=269); Concomitant corticosteroids (n=269).
Continuers - BMI (n=241); Clinical Subtype (n=411); Swollen joints (n=332); Tender joints (n=335); CRP (n=322); ESR (n=329); Patient's global VAS (n=298); Physician's global VAS (n=269); Patient's pain's VAS (n=235); MASES (n=115); SPARCC (n=100) DAS28 (n=247); DAPSA (n=209); HAQ-DI (n=210); Concomitant csDMARDs (n=478); Concomitant corticosteroids (n=478).



Crude responses at 3 months

3 months	Good EULAR response	PsARC response	DAPSA remission	MDA	ASDAS response
Female	43/130 (33.1%)	84/114 (73.7%)	15/121 (12.4%)	1/92 (1.1%)	34/56 (60.7%)
Male	60/88 (68.2%)	72/91 (79.1%)	45/100 (45.0%)	8/46 (17.4%)	35 /53 (66.0%)

Crude responses at 6 months

6 months	Good EULAR response	PsARC response	DAPSA remission	MDA	ASDAS response
Female	51/118 (43.2%)	81/108 (75.0%)	12/117 (10.3%)	81/80 (75.0%)	30/54 (55.6%)
Male	71/99 (71.7%)	87/108 (50.6%)	46/123 (37,4%)	11/41 (26.8%)	45/61 (73.8%)

** p-value<0.001; *p-value<0.05

EULAR: European League Against Rheumatism, DAPSA: Disease Activity Index for Psoriatic Arthritis, PsARC: Psoriatic Arthritis Response Criteria, MDA: Minimal Disease Activity, ASDAS: Ankylosing Spondylitis Disease Activity Score

FIGURE 1. First-line TNFi LUNDEX-corrected response rates of PsA patients from Reuma.pt, according to gender

Objectives: To study gender differences in persistence and response of 1st TNFi in PsA patients.
Methods: PsA patients prospectively followed at the Rheumatic Diseases Portuguese Registry (Reuma.pt), treated with a 1st TNFi, between 2001 and 2016. Drug retention assessed by Kaplan-Meier survival analysis and Cox models, adjusted for the year of starting a TNFi. Response rates measured by EULAR response, DAPSA remission, MDA and ASDAS response, applying LUNDEX method, were compared between genders. Baseline predictors of discontinuation and response were identified (Cox and logistic regression models).
Results: 750 PsA patients, mean age 47.6 (± 11.6) years and 50.3% (n=377) females. PsA females showed significantly different baseline PsA disease characteristics in comparison with males and had more severe peripheral disease activity (Table 1). The overall TNFi survival rate for females was also significantly lower when compared with males. Additionally, females experienced lower rates of response at 3 and 6 months (Figure 1). Female gender was further identified as an independent predictor factor of worse persistence and showed a lower chance of good EULAR response.
Conclusion: PsA females from Reuma.pt have distinct PsA features and worse persistence and response to a 1st TNFi in comparison with males. This might be related to gender dependent inflammatory pathways and was independent of baseline disease activity.

C0192 - REMISSION PERSISTENCE IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS UNDER BIOLOGIC TREATMENT

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Background: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) under biologic treatment are increasingly achieving prolonged remission and tapering treatment is becoming standard practice. However, the optimal timing to start tapering remains unclear and predictors of loss of remission (LOR) are missing. Guidelines disagree on whether to wait for 6 or 12 months of sustained remission before tapering.

Objectives: To determine whether longer sustained remission (6 versus 12 months) influences subsequent LOR rates and to identify predictors of LOR.

Methods: We used the Rheumatic Diseases Portuguese Register (Reuma.pt), to identify RA, PsA and axSpA patients on stable biologic treatment in a single center and retrospectively analyze those who achieved sustained remission for at least 6 and 12 months. Remission was defined as ASDAS <1.3 for axSpA and DAS28 <2.6 for RA and PsA. Survival analysis was used to characterize stability of remission and identify predictors of LOR. The Cox proportional hazards regression was stratified by diagnosis and adjusted for age, gender, smoking, baseline disease activity, type of biologic, previous switches and starting year of biologic treatment.

Results: 195 patients (100 RA, 51 PsA and 44 AxSpA) of 1078 patients (785 RA, 116 PsA, 177 axSpA) registered in Reuma.pt at a single center and treated with biologics between 1999 and 2018, had at least one remission period with a minimal duration of 6 months. This corresponded to 310 individual remission periods longer than 6 months, 232 of which (74.8%) were longer than 12 months. Median remission time (since the start of remission period) was 78.9 weeks overall vs. 99.0 weeks for patients with a minimum 12 months remission (difference in median survival: 20.1 weeks). PsA patients showed significantly longer remission periods (p<0.0001, global log-rank test and Wilcoxon test), followed by axSpA (log-rank p=0.048, Wilcoxon p=0.036 for single flare failure, difference not significant considering persistent flare as failure). We identified female gender (HR 1.764, p=0.007 for the total population; HR 1.448, p=0.18; HR 2.664, p=0.037, HR 1.270, p=0.59 for RA, PsA and axSpA, respectively) infliximab use (HR 1.635, p=0.023 for the total population; HR 2.306, p=0.007; HR 2.445, p=0.098, HR 3.434, p=0.026 for RA, PsA and axSpA, respectively; etanercept used as index category), PtGA (HR 1.011, p=0.012 for the total population; HR 1.002, p=0.73; HR 1.035, p=0.001, HR 1.000, p=0.99 for RA, PsA and axSpA, respectively) and CRP (HR 0.961, p=0.009 for the total population; HR 0.963, p=0.017; HR 0.979, p=0.68, HR 1.052, p=0.59 for RA, PsA and axSpA, respectively) as predictors of LOR. A sensitivity analysis excluding infliximab patients identified the same predictors of LOR: female gender (HR 2.298, p=0.004 for the total population; HR 1.855, p=0.085; HR 22.254, p=0.002, HR 0.599, p=0.264 for RA, PsA and axSpA, respectively), PtGA (HR 1.012, p=0.011 for the total population; HR 0.998, p=0.78; HR 1.045, p<0.001,

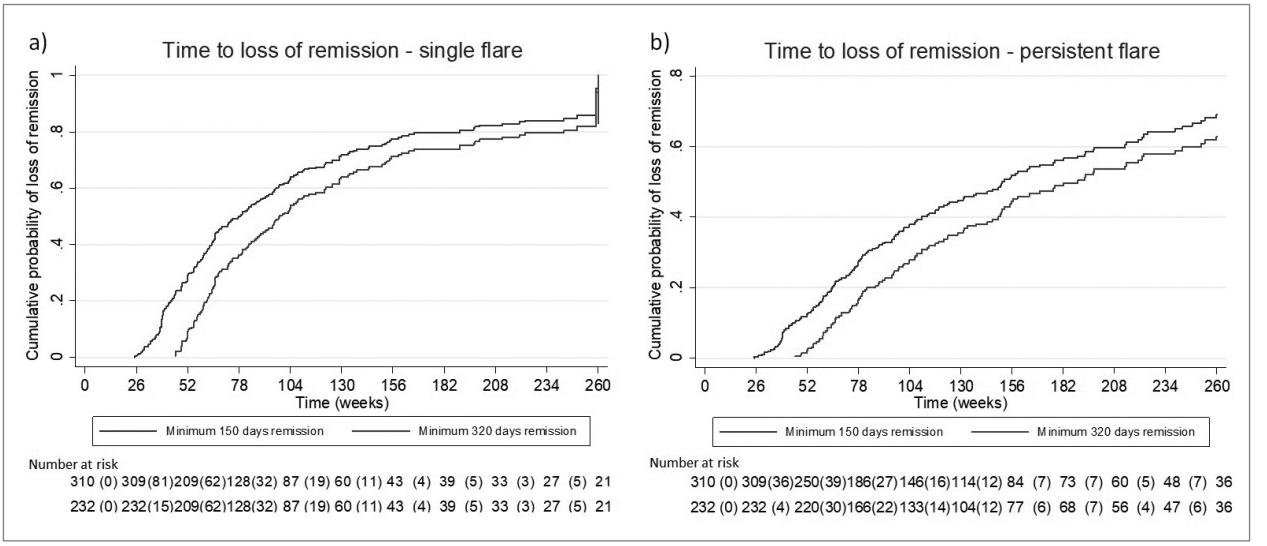

FIGURE 1. Time to loss of remission considering a single flare (a) vs. persistent flare (b).

HR 1.139, p=0.44 for RA, PsA and axSpA, respectively) and CRP (HR 0.964, p=0.018 for the total population; HR 0.962, p=0.023; HR 0.895, p=0.183, HR 1.024, p=0.88 for RA, PsA and axSpA, respectively). Conclusion: 6 vs. 12 months of sustained remission did not influence the subsequent rate of LOR. Female gender, treatment with infliximab, PtGA and CRP were identified as baseline predictors of LOR.

C0193 – CONSTRUCT AND DISCRIMINANT VALIDITY OF THE EUROPEAN PORTUGUESE VERSION OF THE START BACK SCREENING TOOL (SBT-PT)

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Background: The Keele Start Back Screening Tool (SBT) is a brief 9-item instrument developed to stratify low back pain (LBP) patients according to their risk of future persistent and disabling pain so that prognostic subgroups can be matched to the most appropriate treatment- SPLIT Programme. The SBT screens for modifiable predictors of persistent disabling back pain, including the presence of radiating leg pain, pain elsewhere, disability (2 items), fear avoidance, anxiety, pessimistic patient expectations, low mood and how much the patient is bothered by their pain, also providing 2 scores for interpretation: a total score, and a psychosocial distress score. Patients are classified in one of three risk subgroups: Total scores of 3 or less - low risk; If total score is 4 or more: a) Those with psychosocial subscale scores of 3 or less - medium risk; b) Those with psychosocial subscale scores of 4 or more - high risk. The SBT was recently translated into European Portuguese and its face and content validity and reliability were assessed. However, other psychometric properties, such as the construct validity, are unknown. Therefore, the aim of this study is to test the convergent and discriminant construct validity of the European Portuguese SBT in LBP patients.
Methods: A total of 165 patients (mean age 47.5±11.6; 56.4% were female) with nonspecific LBP were recruited from the 7 different community health care units of a specific region of Portugal following standardized inclusion and exclusion criteria. Patients completed a socio-demographic and clinical questionnaire, the SBT-PT, the Portuguese version of the Rolland Morris Disability Questionnaire (RMDQ), and an 11-point numeric pain rating scale (NPRS) (pain at the moment). Convergent construct validity was evaluated by measuring the relation between the SBT-PT (total score/psychosocial sub score) and the RMDQ-PT and the NPRS scores, using Spearman's correlation coefficients. Discriminant validity was assessed through the area under the curve (AUC) derived from receiver operating curves (ROC) for total scores and a psychosocial subscale score of the SBT-PT against baseline reference cases (disability reference standard- RMDQ score ≥7; pain intensity- NPRS≥3). A priori hypothesis was formulated expecting moderate to strong correlations between the SBT-PT and the RMDQ-PT and NPRS, since both questionnaires share at least the same construct. For discriminant validity, this study hypothesized that participants with reference standards would have higher scores on the SBT-PT than participants without this condition.
Results: All the a priori hypotheses were confirmed. Moderate to good correlations were found between SBT-PT total and psychosocial subscale scores with RMDQ-PT (=0.68, p<0.01; =0.55, p<0.01, respectively) and with the NPRS (=0.47, p<0.01; =0.39, respectively). The AUCs for the SBT-PT total score were all above 0.80, indicating excellent discriminative ability [AUC= 0.87 (95% CI 0.81 to 0.94) for disability; [AUC= 0.83 (95% CI 0.75 to 0.91) for pain]. For the psychosocial subscale score, AUCs ranged from 0.78 (disability) to 0.74 (pain), indicating acceptable discriminative ability.
Conclusions: The SBT-PT demonstrated good convergent construct validity and excellent discriminant validity, therefore it may be useful for correctly discriminating between patients with high and low levels of disability and pain.

C0216 - CLINICAL ASSOCIATIONS AND DIAGNOSTIC POTENTIAL OF REGULATORY-LIKE B-CELLS IN SJOGRENS SYNDROME

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Introduction: Some B-cell subsets contribute to the regulation of immune responses, mainly through the secretion of interleukin-10 (IL-10), which suppresses T-helper 1 (Th1) and Th17 cells and induces regulatory T-cells (Tregs). Disturbances in regulatory B-cells (Bregs) have been identified in autoimmune diseases, including pSS. The role of Bregs and Tregs in primary Sjögren's syndrome (pSS) pathogenesis is an active field of research.
Objective: To evaluate the distribution of regulatory and effector T and B-lymphocytes, in patients with pSS and healthy controls (HC), and the relation between regulatory-like B-cell subsets and the pSS phenotype.
Methods: Fifty-seven pSS patients and 24 HC were included. Circulating T and B-lymphocytes were characterized by flow cytometry.
Results: Compared to HC, pSS patients had lower percentages (16.9 vs 32.0%, p<0.001) and absolute numbers (28 vs 81 cells/µL, p<0.001) of Breg-enriched CD24hiCD27+ B-cells, and a decrease in CD24hiCD 38hi B-cells percentages (6.2 vs 7.7%, p=0.09).

Lower frequencies of CD24hiCD27+ B-cells were found in anti-SSA-positive (n=38) compared to anti-SSA-negative (n=19) patients (15.0 vs 19.6%, p=0.170), as well as lower absolute counts (26 vs 31 cells/µL; p=0.173). Anti-SSA-positive patients presented higher CD24hiCD38hi B-cells percentages (6.2 vs 4.2%; p=0.260) and absolute counts (10 vs 5 cells/µL; p=0.343) compared to anti-SSA-negative patients.

Although CD24hiCD27+ B-cells frequencies and absolute counts did not differ between patients with active (n=27) or inactive disease (n=30), (16.9% vs 17.0%, p=0.946; 25 vs 31 cells/µl, p=0.179), patients with higher disease activity (ESSDAI≥5) (n=9) presented lower absolute counts of CD24hiCD27+ B-cells (18 vs 31 cells/µL, p=0.096) and lower CD24hiCD38hi B-cells (4 vs 10 cells/µL, p=0.075), and higher Th1/Breg CD24hiCD27+ ratios, (16.2 vs 9.2, p=0.064).

Considering all patients, a negative correlation was found between the ESSDAI score and the absolute numbers of either CD24hiCD27+ B-cells (r= -0.277; p=0.037) and Tregs (r= -0.311; p=0.019).

Correlations with ESSDAI was stronger when looking at patients with ESSDAI≥5: for the percentages of CD24hiCD27+ B-cells, r=-0.705, p=0.023; for CD24hiCD27+ B-cells absolute counts, r= -0.644; p=0.045; and for the absolute counts of Tregs, r= -0.862; p=0.001.

Using ROC curves to discriminate pSS from HC, better AUCs were obtained for CD24hiCD27+Breg cells (cut-off 34 cells/µL, AUC=0.81), Tregs/CD24hiCD27+ Breg ratio (cut-off 1.98, AUC=0.74) and Th1/CD24hi CD27+Breg ratio (cut-off 12.23, AUC=0.70), corresponding to a specificity for pSS of 0.83, 0.75 and 0.70, respectively, and sensitivity of 0.75, 0.72 and 0.67, respectively.

In pSS, lower CD24hiCD27+ B-cell counts, as well as higher Tregs/CD24hiCD27+Breg and Th1/CD24 hiCD27+Breg ratios, were associated to a higher frequency of autoantibodies and higher gammaglobulin.
Conclusions: Our findings demonstrated a significant decrease in the Breg-enriched CD24hiCD27+ B-cell subset in pSS, which presented a negative correlation with disease activity as evaluated by the ESSDAI. We demonstrated significant differences in the CD24hiCD27+ B-cell subset and respective ratios, presenting a good discriminatory capacity compared to HC. The discriminatory potential of this subset may have diagnostic utility in pSS, as it may support the presence of immune dysregulation in suspected pSS cases, that don't fulfil the classification criteria. Further studies with higher samples and a prospective design are needed to explore this hypothesis.

CO217 - ASSESSING THE QUALITY OF BIOLOGIC SWITCH DECISIONS IN PSORIATIC ARTHRITIS: DEVELOPMENT AND VALIDATION OF OUTCOMES MEASUREMENT TOOLS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease commonly managed by rheumatologists. Switching between biologic therapies is a recommended strategy for PsA patients that show insufficient response or adverse events with a biologic agent. Although the choice of the subsequent biologic may be dependent on many factors (accessibility, clinical aspects, patient's preference), assessing the quality of the switch decision is of utmost relevance.
Objectives: To develop and validate two outcomes measurement tools to evaluate the quality of biologic therapies switch in PsA patients with axial and peripheral phenotypes in clinical practice.
Methods: A Task Force and an Expert Panel were specifically assembled for this purpose. The tool development comprised a modified-Delphi method in a four-step procedure: 1) literature search and experts' opinion collection about quality indicators for PsA management; 2) Delphi design to address the development of the measurement tool; 3) three Delphi questionnaire rounds; 4) consensus meeting to discuss the results and reach a decision regarding outcomes measurement tools' components. This phase resulted in the definition of two measurement tools to evaluate the quality of biologic switch in peripheral and axial PsA. For the validation of these tools, 12 experienced rheumatologists were asked to evaluate and classify the biologic switch of 80 patient profiles (40 with peripheral PsA and 40 with axial PsA phenotypes). Clinical judgement was defined as the "gold standard" against which, tools' output was compared. Each patient profile was evaluated by 3 experts and only those with consensual clinical judgment (agreement between at least 2 of 3 rheumatologists) were included in the validation analysis. The results were used to assess the validity (by sensitivity/specificity analysis) and the reliability, more specifically inter-rater reliability, (by Cohen's kappa) of both tools.
Results: The developed tools consisted of 6 domains (disease activity, dactylitis, enthesitis, skin and nail manifestations, physical function and quality of life), their respective instruments and thresholds. The classification of the biologic switch was divided into three quality levels: "Good", based on treat-to-target thresholds; "Moderate", based on improvement from baseline thresholds; and the remaining as "Insufficient". In the validation phase, an agreement (i.e. clinical judgement versus tools' output) of 75% was obtained for peripheral PsA and 63% for axial PsA. The peripheral PsA tool was found to be more sensitive (92%) with the "Good" quality level and more specific (97%) with the

TABLE I. RESULTS OF THE TWO OUTCOMES MEASUREMENT TOOLS, COMPARED WITH THE "GOLD STANDARD" (CLINICAL JUDGEMENT)

Peripheral PsA Tool	*"Good"*	*30/40 (75%)*	*92%*	*89%*	*0.71 (95% CI = 0.59-0.83)*
	"Moderate"		*73%*	*85%*	
	"Insufficient"		*75%*	*97%*	
*Axial PsA Tool**	*"Good"*	*22/35 (63%)**	*100%**	*100%**	*0.94* (95% CI = 0.88-1.00)*
	"Moderate"		*100%**	*96%**	
	"Insufficient"		*87%**	*100%**	

1 All patient profiles (40 with Peripheral PsA and 40 with Axial PsA) were evaluated by 3 experts and the biologic switch was classified into three quality levels: "Good", "Moderate" or "Insufficient"
2 The level of agreement is defined when at least 2 of 3 experts rate the patient profile with the same switch classification as the outcomes measurement tool
3 "Sensitivity": Only of those consensual patient profiles, proportion (%) correctly classified as "Good"; "Moderate" or "Insufficient"
4 "Specificity": Only of those consensual patient profiles, proportion (%) correctly classified as not "Good"; "Moderate" or "Insufficient"
5 Reliability (i.e. inter-rater reliability) was calculated by Cohen's Kappa calculation; values above 0.61 are considered a good level of agreement
** Preliminary results: the clinical judgement corresponding to the validation of the Axial PsA outcomes measurement tool is not yet completed; only 35 of the 40 patient profiles were fully analysed by the 3 Experts*

"Insufficient" quality level. Regarding the axial PsA tool, higher sensitivity and specificity was obtained for all quality levels, as well as a higher Cohen's kappa than Peripheral PsA tool (0.94 vs 0.71).

Conclusion: The two developed outcomes measurement tools address the quality of treatment decisions regarding biologics' switch in PsA clinical practice. The data in the validation part support the tools' reliability for both peripheral and axial PsA and could complement clinical judgment too. Therefore, these fully developed and validated tools are expected to support rheumatologists in making better and more informed therapeutic decisions.

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