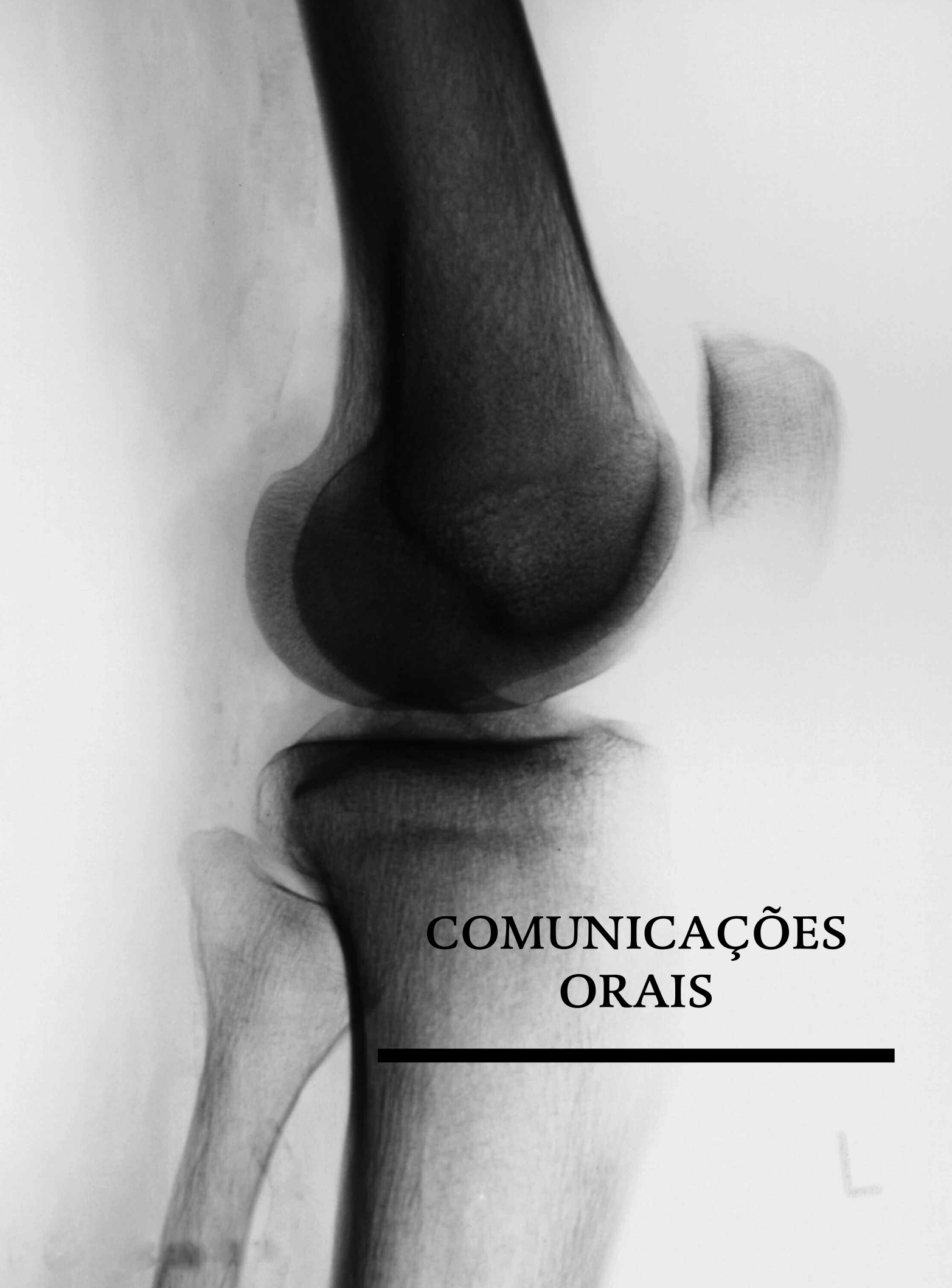

COMUNICAÇÕES ORAIS

Comunicações orais

ACTA REUMATOL PORT. 2018:43:25-45 (SUP)

CO1 – PROGRESSION OF STRUCTURAL DAMAGE ON MRI OF THE SPINE AND SACROILIAC JOINTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IS LIMITED: THE 5–YEAR RESULTS IN THE DESIR COHORT

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Background: Reliably detecting radiographic structural change in patients with axial spondyloarthritis (axSpA), especially in the sacroiliac joints (SIJ), is notoriously difficult. Magnetic resonance imaging (MRI) is an alternative for radiographs to assess structural damage. However, so far the utility of MRI in capturing change in structural damage over time has been poorly studied.

Objectives: We aimed to evaluate the change over time of structural lesions on MRI of the SIJ and spine in patients with axSpA.

Methods: Patients with recent onset (≤3 years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline and 5 years and scored by 3 trained central readers unaware of the chronology. Structural damage in the SIJ (MRI-SIJ-STR) and in the spine (MRI-spine-STR) was defined according to 3 binary rules (A1: ≥5 fatty lesions and/or erosions; B1: ≥3 erosions; and C1: ≥3 fatty lesions) and 3 continuous scores (A2: number of fatty lesions /erosions; B2: number of erosions; and C2: number of fatty lesions). For binary outcomes, structural damage was defined by the agreement of at least 2 out of 3 readers and the % of net progression by subtracting the number of patients that 'improved' from those that 'worsened' divided by the total number of patients with complete baseline and 5-year data. For continuous outcomes, the mean of the 3 readers was used and the difference between year 5 and baseline was calculated.

Results: In total, 151 and 145 patients had complete MRI-SIJ and MRI-spine data available from 3 readers, respectively. The percentages of net progression at SIJ level are summarized in the Figure 1. These were 6.6%, 0.7% and 7.9% for the binary outcomes A1, B1 and C1 respectively. Notably, the percentage of 'improvement' (4.6%) was almost as high as the percentage of 'worsening' (5.3%) for definition B1 (≥3 erosions); while no 'improvements' were seen by the 3 readers for definition C1 (≥3 fatty lesions). Similar differences were seen for the mean (standard deviation) change of the 3 MRI-SIJ-STR continuous outcomes (A2: 1.02 (2.60); B2: 0.20 (1.39); and C2: 0.83 (2.20); p<0.01 for all). MRI-spine-STR net change over time was almost absent (A1: -0.7%; B1: 0.0%; C1: 0.7%) considering the binary outcomes, and small (though statistically significant) considering definition A2 (0.18 (0.52); p<0.01) and C2 (0.14 (0.48); p<0.01) but absent for

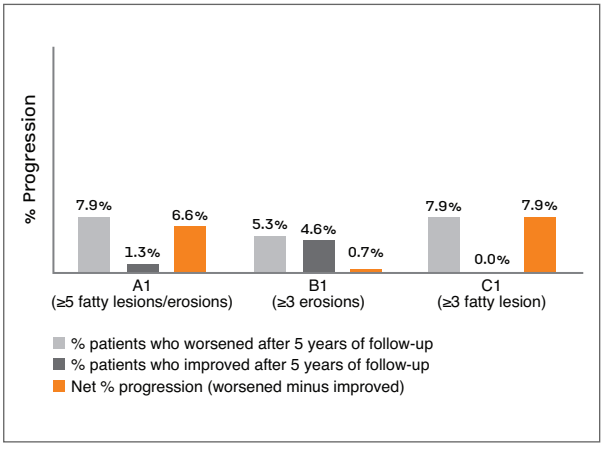

FIGURE 1. Changes in different binary MRI-SIJ-STR outcome measures. All outcomes are assessed according to the '2 out of 3' definition in the completers population (N=151). MRI-SIJ-STR, structural damage on magnetic resonance imaging of the sacroiliac joints.

definition B2 (0.03 (0.24); p=0.109).
Conclusion: These results suggest that patients with early axSpA only show modest structural progression in the MRI of the SIJ and that fatty lesions are more sensitive to change compared to erosions. In this early axSpA population, MRI-detected structural progression in the spine is very limited/absent.

CO8 – PERFORMANCE OF REFERRAL STRATEGIES FOR SPONDYLOARTHRITIS: A POPULATION-BASED NATIONWIDE STUDY

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Background: Several strategies have been proposed to promote early referral of patients with axial spondyloarthritis (axSpA), but consensus on the 'best' strategy is yet to be achieved. Moreover, few studies compared referral strategies (RS) head-to-head and, up to now, none has neither evaluated these in a 'nationwide' setting (external validity) nor assessed the entire spectrum of SpA (i.e. axSpA and peripheral SpA).
Objectives: To evaluate the performance of the screening strategy for SpA of a nationwide epidemiological study (EpiReumaPt), as compared to previously proposed RS.
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 (RD), such as SpA. In the second phase, positive screenings for ≥1 rheumatic complaint plus 20% negative screenings were invited for an assessment by the rheumatologist. Finally, 3 rheumatologists revised all the information and defined the final diagnosis by consensus. All participants of the second phase were included (N=3,877). Each RS (Table I) was tested against the SpA revised diagnosis using the following metrics:

TABLE I. PERFORMANCE OF THE REFERRAL STRATEGIES AGAINST THE RHEUMATOLOGIST CLINICAL DIAGNOSIS (N=3,877; PRE-TEST PROBABILITY: 1.6% – WEIGHTED NATIONAL SPA PREVALENCE)

	Sensitivity (%)	Specificity (%)	PPV (%)	1-NPV (%)
ASAS	85.4	38.8	2.2	0.6
EpiReumaPt	72.1	67.6	3.5	0.7
CafaSpA one	56.3	69.7	2.9	1.0
Brandt I	49.2	79.3	3.7	1.0
Braun IBP	47.5	78.7	3.5	1.1
MASTER	36.7	87.7	4.6	1.2
Brandt II	27.7	92.4	5.6	1.3
Hermann	22.4	93.2	5.1	1.3
CafaSpA two	15.2	95.2	4.9	1.4
Braun 2 step	15.1	95.7	5.3	1.4
Brandt III	7.9	98.4	7.6	1.5

ASAS (≥1/5+): IBP (ASAS definition), good response to NSAIDs, family history of SpA, peripheral manifestations (arthritis, enthesitis and/or dactylitis), extra-articular manifestations (uveitis, psoriasis and/or IBD); **EpiReumaPt (≥1/5+):** previous SpA/PsA diagnosis, IBP (≥3/8 features), CBP (≥3 months) starting <45 years and ≥1/6 SpA features, dactylitis, enthesitis; **CafaSpA one (≥1/3+):** IBP (ASAS definition), good response to NSAIDs, family history of SpA; **CafaSpA two (≥2/3+):** see CafaSpA one; **Brandt I (≥1/1+):** IBP (morning stiffness >30 min, pain at night/early morning, improvement by exercise; ≥1/3); **Brandt II (≥1/1+):** ≥3/3 IBP features (see Brandt I); **Brandt III (≥1/1+):** ≥3/3 IBP features (see Brandt I); **Braun IBP (≥2/5+):** start BP ≤35 years, waking second half of the night, alternating buttock pain, improvement by movement, not rest; **MASTER (≥2/3+):** IBP (morning stiffness >30 min, improvement exercise, not rest, awakening in the night because of BP), good response to NSAIDs, family history of AS; **Hermann (≥1/1):** IBP (Calin's criteria): **Braun 2 step (≥ 2/3):** psoriasis, alternating buttock pain, improvement BP by exercise. HLA-B27 excluded from ASAS, Brandt I-III and Braun 2 step; elevated CRP/ESR excluded from ASAS.
PPV: positive predictive value; 1-NPV 1:negative predictive value

sensitivity, specificity, positive predictive value (PPV), and post-test probability of disease given a negative test (1-negative predictive value). RS with an imaging (e.g. MRI) or laboratory component (e.g. CRP, HLA-B27) were modified (by excluding these components) given limited data obtained in the survey (Table I). A weighting factor was used to take the survey design into account.

Results: From the total 3,877 participants, 92 received a SpA diagnosis [weighted prevalence: 1.6% (95%CI: 1.2; 2.1)], 3,107 other RD diagnosis [e.g. knee osteoarthritis (31%)] and 678 no RD diagnosis. The ASAS RS was the most sensitive (85%) followed by the EpiReumaPt strategy (72%) (Table I). The ASAS and EpiReumaPt RS had the lowest post-test probabilities of SpA in the presence of negative screening (0.6% and 0.7% respectively), thus, yielding a marked decrease in the probability of disease if negative [(1.6--0.6)/1.6*100=63%; (1.6-0.7)/1.6*100=56% respectively). On the other hand, the likelihood of SpA increased by 38% (2.2-1.6)/1.6*100) and 119% (3.5--1.6)/1.6*100) in case of a positive ASAS and EpiReumaPt RS, respectively. Brandt III was the least sensitive strategy in this study and not contributive to excluding SpA (1-NPV: 1.5%; pre-test probability: 1.6%), but expectedly increased the likelihood of SpA by 3.8 times if positive. The performance of the remaining RS is described in the Table I.

Conclusion: For the first time, a wide range of SpA RS were tested head-to-head in a population-based setting where the ASAS and EpiReumaPt RS were shown to be the most sensitive. Our data suggest that these strategies can be effectively used as screening tools for SpA especially when laboratory and imaging data are not available.

CO15 - ELIGIBILITY CRITERIA FOR TNFi THERAPY IN axSpA: GOING BEYOND BASDAI

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Background: A BASDAI ≥4 has been often required to start TNFi therapy in patients with axSpA. However, this cut-off of high disease activity (HDA) is largely arbitrary. Unlike BASDAI, ASDAS incorporates objective measures (e.g. CRP) and has a validated definition of HDA (≥2.1). It has thus been suggested that ASDAS could also be used to guide treatment decisions, but evidence to support this is still scarce.

Objective: To compare the impact of applying the ASDAS and BASDAI definitions of HDA in selecting patients for TNFi-treatment in daily clinical practice.

Methods: Patients from Reuma.pt (Rheumatic Diseases Portuguese Register), with diagnosis of axSpA according to their rheumatologists (both treated and not treated with their first TNFi), with complete baseline BASDAI and ASDAS data, and complete 6-month of follow-up (i.e. baseline, 3 and 6 months visits available) were included. Four subgroups [cross-tabulation between ASDAS (≥2.1) and BASDAI (≥4) definitions of HDA], were compared according to baseline demographic and clinical characteristics in the 'eligible population' (i.e. irrespective of TNFi-treatment). In addition, for patients starting TNFi and with complete follow-up BASDAI/ASDAS data ('efficacy population'), the subgroups were also compared according to different response criteria (see Table I), at 3 and 6 months.

Results: In total, 466 patients were included (59% males and 66% HLA-B27 positive). The large majority

TABLE I. TNFi RESPONSE CRITERIA ACROSS SUBGROUPS ACCORDING TO BASDAI/ASDAS CATEGORY ('EFFICACY POPULATION')

Variables	Overall (N=296)*	ASDAS ≥2.1		ASDAS <2.1		p-value**
		BASDAI ≥4 (N=256)	BASDAI <4 (N=34)	BASDAI ≥4 (N=1)	BASDAI <4 (N=5)	
Outcomes – 3 months, n (%)						
ASAS20	159 (59)	142 (60)	15 (56)	0 (0)	2 (40)	0.48
ASAS40	127 (47)	111 (46)	14 (52)	0 (0)	2 (40)	0.74
ASAS PR	73 (26)	56 (22)	14 (56)	0 (0)	3 (60)	<0.01
BASDAI50	184 (62)	160 (63)	21 (62)	0 (0)	3 (60)	0.64
ASDAS CII	207 (70)	179 (70)	26 (77)	0 (0)	2 (40)	0.16
ASDAS MI	123 (42)	111 (43)	12 (35)	0 (0)	0 (0)	0.16
ASDAS ID	90 (30)	66 (26)	20 (59)	0 (0)	4 (80)	<0.01
Outcomes – 6 months, n (%)						
ASAS20	160 (61)	139 (61)	18 (62)	0 (0)	3 (60)	0.67
ASAS40	124 (46)	104 (45)	17 (57)	0 (0)	3 (60)	0.43
ASAS PR	74 (27)	57 (24)	13 (48)	0 (0)	4 (80)	<0.01
BASDAI50	188 (64)	167 (65)	18 (53)	0 (0)	3 (60)	0.29
ASDAS CII	216 (73)	190 (74)	25 (74)	0 (0)	1 (20)	0.02
ASDAS MI	128 (43)	117 (46)	11 (32)	0 (0)	0 (0)	0.08
ASDAS ID	84 (28)	63 (25)	17 (50)	0 (0)	4 (80)	<0.01

*axSpA patients treated with TNFi, with complete 6 months of follow-up and data for BASDAI/ASDAS at every time-point; **comparison between subgroups according to BASDAI/ASDAS category of disease activity (ANOVA for continuos variables and Chi2 for categorical variables).
ASDAS CII: ASDAS clinically important improvement; ASDAS MI: ASDAS major improvement; ASDAS ID: ASDAS inactive disease

(n=382; 82%) fulfilled the definition of HDA according to both BASDAI and ASDAS at baseline (i.e. BASDAI≥4 and ASDAS≥2.1). The frequency of ASDAS≥2.1, if BASDAI<4, was much higher than the opposite condition (i.e. ASDAS<2.1, if BASDAI≥4) (70% vs 0.5%). Compared to patients fulfilling both definitions, those who were ASDAS≥2.1 only, were more likely to be male (82.5% vs 54%), HLA-B27 positive (79% vs 54%), to show higher levels of CRP (2.6 ± 2.5 vs 2.2 ± 2.8mg/dL) and lower BASFI (3.1 ± 2.6 vs 5.6 ± 2.3). In the 'efficacy population' (n=296), better responses were observed among patients with ASDAS≥2.1 only, especially for the most 'stringent' outcomes [e.g. ASDAS inactive disease (ASDAS ID): 59% and 50%, at 3 and 6 months respectively], compared to patients fulfilling both definitions (ASDAS ID: 26% and 25% at 3 and 6 months respectively) (Table I).

Conclusion: Our results show that the ASDAS-HDA definition (ASDAS≥2.1) is more inclusive than the BASDAI-HDA definition (≥4) in selecting axSpA patients for TNFi treatment. Importantly, the additionally 'captured' patients respond better and have higher likelihood of predictors thereof. These results support the use of ASDAS≥2.1 as a selection criterion for treatment decisions.

Disclosures: Supported in part by a research Grant from Investigator-Initiated Studies program of MSD.

C035 – PATTERN OF DRUG USE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND REASONS FOR DRUG DISCONTINUATION IN REAL WORLD CLINICAL PRACTICE

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Background: Pharmacological treatment for systemic lupus erythematosus (SLE) is aimed at reducing disease activity, preventing flares and minimizing the damage. The use of medication varies widely and therapeutic strategies are well defined only for certain organ manifestations. Hydroxychloroquine is the standard treatment for most SLE patients during the entire disease course, while immunosuppressants are recommended for those with severe organ involvement. Belimumab is the only biological currently licensed for SLE, although others are used off-label in clinical practice.
Objectives: To describe the real-world patterns of drug use in SLE patients, and their relationship with disease phenotype. To describe reasons for drug discontinuation and drug retention (DR) in SLE patients.
Methods: Observational study of adult SLE patients registered in Reuma.pt, who have clinical diagnosis of SLE, followed for at least 1 year and with available data on medication. Sociodemographic and clinical characteristics were compared among treatment groups de-

TABLE I. SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS ACCORDING TO TREATMENT GROUPS

	Sensitivity (%)	Specificity (%)	PPV (%)	1-NPV (%)
ASAS	85.4	38.8	2.2	0.6
EpiReumaPt	72.1	67.6	3.5	0.7
CafaSpA one	56.3	69.7	2.9	1.0
Brandt I	49.2	79.3	3.7	1.0
Braun IBP	47.5	78.7	3.5	1.1
MASTER	36.7	87.7	4.6	1.2
Brandt II	27.7	92.4	5.6	1.3
Hermann	22.4	93.2	5.1	1.3
CafaSpA two	15.2	95.2	4.9	1.4
Braun 2 step	15.1	95.7	5.3	1.4
Brandt III	7.9	98.4	7.6	1.5

ASAS (≥1/5+): IBP (ASAS definition), good response to NSAIDs, family history of SpA, peripheral manifestations (arthritis, enthesitis and/or dactylitis), extra-articular manifestations (uveitis, psoriasis and/or IBD); **EpiReumaPt (≥1/5+)**: previous SpA/PsA diagnosis, IBP (≥ 3/8 features), CBP (≥ 3 months) starting <45 years and ≥ 1/6 SpA features, dactylitis, enthesitis; **CafaSpA one (≥1/3+)**: IBP (ASAS definition), good response to NSAIDs, family history of SpA; **CafaSpA two (≥2/3+)**: see CafaSpA one; **Brandt I (≥ 1/1+)**: IBP (morning stiffness>30 min, pain at night/early morning, improvement by exercise; ≥1/3); **Brandt II** (≥ 1/1+): ≥2/3 IBP features (see Brandt I); **Brandt III** (≥ 1/1+): ≥3/3 IBP features (see Brandt I); **Braun IBP (≥ 2/5+)**: start BP≤35 years, waking second half of the night, alternating buttock pain, improvement by movement, not rest; **MASTER (≥ 2/3+)**: IBP (morning stiffness>30 min, improvement exercise, not rest, awakening in the night because of BP), good response to NSAIDs, family history of AS; **Hermann (≥1/1)**: IBP (Calin's criteria): **Braun 2 step (≥ 2/3)**: psoriasis, alternating buttock pain, improvement BP by exercise. HLA-B27 excluded from ASAS, Brandt I-III and Braun 2 step; elevated CRP/ESR excluded from ASAS.
PPV: positive predictive value; 1-NPV 1:negative predictive value

fined as: group 1 antimalarials ± glucocorticoids (GCs); group 2 immunosuppressants (azathioprine (AZA)/mycophenolate mofetil (MM)/methotrexate (MTX)) ± (antimalarials ± GCs); group 3 biologics ± immunosuppressants ± (antimalarials ± GCs). To assess possible differences between the groups, univariate regression analyses were made. DR was assessed by Kaplan-Meier survival analysis. In all analyses significance level was set at 0.05.

Results: A total of 824 SLE patients were included, mean age of 47.3±14.4 years, 92.3% female. The mean age at first symptoms was 31.6±14.1 and at SLE diagnosis of 34.1±14.3 years. On their last assessment, 678 (82.3%) were being treated with antimalarials, 463 (56.2%) GCs, 343 (41.6%) immunosuppressants (149 AZA, 99 MM, 67 MTX, 14 cyclosporine, 11 cyclophosphamide (CP), 3 leflunomide), 53 (6.4%) biologics (32 rituximab, 21 belimumab) and 26 (3.2%) were off medication. The sociodemographic and clinical characteristics according to treatment groups are shown in Table I. Gender distribution was similar across groups. A high prevalence of women, Caucasians, non-smokers, acute cutaneous lupus and arthritis was found in all groups. Patients in group 1 had lower disease activity measured by SLEDAI, less organ damage measured by SLICC and lower score on physician's global assessment. In group 2 patients were younger and had higher prevalence of renal involvement. Patients in group 3 had higher SLEDAI score and damage, higher prevalence of mucocutaneous, articular, neurologic and hematologic involvement and more use of GCs. The main reported reasons for discontinuation of antimalarials and rituximab were adverse events (AE) in 19 (41.3%) and 4 (33.3%), respectively; AZA, MM, MTX and belimumab was loss of response in 25 (60.9%), 7 (38.9%), 8 (33.3%) and 4 (30.8%), respectively; CP was remission in 5 (50%). DR was higher with antimalarials (9.3 years (mean)) and smaller with belimumab (1.9 years (mean)).

Conclusion: Almost all SLE patients with established disease were chronically medicated, most with antimalarials ± GCs. As expected, this group 1 had less severe disease. Patients under immunosuppressants had a higher frequency of renal involvement, which denotes a targeted therapeutic strategy. In routine clinical settings biologics are rarely used, being restricted to patients with very active SLE and multiple clinical manifestations. Treatment persistence on antimalarials is high, and AE are the most frequent reason for its discontinuation.

C040 – REUMAHEART: CARDIOVASCULAR RISK IN INFLAMMATORY RHEUMATIC DISEASE – A PORTUGUESE POPULATION BASED STUDY

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Introduction: Individuals diagnosed with rheumatic diseases have shown an increased risk of developing several comorbid conditions, of which cardiovascular (CV) comorbidities are the most common and have the greatest effect on mortality. Our global aim is to assess the impact of Inflammatory Rheumatic Diseases (IRD) in the development of cardiovascular diseases controlling for traditional CV risk factors in a Portuguese national-wide population-based cohort.

Methods (study design, setting, participants, exposure, outcome, analytics): This study used data from a population-based longitudinal cohort study – the EpiDOC cohort. IRD participants ere selected according to Rheumatoid Arthritis (RA), Systemic Lupus Erythematous (SLE), Ankylosing Spondylitis (SpA) and polymyalgia rheumatic (PMR) diagnosis criteria fulfilment. Outcome was defined as a composite of myocardial infraction or angor pectoris (ischemic heart disease), arrhythmias, valvular disease, stroke or transient ischemic attack and peripheral artery disease. Multivariate logistic regression models were used to assess

predictors of CV events in IRD participants. Calibration and discrimination of a predictive model were assessed by goodness-of-fit and area under receiver operating characteristic curve.

Results: In a national cohort of 10 661 people, patients with RA (n=61), SLE (n=13), SpA (n=92), PMR (n=8) were identified. Patients with IRD had similar age as non-IRD (mean age 55 vs 53-year-old; 72,1% female), with a predominance of dyslipidaemia diagnosis (40.7% vs 31.4%; p=0,033) and sedentary lifestyle (exercise practise 22.7% vs 33%; p=0,016). IRD participants were followed by a median follow-up of 2.6 years compared with 2.4 years in the non-IRD group (p<0,01). Cardiovascular events were proportional in both populations, leading ischemic heart disease on IRD group (34.6%) and arrhythmias in controls (29.4%). After adjustment for risk factors, the odd of cardiovascular event is high (OR 1.64, 95% CI: 1.04--2.58; p=0.03). A stepwise approach to find the best predictive model attained that gender, age, history of hypertension, body mass index, IRD and follow-up time are the most important predictive variables of CV event, with an area under ROC of 0,80.

Conclusions: We report an increase odd of major CV events in inflammatory rheumatic disease in Portugal adjusting for potential modifiers. This study brings forward a contemporary awareness of physicians and patients with IRD for a premature identification and control of higher risk patients among this population.

C045 – DETERMINANTS OF NON-NOCICEPTIVE PAIN IN RHEUMATOID ARTHRITIS

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Introduction: Neuropathic component (NP) of Rheumatoid Arthritis (RA) pain was described in nearly a third of the patients. Radiographic damage is a reflection of cumulative disease activity and other pathophysiological processes. Some clinical predictors of RA NP were recently identified by our group, but association and adjustment for radiographic damage were not studied.

Objectives: To estimate the clinical predictors of NP in RA patients adjusting for their radiographic damage.

Methods: Cross-sectional study was performed with RA patients followed at our Rheumatology department. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit. Demographic, clinical and laboratorial data were collected and two questionnaires were applied to assess NP: the Leeds Assessment of Neuropathic Symptoms (LANSS) and the painDETECT (PDQ). Wrists, hands and feet radiographic studies from the previous 12 months were classified according to the modified van der Heijde Sharp s method by one trained reader, blinded for patient clinical variables and treatment allocation. Univariate and multivariate logistic regression were performed adjusting for global radiographic score (GS). Significance level was set as <0.05.

Results: Ninety one RA patients were included. Seventy (77%) were women, with a mean (SD) age of 55.6 (10.8) years and median disease duration of 12 years (range: 2–41); 84% patients were seropositive for Rheumatoid Factor and/or ACPA; 85 (93%) were treated with DMARDs and 41% with a biological DMARD (bDMARDs). The mean (SD) DAS28 4V CRP was 3.15 (0.77). The median joint erosion score (JE) was 28 (range: 3-143) and the median joint space narrowing (JN) was 46 (range: 10-133). Forty-two (46%) patients had NP by the LANSS (≥12) and 29% had a possible/likely NP in the PDQ (>12). JN was a significant negative predictor of LANSS NP (OR: 0.98, p=0.02). After adjusting for GS, gender was not associated with NP. Pain VAS, patient global activity and the tender joint count were positive predictors of NP by both tests. Swollen joint count, ESR or CRP levels were not significantly associated with NP. DAS 28 CRP was a significant positive predictor of NP by both tests (OR 1.89 for LANSS; OR: 2.06 for PDQ, p<0.05); as well as the HAQ score (OR: 2.68 and OR: 4.85, respectively, p<0.05). Positivity for ACPA was a negative predictor of LANSS NP once more (OR: 0.31, p=0.048). Current methotrexate had lower odds of LANSS NP (OR: 0.35, p=0.04) but did not remained significant after adjustment for DAS28 CRP. Previous/current Hydroxychloroquine (HCQ) treatment was again a negative predictor for PDQ NP (OR: 0.11, p<0.04) and remained significant after adjustment for DAS28 CRP. Previous/current leflunomide (LFN) was newly a positive predictor of NP in both tests (OR: 3.41 for LANSS and

OR: 2.95 for PDQ, p<0.05), persisting significant after disease activity adjustment. No other significant associations were found.

Conclusions: Consistently with our previous data, this study supports an association between NP and disease activity/functional scores but not with objective inflammatory measures. Possible increased risk of NP in LFN treated patients was newly pointed and protective role of ACPA positivity and HCQ was reinforced.

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C053 – MEMBRANOUS VERSUS PROLIFERATIVE LUPUS NEPHRITIS: TWO DIFFERENT DISEASES?

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Background: Lupus nephritis (LN) is currently classified according to the 2003 International Society of Nephrology/Renal pathology Society (ISN/RPS) classification system, which is based on histology.(1) Most patients have proliferative lupus nephritis (PLN), which has been the most studied type of LN. Membranous lupus nephritis (MLN) is less frequent, accounting for 10-20% of the cases.(2) In some patients there is a combination of the two types.

Objectives: To compare MLN and PLN with respect to demographic, clinical and laboratory characteristics.

Methods: Single-centre retrospective observational study. All patients with biopsy-proven proliferative (class III and IV), membranous (class V) and mixed (class III or IV + V) LN (according to the 2003 ISN/RPS classification), followed at UCLH Rheumatology department from 1975 to 2017, were included. Individual clinical files were reviewed to obtain demogra-

TABLE I. COMPARISON BETWEEN THE THREE GROUPS OF PATIENTS

	Class III and IV	Class V	III+V or IV+V	p
Total, N	135	38	14	
Sex				
F, N (%)	123 (91)	33 (87)	11 (79)	0.303
M, N (%)	12 (9)	5 (13)	3 (21)	
Ethnicity				
Caucasian, N (%)	67 (50)	12 (32)	3 (21)	0.044
Afro-Caribbean, N (%)	35 (26)	18 (47)	6 (43)	
Asian, N (%)	33 (24)	8 (21)	5 (36)	
uPCR at LN diagnosis, median; IQR	261.5; 372	254.0; 276	143.0; 195	0.663
Creatinine at LN diagnosis, median; IQR	73.5; 40	54.5; 17	73; 58	0.106
Albumin at LN diagnosis, median; IQR	32.5; 13	31; 9	35; 4	0.624
C3 at LN diagnosis, median; IQR	0.61; 0.34	0.81; 0.57	0.64; 0.32	0.002
Anti-dsDNA at LN diagnosis, median; IQR	863.0; 1616.75	80; 149.5	296; 242	0.000
Ever Low C3, N (%)	107 (80)	35 (92)	11 (79)	0.203
Ever anti-dsDNA positive, N (%)	111 (83)	32 (84)	12 (86)	0.950
Ever anti-Sm positive, N (%)	25 (19)	16 (42)	6 (43)	0.004
Ever anti-RNP positive, N (%)	42 (31)	19 (50)	8 (57)	0.030
Ever anti-Ro positive, N (%)	54 (40)	16 (42)	10 (71)	0.081
Ever anti-La positive, N (%)	21 (16)	3 (8)	4 (29)	0.168
Use of antimalarials, N (%)	82 (66)	27 (73)	9 (69)	0.732
Use of immunosuppressants, N (%)	121 (95)	35 (95)	14 (100)	0.669
Use of corticosteroids, N (%)	125 (97)	36 (95)	13 (93)	0.668

F: females; M: males; uPCR: urinary protein-creatinine ratio; LN: Lupus nephritis; N: number; IQR: interquartil range

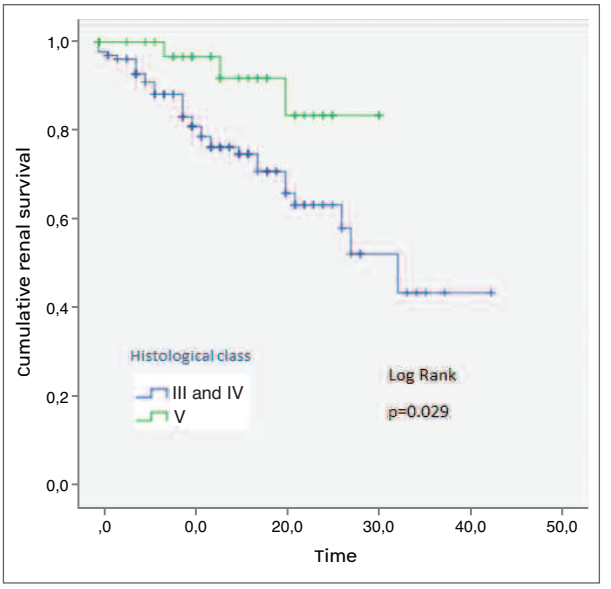

FIGURE 1. Kaplan-Meier curves showing renal survival for patients with membranous and proliferative lupus nephritis

phic, clinical, laboratory and pathological data. We also recorded data on treatment with corticosteroids, immunosuppressants and antimalarials. We compared groups using Pearson's chi-squared test for qualitative variables and Mann-Whitney test for quantitative variables. Renal survival was analysed through the Kaplan--Meier method. Significance level was defined at 0.05.

Results: 187 patients were included (Table I). Age at diagnosis was not significantly different between groups (p=0.474). The groups differ regarding ethnicity – higher proportion of Caucasians with PLN versus higher proportion of Afro-Caribbeans with MLN. Patients with MLN present with higher C3 levels and significantly lower anti-dsDNA levels than the ones with proliferative changes. Conversely, the proportion of positive anti-Sm and anti-RNP antibodies is lower in patients with pure PLN. Thirty-four patients with PLN, 3 with MLN and 2 with mixed nephritis, progressed to end-stage renal disease. Cumulative renal survival rates at 5, 10, 15 and 20 years were 91, 81, 75 and 66% for PLN and 100, 97, 92 and 84% for MLN, respectively (Figure 1).

Conclusions: In spite of presenting in the context of the same autoimmune systemic disease, PLN and MLN appear to be very different entities, showing significant differences regarding serologic profiles and renal survival.

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C055 – COMPARATIVE LONG-TERM EFFECTIVENESS OF SWITCHING TO ANOTHER TUMOUR NECROSIS FACTOR ANTAGONISTS, TOCILIZUMAB OR RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO A FIRST-LINE TNF INHIBITOR

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Background: Tumour necrosis factor inhibitors (TNFi) are highly effective treatments for active Rheumatoid Arthritis (RA). However, up to 40% of patients either fail to respond adequately to TNFi or lose response over time. Options available for these patients include treatment with a second TNFi or switching to a biological therapy with a different target such as Tocilizumab (TCZ) or Rituximab (RTX).

Objectives: To compare the effectiveness of a 2nd TNFi, TCZ or RTX, measured by stratified persistency rates, in RA patients with previous inadequate response to their 1st TNFi; to compare the response rates of TNFi, TCZ

TABLE I. PERCENTAGE OF PATIENTS WHO REMAINED ON THERAPY, AT 6 MONTHS, 1, 2, 3, 4 AND 5 YEARS, FOR EACH THERAPEUTIC GROUP

Survival Rate n(%)	TNF inhibitor n=390	Tocilizumab n=147	Rituximab n=106
6 Months	71%	81%	85%
1 Year	62%	78%	82%
2 Years	52%	77%	78%
3 Years	46%	73%	72%
4 Years	41%	70%	67%
5 Years	29%	64%	50%

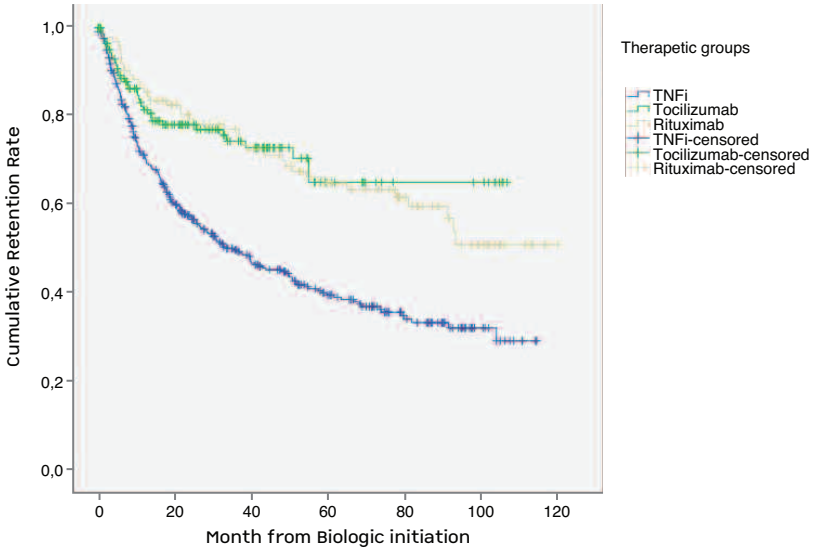

FIGURE 1. Persistency by months for each group therapeutic.

or RTX at 6 months, 1 and 2 years; to clarify the frequency and reasons for treatment discontinuation.

Methods: Non-interventional prospective study of RA patients exposed to a 2nd TNFi, TCZ or RTX treatment after previous TNFi descontinuation using real-world data from the Reuma.pt database. Patient baseline characteristics (demographic data, disease characteristics and activity), disease activity at follow-up (6 and 12 months and every year thereafter), discontinuation date and reason were collected and compared according to biologic class. Persistency of RTX, TCZ and TNFi were estimated using Kaplan-Meier analysis, from initiation of each therapy until discontinuation/ switch and last follow-up visit. All analyses were performed with SPSS v23 and significance level was set at 0.05.

Results: 643 patients were included, 88.8% females, with a mean age of 59.4 (±12.8) years and mean disease duration until 1st biologic of 10.1 (±8.5) years. After 1st TNFi discontinuation, 390 (60.7%) patients initiated a 2nd TNFi, 147 (22.9%) TCZ and 106 (16.5%) RTX. There were no significant differences in patient and disease characteristics among the 3 groups, except for extra-articular manifestations, higher in RTX group (p=0.013), education (p=0.002) and current full-time employment (p<0.001), both lower in RTX patients. At baseline, TNFi group included more patients treated with concomitant methotrexate (p=0.002) and a higher swollen joint count-28 (p=0.010). However, the disease activity according to DAS28, CDAI and SDAI were similar between the different therapy groups at baseline. The persistency rates according to Kaplan-Meier survival curve were significantly greater (log rank test, p<0.001) among patients who initiated TCZ or RTX after TNFi failure,

compared with those who initiated a 2nd TNFi (Figure 1, Table I). The multivariate analysis showed a lower risk of discontinuation for TCZ (HR 0.39, 95% CI 0.23 to 0.64, p<0.001) and RTX (HR 0.42, 95% CI 0.25 to 0.72, p=0.001) and a significant risk for discontinuation for smoking (HR 2.43, 95% CI 1.50 to 3.95, p<0.001) and higher HAQ at baseline (HR 1.51, 95% CI 1.14 to 2.00, p=0.004), adjusted for gender, disease duration and comorbidities. The proportion of patients with a EULAR good response at 6 months (p<0.001), 1 (p<0.001) and 2 years (p=0.021) were, respectively, 23.7%, 28.0%, 31.4% for TNFi, 51.7%, 54.4%, 55.9% for TCZ and 27.5%, 23.1%, 25.6% for RTX. The main reason for discontinuation was inefficacy in the case of TNFi and RTX and adverse events in the case of TCZ (p<0.001).

Conclusions: Our findings showed a significantly higher drug retention for RTX and TCZ compared with 2nd TNFi and a similar persistence among RTX and TCZ, in patients with a previous TNFi discontinuation. These data corroborate the notion that switching to a biologic with a different mechanism of action might be more effective after prior TNFi discontinuation.

C087 – FALL DETERMINANTS IN THE ADULT PORTUGUESE POPULATION

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Introduction: Falls are a major public health issue, given its prevalence and social impact. This study aimed to (1) characterize fallers in the adult Portuguese population as well as (2) identify falls determinants.

Methods: Our data of 7403 adults (≥18 years) was retrieved from phase 1 survey of EpiReumaPt, a representative sample of adult Portuguese population. We analyzed sociodemographic variables and the presence of chronic diseases, which was evaluated by self-report. Anxiety/depression symptoms were assessed using The Hospital Anxiety and Depression Scale (HADS). Fall was defined by the presence of a self-report fall in the previous 12 months to the interview. Univariate and Multivariable logistic regression were used to assess fall determinants. Analyses were conducted in Stata v13.

Results: The estimated prevalence of falls in the Portuguese population is 24,1%. Women are at 2.12 times higher risk of fall than man (95% CI 1.79 – 2.51) and there's also a progressive increasing association between age and falls, with people with 75+ years having greater odds of falling (OR = 1.86 95% CI 1.49 – 2.31). Different chronic health conditions were identified as major determinants of falls in the Portuguese population. Neurologic (OR = 1.64 95% CI 1.17 – 2.32) and rheumatic (OR = 1.44 95% CI 1.18 – 1.74) disease were significantly and independently associated with falls. Similar results were found for presence of anxiety (OR = 1.33 95% CI 1.04 – 1.71) or depression (OR = 1.61 95% CI 1.20 – 2.15) symptoms.

Conclusion: Our results show a perspective of the determinants of falls in the Portuguese population, allowing us to know that women and elders are at greater risk. We have showed that some chronic diseases are associated with falls, in particular musculoskeletal and mental diseases. Implementing specific and adapted prevention strategies might reduce the number and complications of falls ultimately improving Portuguese overall health.

C093 – RETENTION OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS WITH CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS: A STUDY FROM THE TOCERRA COLLABORATION

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TABLE I. BASELINE CHARACTERISTICS

	TCZ mono (N=585)	TNFicombo (N=4163)	p
Age, yr (median, IQR)	57.8 [44.2-65.5], n=585	54.3 [44.2-61.7], n=4161	<0.001
Female gender, N (%)	485 (82.9%), n=585	3333 (80.1%), n=4161	0.12
Disease duration, yr (median, IQR)	9.7 [4.5-16.7], n=569	7.8 [3.3-14.3], n=3575	<0.001
Seropositivity (RF and/or ACPA), N (%)	445 (83.6%), n=532	2573 (81.0%), n=3175	0.17
N previous bDMARDs, N (%)			<0.001
1	250 (42.7%)	2882 (69.2%)	
2	206 (35.2%)	526 (12.6%)	
≥3	129 (22.1%)	755 (18.1%)	
Glucocorticoids	193 (33.0%), n=585	2487 (59.7%), n=4163	<0.001
Concomitant csDMARD			–
MTX	–	1766 (42.4%)	
MTX + other	–	1291 (31.0%)	
Other	–	1106 (26.6%)	
CDAI (mean, SD)	23.2 (16.1), n=322	21.9 (14.7), n=3021	0.25
HAQ (mean, SD)	1.4 (0.7), n=226	1.1 (0.7), n=2429	<0.001

IQR: interquartil range; yr: years; N: number; RF: rheumatoid factor; ACPA: anti–citrullinated peptide antibodies; MTX: methotrexate; SD: standard deviation

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Background: Tocilizumab (TCZ) as monotherapy has been shown to be more efficacious than the TNF inhibitor (TNFi) adalimumab as monotherapy in patients with rheumatoid arthritis (RA). However, effectiveness data comparing TCZ as monotherapy versus TNF inhibitors in combination with csDMARDs are limited.
Objectives: To examine retention of TCZ administered alone (TCZ mono) versus TNFi in combination with csDMARDs (TNFi combo) in patients with RA who had an inadequate response to ≥1 TNFi (TNFi-IR).
Methods: Patients with RA who were TNFi-IR and treated with TCZ mono or TNFi combo with baseline (BL) data, not immediately lost to follow-up and started treatment after TCZ was available across 9 European registries in TOCERRA from 2009 to 2016 were included. The hazard for TCZ discontinuation was modeled using a country-stratified Cox proportional hazards model, adjusting for age, gender, disease duration, seropositivity, HAQ and CDAI at BL, number of previous csDMARD and biologic DMARD (bDMARD), glucocorticosteroid and calendar year of treatment initiation. Missing data on covariates were imputed using multiple imputation with chained equations.
Results: A total of 4748 patients were eligible, including 585 who received TCZ mono and 4163 who received TNFi combo. Patients who received TCZ mono were older with a longer disease duration, more previous bDMARDs and less glucocorticosteroids at baseline (Table I) compared with patients who received TNFi combo. The crude median retention for TCZ mono was 1.82 years (95% CI: 1.59–2.09) and 1.54 years (95% CI: 1.43–1.64) for TNFi combo, (P=0.65). Causes of discontinuation differed between TCZ mono and TNFi combo (P<0. 001): TCZ mono stopped more frequently for ineffectiveness (25.7% vs. 13.8%) and TNFi combo stopped more frequently for safety issues (18.3% vs. 12.8%). In a country-stratified, covariate-adjusted analysis, we found that hazards of discontinuation were significantly lower among patients who

received TCZ mono (HR: 0.71, P<0.001). More previous treatment with bDMARDs and a greater HAQ and CDAI at BL were significantly associated with greater risk of discontinuation.

Conclusions: In routine care across 9 European countries, TCZ mono retention is better than TNFi combo in patients with RA who were TNFi-IR.

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DISCLOSURE OF INTEREST

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CO104 – A PHASE 3 RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF UPADACITINIB (ABT-494), A SELECTIVE JAK-1 INHIBITOR, IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS

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Background/Purpose: Upadacitinib (UPA) is an oral, selective JAK-1 inhibitor in development for the treatment of patients (pts) with moderate to severe rheumatoid arthritis (RA) and other immune-mediated diseases.

Methods: This Phase 3 study in pts with inadequate response (IR) to csDMARDs included a double blind placebo (PBO)-controlled period (Period 1, reported here), during which pts were randomized 1:1:1 to receive once-daily (QD) extended-release formulation of UPA at 15 mg or 30 mg, or PBO for 12 weeks (wks). The primary efficacy endpoints were the proportion of pts who achieved an ACR20 response and the proportion who achieved DAS28-CRP low disease activity (LDA, ≤3.2) at Wk 12, using non-responder imputation (NRI).

Results: Of 661 pts who were randomized, all received study drug, and 618 (93.5%) completed Period 1. At baseline, demographics and disease characteristics were similar across arms. The study met all primary and key secondary endpoints with p values < 0.001 for both doses. At Wk 12, significantly more pts receiving UPA 15 mg and 30 mg QD vs PBO achieved an ACR20 response (63.8% and 66.2% vs 35.7%, p<.001), and DAS28-CRP LDA (48.4% and 47.9% vs 17.2%, p<.001) (Table I). Onset of action was rapid with significantly more pts in both UPA arms achieving ACR20 at Wk 1 vs PBO. At Wk 12, significantly more pts met ACR50 and ACR70 in the UPA 15 mg (38% and 20.8%) and 30 mg QD arms (43.4% and 26.5%) vs PBO (14.9% and 5.9%). Significantly more patients receiving UPA 15 mg and 30 mg QD vs PBO achieved DAS28-CRP <2.6 (30.8% and 28.3% vs 10%, p<.001)] and CDAI-LDA (40.3% and 42% vs 19%, p<.001), and pts receiving UPA at both doses experienced significantly greater improvements in DAS28--CRP, HAQ-DI, morning stiffness and FACIT-F vs PBO (p<.001).

Adverse events (AEs) and serious AEs were numerically higher with UPA than PBO (Table II). The overall incidence of infection was higher for UPA 15 mg and 30 mg QD vs PBO, but few were serious infections. There were 4 cases of herpes zoster/Varicella Zoster Virus infection (1 on PBO). Asymptomatic CPK elevations were only reported for patients on UPA. Two malignancies and 3 adjudicated cardiovascular events were reported. There were no deaths, cases of TB or GI perforations. Types and frequency of laboratory abnormalities were similar to findings in Phase 2 studies with UPA.

Conclusion: The efficacy of UPA at 15 mg and 30 mg QD vs PBO was demonstrated in this csDMARD-IR study population. The most notable responses were observed in the more stringent endpoints of LDA (by either DAS28-CRP or CDAI) and ACR70. The safety and tolerability profile was consistent with observations in the Phase 2 studies with UPA.

TABLE I. EFFICACY ENDPOINTS AT WEEK 12#

Endpoint	Placebo N=221	Upadacitinib 15 mg QD N=221	Upadacitinib 30 mg QD N=219
Primary Endpoints			
ACR20 (%)	35.7	63.8***	66.2 ***
DAS28-CRP LDA (%)	17.2	48.4***	47.9 ***
Key Secondary Endpoints			
ACR20 at Week 1 (%)	8.6	22.2***	28.3***
ACR50 (%)	14.9	38.0***	43.4***
ACR70 (%)	5.9	20.8***	26.5***
DAS28-CRP <2.6 (%)	10.0	30.8***	28.3***
CDAI LDA (%)	19.0	40.3***	42.0***
Δ DAS28-CRP	-1.02	-2.20***	-2.34***
Δ HAQ-DI	-0.25	-0.59***	-0.54***
Δ SF-36 PCS	3.03	7.58***	8.01***
Δ Morning Stiffness Duration (min.)	-34.27	-85.28***	-85.13***
Δ FACIT-F	2.96	7.91***	7.74***

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; DAS28-CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire disability index; SF-36 PCS, short form 36- physical component score; LDA, low disease activity; FACIT-F, functional assessment of chronic illness therapy-fatigue (FACIT-F)
#Results for binary endpoints are based on NRI analysis. Results for DAS28-CRP and HAQ-DI are based on Multiple Imputation analysis. Results for other continuous endpoints are based on MMRM (Mixed Effect Model Repeat Measurement) analysis.
***p< .001

TABLE II. ADVERSE EVENTS SUMMARY

n (%)	Placebo N=221	Upadacitinib 15 mg QD N=221	Upadacitinib 30 mg QD N=219
Any Adverse Event (AE)	108 (48.9)	125 (56.6)	118 (53.9)
Serious AE	5 (2.3)	9 (4.1)	6 (2.7)
AE Leading To Discontinuation Of Study Drug	7 (3.2)	7 (3.2)	13 (5.9)
Severe AE	5 (2.3)	8 (3.6)	7 (3.2)
AE of Special Interest			
Infection	47 (21.3)	64 (29.0)	69 (31.5)
• Serious Infection†	1 (0.5)	1 (0.5)	3 (1.4)
• Opportunistic Infection ǂ	1 (0.5)	0	3 (1.4)
Anemia	3 (1.4)	0	3 (1.4)
Neutropenia	1 (0.5)	4 (1.8)	8 (3.7)
Herpes Zoster	1 (0.5)	1 (0.5)	2 (0.9)¥
Hepatic disorder	5 (2.3)	4 (1.8)	6 (2.7)
CPK elevation	0	5 (2.3)	6 (2.7)
Malignancy (including NMSC)	0	0	2 (0.9)
Cardiovascular event (adjudicated)[6]	0	2 (0.9)	1 (0.5)

AE, adverse event; CPK, creatine phosphokinase; NMSC, non-melanoma skin cancer
† Serious Infection events: PBO: pneumonia; UPA 15 mg: enterocolitis infection; UPA 30 mg: 1 varicella zoster, 1 viral upper respiratory tract infection, 1 staphylococcal wound infection
ǂ Opportunistic infection events: PBO: oral candidiasis; UPA 30 mg: 2 oral candidiasis, 1 varicella zoster pneumonia
¥ 1 pt on UPA 30 mg was exposed to chicken pox and had primary varicella infection
γ Malignancies: UPA 30 mg: 1 case of basal cell carcinoma in pt with history of skin cancer, 1 case of chronic lymphocytic leukemia/small lymphocytic lymphoma. Both were deemed unrelated to study drug by the investigator
6. Cardiovascular events (adjudicated): UPA 15 mg: 1 congestive cardiac failure, 1 stent placed in pt with prior history of angina, coronary artery disease and transient ischemic attack; UPA 30 mg: ischemic stroke in pt with history of hypertension

DISCLOSURE

G. R. Burmester, AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB.,5,AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB., 8; J. Kremer, Corrona,1,Corrona, 3,AbbVie, 2,BMS, Genentech, Gilead, GSK, Eli Lilly and Pfizer, 5; F. van Den Bosch, AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 5,AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 8; Y. Li, AbbVie, 1,AbbVie, 3; Y. Zhou, Abbvie, 1,AbbVie, 3; A. Othman, AbbVie, 1,AbbVie, 3; A. L. Pangan, AbbVie, 1,AbbVie, 3; H. S. Camp, AbbVie, 1,AbbVie, 3.

C0134 – ASSOCIATION BETWEEN MEMORY B-CELLS AND PHENOTYPIC FEATURES OF PRIMARY SJÖGRENS SYNDROME

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Background: B-cells play a pivotal role in primary Sjögren's syndrome (pSS) pathogenesis and evolution. In pSS, the distribution of peripheral B-cell subpopulations is reported to be altered, with an increase of the naive subset and the decrease of circulating memory cells. A decreased frequency of memory cells has also been identified in patients Sicca syndrome without criteria for pSS. The identification of distinct B-cell subset profiles that may have a role in the diagnosis of autoimmune diseases is of great interest.

Objectives: Our study aims to evaluate the distribution of B-cell subsets in patients with pSS and sicca syndrome through flow cytometry and to establish cut-off points for pSS classification in relation to healthy controls. Moreover, we aim to evaluate the relation between lymphocyte subpopulations and phenotypic features in pSS patients.

Methods: Fifty-seven pSS patients, 68 non-Sjögren Sicca and 24 healthy controls were included. Frequencies of circulating B-cells were determined by flow cytometry. B-cells were characterized as naïve and memory (switched and unswitched) subsets, and classified from Bm1 to Bm5, based on surface marker expression of the following monoclonal antibodies: CD19, CD24, CD27, CD38, Anti-IgD and Anti-IgM.

Kruskal-Wallis test was applied for groups' comparison, with multiple comparisons used whenever suitable. Receiver Operating Characteristic (ROC) curves were used to establish cut-off points in the B-cells subset levels and to estimate corresponding sensitivity and specificity. Data analysis was performed using R-programme.

Results: Absolute numbers of lymphocytes in pSS patients were lower compared to controls, particularly the memory subset. pSS had higher percentage of naïve and lower percentage of memory B-cells than controls. Absolute numbers of memory B-cells in Sicca were intermediate between pSS and controls.

Significant differences were found between pSS and controls in absolute counts of all memory subsets: total memory (TMem) (CD19+CD27+), switched memory (SwM) (CD19+IgD-CD27+) and unswitched memory (UnSwM) ($p<0.001$ for all). Comparing pSS with controls, we found a weak evidence of lower percentages of TMem B-cells ($p=0.078$) in patients, and more significant differences in the UnSwM subset ($p=0.043$). Percentages of memory B-cells in Sicca were similar to pSS and lower than controls, but the differences were not statistical significantly. Absolute memory B-cells numbers in Sicca were intermediate between those of pSS and controls.

Through ROC curves, the B-cell subsets that better discriminate between pSS and controls were TMem and SwM. A cut-off of ≤58 TMem cells/µl yelded a specificity of 0.88 and a sensitivity of 0.60 for pSS, and was met by 59.6% of pSS patients, 12.5% of controls and 38.8% of Sicca patients, and a cut-off of <23.5 SwM cells/µl yelded a specificity of 0.88 and a sensitivity of 0.54 and was met by 54.4% of pSS patients, 12.5% of controls and 37.3% of Sicca patients.

pSS patients with cell counts lower than the cut-off points had longer disease duration, higher disease activity (ESSDAI), and were more likely to present auto-antibodies and positive biopsy. Several Sicca also presented memory B-cell subsets counts lower than the pSS cut-off.

Conclusions: Decreased numbers of memory B-cell subsets clearly discriminate pSS patients from healthy

controls. Lower memory B-cells counts is associated with more active pSS disease profile. It remains to be clarified whether decreased memory B-cells in Sicca represents pSS and if B-cell profiling could help in the diagnosis of pSS.

CO149 – THIRTY MONTHS OF REUMA.PT/SCLERODERMA – SPECIAL FOCUS ON INTERSTITIAL LUNG DISEASE

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Background: Systemic sclerosis (SSc) is a rare systemic rheumatic disease (SRD) characterized by inflammation and fibrosis. Lung involvement, particularly interstitial lung disease (ILD), is a major cause of morbimortality. Reuma.pt allows the follow-up of patients (pts) with different SRD and is very useful in daily practice. In September 2015 a new protocol for scleroderma (Reuma.pt/Scl) was launched.

Objectives: Characterize clinical features of SSc national cohort, particularly ILD; identify predictors for ILD diagnosis and progression.

Methods: Multicenter prospective cohort study using Reuma.pt/Scl was performed. Demographic and clinical data until 25th February 2018 were retrieved. ILD was defined by fibrosis in chest x-ray and/or high-resolution computed tomography (HRCT) and disease progression by an increase from baseline in the area of lung involved and/or development of honeycombing in pts with previous ground glass and/or reduction ≥15% in diffusing capacity of carbon monoxide (DLCO) or reduction ≥10% in forced vital capacity (FVC) in pts with established ILD. Logistic regression analysis was used to identify variables independently associated with ILD and Cox regression for predictors of ILD progression.

Results: 575 SSc pts from 16 centres were registered in Reuma.pt/Scl; 87.5% female, with mean age of 59.9±15.9 years (yrs) and mean disease duration of 8.8±7.2yrs (min 2months, max 37.6yrs). Limited cutaneous SSc (lSSc) occured in 262 (45.6%)pts, diffuse cutaneous SSc (dSSc) in 164 (28.5%), overlap syndrome in 51 (8.9%), very early diagnosis SSc in 49 (8.5%) and SSc sine scleroderma in 12 (2.1%); 97 missing data. Antinuclear antibodies were positive in 392 (68.2%)pts (154 missing data). Anticentromere (ACA)

TABLE I. DIFFERENCES BETWEEN SCL PATIENTS WITH AND WITHOUT ILD (N=276)

	ILD(n=106)	Non-ILD(n=170)	p-value
Age(years)	62.9 ± 15.2	59.1 ± 15.5	0.12
Disease duration(years)	10.3 ± 7.8	7.7 ± 6.2	0.014
Female gender	86.8%	89.4%	0.555
ACA +	21.7%	40.6%	<0.001
Anti-Scl70 +	47.2%	9.4%	<0.001
dSSc subset	44.3%	11.2%	<0.001
lSSc subset	45.3%	70.6%	<0.001
Presence of digital ulcers	47.2%	24.7%	0.044
Presence of calcinosis	18.9%	8.8%	0.157
SSc pattern in NCP	37.7%*	48.8%*	0.147
Late pattern in NCP	17.9%	9.4%	0.001

*60 patients in the ILD group and 61 in the non-ILD group didn't have any NCP
ACA – anticentromere antibody; dSSc – diffuse cutaneous SSc; lSSc – limited cutaneous SSc; NCP – nailfold capillaroscopy; ILD – interstitial lung disease

occurred in 202 (35.1%)pts, anti-Scl70 in 98 (17%), anti-Pm/Scl in 13 (2.3%), anti-U1RNP in 12 (2.1%), anti-U3RNP in 9 (1.6%), anti-RNA polymerase III in 8 (1.4%), anti-ThTo in 2 and anti-Ku in 1. ACR/EULAR 2013 classification criteria were fulfilled in 276 pts (219 missing data). Nailfold capillaroscopy was available in 155 of them, with 123pts showing a SSc pattern (39 early, 49 active and 35 late).

From these 276 pts, 106 (38.4%) developed ILD, 3.4±8.2yrs after SSc diagnosis. Eighteen were current/previous smokers. Table I shows differences between pts with and without ILD. In multivariate analysis, anti-Scl70 (OR:3.73 95%CI 1.59-8.76), current/previous digital ulcers (OR:1.94 95%CI 1.01--3.76) and longer disease duration (OR:1.07 95%CI 1.02-1.12) were associated with ILD diagnosis. ACA (OR:0.36 95%CI 0.15-0.82) had a protective effect. At baseline, 16.9% had a restrictive pattern in PFR and 29.2% a description of honeycombing in HRCT. Treatment options included cyclophosphamide (CYC) in 18 pts, azathioprine in 9 (4 as maintenance therapy after CYC) and 17 mycophenolate mofetil (6 as maintenance therapy after CYC). Three pts received rituximab and 1 nintedanib. During follow-up (7.8±4.8yrs), ILD progressed in 31 pts (40.1%). Higher FVC at baseline had a negative association with ILD progression (HR:0.94 %CI0.9-0.98). Death occurred in 10 pts with ILD, in 8 of them related to lung disease, 13.8yrs after the diagnosis.

Conclusions: In our cohort ILD occurred in about 40% of the pts and was associated with a mortality rate of 3%. Our results confirm that some clinical and laboratorial variables are associated with ILD diagnosis and progression. In clinical practice, their identification may help identifying pts at risk for diagnosis and/or progression of ILD. Reuma.pt/Scl is undoubtedly useful for systematic and prospective recording of data in these pts.

CO185 – SELF-REPORTED LOW-ENERGY FRACTURES AND ASSOCIATED RISK FACTORS IN DIABETIC PORTUGUESE PATIENTS: A CROSS-SECTIONAL POPULATION-BASED STUDY

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Introduction: Patients with diabetes have an increased risk of low-energy bone fractures (LEF). Traditional clinical risk factors and bone mineral densitometry underestimate LEF risk in diabetics. We aim to estimate the prevalence of LEF among diabetics and compare with subjects without diabetes. We also aim to evaluate the associated risk factors for LEF in the diabetic subjects.

Methods: National, cross-sectional and population--based study to describe the prevalence of self-reported LEF in diabetic subjects over 40 years-old. Estimates were computed as weighted proportions/means, considering sample design. Multivariate logistic regression models were used to assess predictors of LEF in the diabetic.

Results: In a national survey of 10 661 people, 7675 subjects were over 40 years-old, of which 1173 were diabetic. Compared to nondiabetic, diabetic patients were older (mean age 66.0±11.49 years-old; 55.8% female), more overweight or obese (81.1% vs. 61.3%) and more frequently reported osteoporosis (20.4% vs. 15.4%) and falls in the previous 12 months (32.4% vs. 22.9%). Estimated prevalence of self-reported LEF was 16.2% (95% CI: 13.68-19.13, n=203) among the diabetic, compared to 13.3% (95% CI: 12.14-14.57, n=931) in nondiabetic (crude OR for the association between diabetes and LEF: 1.26, 95% CI: 1.01-1.58, p=0.045; in women, adjusted OR: 1.41, 95% CI: 1.05-1.89; in men, adjusted OR: 0.86, 95% CI: 0.57-1.31, p=0.481; p-value for the interaction between diabetes and gender: 0.008). In the diabetic subjects, LEF were more frequent among women and increased with age; LEF of distal forearm were the most prevalent (13.9%, 95% CI: 9.26-20.28), followed by hip (5.2%, 95% CI: 2.54-10.49) and vertebral fractures (3.2%, 95% CI: 1.35-7.59). A third of the diabetic (95% CI: 25.80--35.0) reported at least one major LEF (hip, vertebral or distal forearm) and 70% (95% CI: 65.39-74.36) in other sites. Self-reported LEF were associated with female gender (adjusted OR 1.66, 95% CI: 1.07 - 2.56, p=0.023) and the occurrence of falls in the previous 12 months (adjusted OR 1.72, 95% CI: 1.12--2.63, p=0.013) in the diabetic subjects.

Conclusion: Diabetics reported more falls and had a higher prevalence of self-reported LEF than nondia-

betic. Female gender and falls were associated with LEF in the diabetic. Our findings emphasize the need for fracture and falls preventive measures in diabetic patients.

CO198 – DRUG CONCENTRATIONS AND ANTI-DRUG ANTIBODIES ANALYSIS OF A SYSTEMATIC SWITCH FROM ORIGINATOR INFLIXIMAB TO BIOSSIMILAR (CT-P13) IN ROUTINE CARE

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Introduction: Biotechnological drugs (BioTx) are a fundamental resource for the treatment (Tx) of rheumatic patients. Patent expiry of some BioTx created the opportunity for biopharmaceutical manufacturers to develop biosimilar drugs intended to be as effective as the originator product but with a lower cost to healthcare systems.

In our center, in 2016, we promoted a switch from originator infliximab (IFX) to biosimilar infliximab (CT-P13) in all patients (Pts) with inflammatory arthritis treated in routine care.

Objectives: The aim of this study was to investigate the fraction of switchers who changed serum IFX concentrations (sIFX) status (i.e. high to low or vice versa) or anti-drug antibodies (ADA) status (i.e. negative to positive or vice versa) during follow-up and analyze if these changes were associated with higher activity scores and IFX withdrawal.

Methods: Inclusion criteria were rheumatic patients followed at our Day-Care Unit who switched from IFX to CT-P13 ("switchers") up to February 2018 who had blood samples available before and after switch.

Blood samples were drawn at baseline (right before the first CT-P13 Tx) and during follow-up. Serum IFX and CT-P13 were measured using assays utilizing a common immobilized tumor necrosis factor in solid phase and assay-specific lanthanide-labelled tracers.

The sIFX were dichotomized as low (<3 µg/mL) and high (>6 µg/mL). ADA levels were dichotomized into detectable (>10 ng/ml, positive) or non-detectable (<10 ng/ml, negative). CT-P13 Tx withdrawal and drug persistence were used as effectiveness outcomes. Clinical data was collected from the Reuma.pt registry.

Results: In total, 28 switchers were included (Table I). The minimum follow up was of seven months (median 10 months). A total of 21 (75%) patients had unaltered sIFX levels and ADA status during follow up. At base-

TABLE I. BASELINE CHARACTERISTICS OF PATIENTS SWITCHED TO BIOSIMILAR INFLIXIMAB (CT-P13) DISEASE ACTIVITY SCORE IN 28 JOINTS (DAS28); ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE (ASDAS)

	RA	PsA	AS	Total
Number of patients	13	2	13	28
Female patients (%)	11 (84.6%)	0	2 (15.4%)	13 (46.4%)
Median age, years (min-max)	57.6 (51.1-68.7)	52.4 (49.6-55.3)	49.5 (37.5-57.3)	53.6 (41.2-60.9)
Concomitant methotrexate therapy, n (%)	12 (92.3%)	2 (100%)	11 (84.7%)	25 (89.3%)
Median Disease duration, years (min-max)	17.7 (13.4-24.4)	21.9 (21.7-22.2)	11.0 (9.9-17.9)	15 (10.3-22.4)
Median IFX treatment duration, years (min-max)	8.7 (7.0-12.9)	9.1 (8.4-9.7)	7.8 (6.1-9.4)	8.0 (6.9-11.6)
Median IFX dose, mg (min-max)	243 (189-282)	340 (297-383)	325 (252-395)	264 (214-351)
Median IFX interval, weeks (min-max)	7 (6-8)	8 (8-8)	8 (7-9)	8 (6-8)
Median DAS 28 baseline (min-max)	2.2 (1.5-2.8)	1.2 (1.2-1.3)	–	–
Median ASDAS baseline (min-max)	–	–	1.6 (1.1-2.0)	–

RA - rheumatoid arthritis; PsA - psoriatic arthritis; AS - ankylosing spondylitis

line one patient (Pt) had low sIFX with no detectable ADAs, which were maintained after switch. This Pt had no variation in disease activity (ASDAS) before and after switch.

4 Pts (14.3%) had detectable ADA at baseline with low sIFX levels. After switch, ADAs became negative in 3 of those Pts, with normalization of sIFX (CT-P13). The other Pt kept detectable ADA levels after switch. This Pt had a minor elevation of DAS28, based on patient global assessment (PtGA) of disease activity and erythrocyte sedimentation rate.

ADAs became positive in 3 Pts after switch (10.7%). Of these, sIFX (CT-P13) changed from high to low accompanied by an elevation of Ankylosing Spondylitis Disease Activity Score (ASDAS) in 2 Pts.

Apart from the Pts that developed ADAs, no other Pt changed from high to low sIFX (CT-P13).

One Pt with spondyloarthritis stopped IFX therapy after switch to CT-P13. He had worsening of ASDAS caused only by PtGA elevation. This Pt had unaltered sIFX (CT-P13) level (medium levels) and ADA status (negative).

Conclusion: This real-world study demonstrated that Pts who had received originator IFX and switched to biossimilar IFX had few changes in sIFX and ADAs levels after switch. The observed changes were not associated with higher disease activity and did not lead to stopping IFX Tx. The Pt who stopped IFX Tx after switch did not have a change in sIFX or ADA levels. We can also conclude that the Pt that had detectable ADA levels and low sIFX at baseline with increasing disease activity after switch, probably would benefit to switch to another BioTx. Regarding the Pt with detectable ADA levels, low sIFX and sustained low disease activity, suspension of IFX should be considered since he probably does not need BioTx.

CO200 – EFFICACY AND COST ANALYSIS OF A SYSTEMATIC SWITCH FROM ORIGINATOR INFLIXIMAB TO BIOSSIMILAR CT-P13 OF ALL PATIENTS WITH INFLAMMATORY ARTHRITIS FROM A SINGLE CENTER

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Background: The aim of this study was to analyze efficacy, safety and cost savings of switching from infliximab originator (IFXor) to the biosimilar (BS) CT-P13 in a single center.

Methods: Eligible patients were those older than 18 years old with the diagnosis of rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) on treatment (Tx) with IFXor for at least 6 months and with stable disease activity. In December 2016 all eligible patients were proposed to switch to CT-P13. At the day of the last Tx with IFXor, informed consent, data and blood samples were collected. On the next Tx day, CT-P13 was administered after standard evaluation of efficacy and safety. Efficacy was measured considering change from baseline in Disease Activity Score in 28 joints (DAS28) for RA and PsA and in Ankylosing Spondylitis Disease Activity Score (ASDAS) for SpA and disease worsening was considered when an increase of 1.2 from baseline in DAS28 or an increase of 1.1 in ASDAS occurred. A cost analysis was done based on the purchasing prices of the 2 drugs at our center.

Results: In a 12 months period switch to CT-P13 was performed in 60 patients: 36 patients with SpA, 16 with RA and 8 with PsA. 65% were females with a median age of 53 years. The median disease duration previous to switch was 17 years. The median time on IFXor Tx before switch was 7 years and the median time of follow-up after switch to CT-P13 was 9 months.

In the SpA group, 30 patients were male patients, with a median age of 50 years. In 86% patients, IFX was the first biologic therapy. The median disease duration previous to switch was 16 years and the median duration of IFXor Tx until switch was 8 years. The median time of follow-up after switch was 9 months.

In the RA group, 14 patients were female and the median age was 59 years. In 10 patients, IFX was the first biologic drug prescribed. The median disease duration previous to switch was 18 years. The median INFor Tx until switch was 8 years and the median time of follow-up after switch was 10 months.

In the PsA group, 7 patients were male and the median age was 55 years. In all patients, IFXor was the first biologic Tx. The median time of disease duration

TABLE I. INFLAMMATORY PARAMETERS AND PATIENT' AND PHYSICIAN' GLOBAL ASSESSMENTS THROUGH FOLLOW-UP

	Baseline	3 Months after switch	6 Months after switch	9 Months after switch	Variation from baseline to 9 Months after switch
ESR (mm/h)	15 (10-21)	17 (9-29)	15 (9-24)	15 (9-24)	0
CRP (mg/dL)	0.18 (0.80-0.57)	0.17 (0.06-0.50)	0.19 (0.10-0.46)	0.25 (0.10-0.72)	0.07
PtGA (0-100)	30 (20-50)	20 (30-50)	30 (3-50)	30 (15-50)	0
PhGA (0-100)	20 (10-30)	20 (10-30)	20 (0-30)	20 (10-30)	0

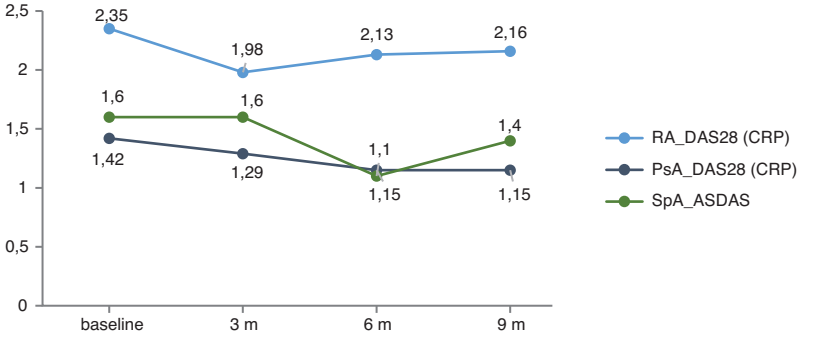

FIGURE 1. Variation of disease ativity scores after switch to CT-P13
ILD – interstitial lung disease

previous to switch was 16 years. The median IFXor Tx until switch was 8 years and the median time of follow-up after switch was 9 months.

Disease activity (DA) was stable over the observation period and similar to the values observed with IFXor.

Median follow-up time was 261 days during which disease worsening occurred in 3 (5%) patients. One was a PsA patient with aggravation of the skin manifestations, the second was a SpA patient with ASDAS worsening caused only by PtGA elevation, the third was a SpA patient with an ASDAS exacerbation driven by CRP, ESR and PhGA elevation. One patient had a minor adverse event (lip edema). These 4 patients (6.7%) stopped the BS. One returned to IFXor and the other 3 switched to another drug. The switch to CT-P13 represented a 26.4 % reduction of costs in the use of IFX Tx in these patients.

Conclusions: The switch in routine care of a group of RA, SpA and PsA patients from IFXor to CT-P13 did not affect the overall efficacy and safety and reduced costs in 26.4%. Possible interpretations for the causes of the 4 drop outs are very limited. Fluctuations in disease activity and nocebo effect can justify the 3 patients that appeared to be more symptomatic while the frequent immunogenic reactions to IFX/CT-P13 can justify the adverse effect that occurred.