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LONDON 8/11 JUNE 2016

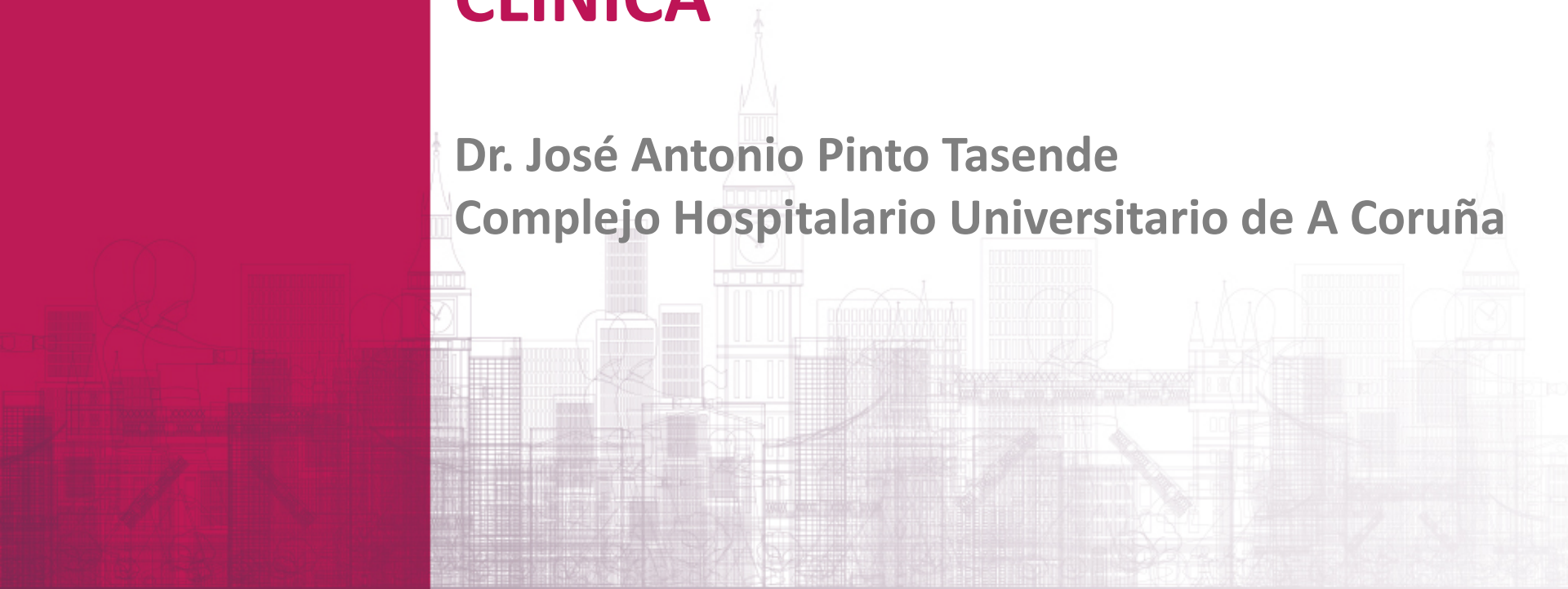
REVIEW
Annual European Congress
of Rheumatology

Con la colaboración de
 **NOVARTIS**

 **Sociedad Española de
Reumatología**

ARTRITIS PSORIÁSICA CLÍNICA

Dr. José Antonio Pinto Tasende
Complejo Hospitalario Universitario de A Coruña



Friday 10.06.2016 10:15 - 11:45
What is New (WIN) - ICC Auditorium
WIN Session 5

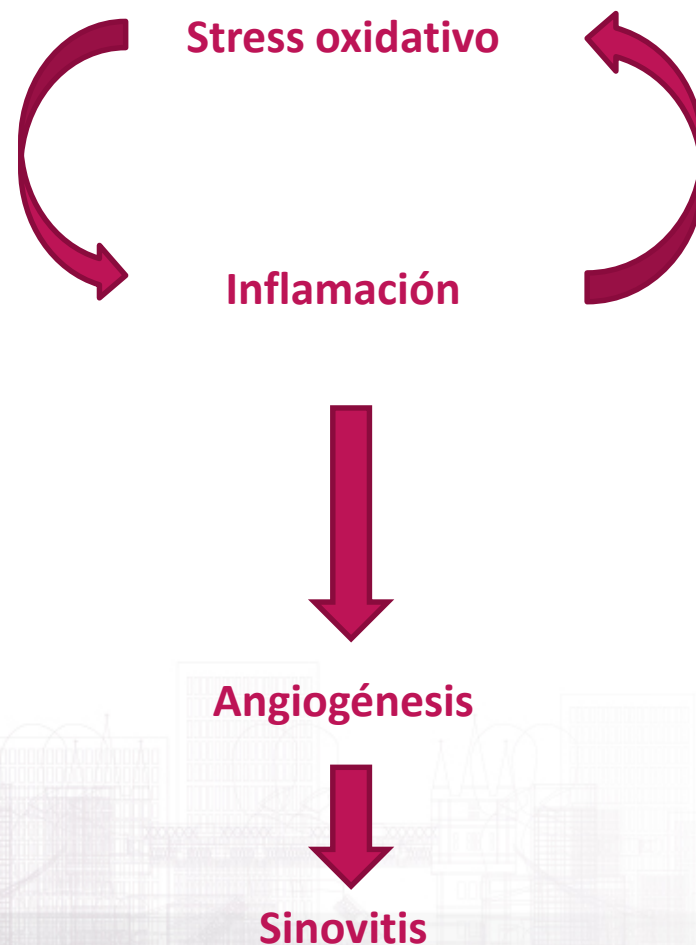
- ▶ **Speaker Veale Douglas (Ireland)**
Psoriatic arthritis



► **Importancia del stress oxidativo**

► **Riesgo de comorbilidad está aumentado, el 42% tienen 3 ó más comorbididades, sobretodo:**

- ▼ **Obesidad**
- ▼ **HTA**
- ▼ **Dislipemia**
- ▼ **Enfs CV**



FRI0440

PROGRESSION OF RADIOGRAPHIC AXIAL DAMAGE IN PATIENTS WITH PSORIATIC ARTHRITIS. RELATION WITH CLINICAL AND ANALYTICAL FACTORS

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- ▶ **Background:** Axial involvement in psoriatic arthritis (PsA) is a controversial issue. Lack of unanimity in the definition has led to a wide range of levels of prevalence. Moreover, although radiographic progression in patients with spondylitis (AS) is widely known, the different radiographic characteristics of both entities advise against establishing a parallelism between the evolution of the different lesions or the clinical factors which may have an influence on them.
- ▶ **Objectives:** Measure radiographic progression over four years in patients with PsA and axial involvement. Relate radiographic damage with clinical and analytical factors.
- ▶ **Methods:** Prospective study with patients diagnosed with PsA according to the CASPAR criteria. Axial involvement was defined as the presence of inflammatory back pain along with sacroiliitis and/or syndesmophytes. Patients with less of five years of evolution from the onset were included. The radiographic damage was measured with the PASRI method. The difference between both measurements was four years. The assessment was carried out by two observers. The clinical factors measured were: age, sex, peripheral involvement, smoking, use of NSAIDs (continuous vs on-demand), biological treatment, measures of activity (BASDAI), function (BASFI) and mobility (BASMI). The analytical variables measured were: VSG, PCR, B-CrossLaps, P1NP and HLA-B27. The presence of a dorsal or lumbar fracture was also assessed according to the semiquantitative Gennant method.
- ▶ **Results:** 45 patients with PsA and axial involvement were included. The average age was 53.5 years (SD: 12.9). 31 patients were men. The kappa coefficient between both raters was 0.70. Radiographic progression was higher in men (3.13 vs 1.14, $p=0.04$; in the multivariate analysis: $p=0.04$, OR: 0.61, 95%CI: 0.39-0.98) and in smokers (active and ex-smokers) (3.81 vs 1.14, $p=0.04$; in the multivariate analysis: $p=0.04$, OR: 0.61, 95%CI: 0.48-0.93). The presence of vertebral fracture was associated to patients with a higher radiographic progression (4.85 vs 1.82; $p=0.001$; in the multivariate analysis: $p=0.008$, OR: 0.59, 95%CI: 0.39-0.87). No differences were found regarding the presence of peripheral manifestations (2.32 vs 3.57, $p=0.3$), peripheral joints erosions (2.61 vs 3.1, $p=0.4$), continuous use of NSAIDs (1.67 vs 2.91, $p=0.3$), biological prescription (2.04 vs 3.72, $p=0.3$) or HLA-B27 (2.00 vs 2.79, $p=0.5$). A correlation was observed between radiographic progression and the initial PASRI score ($p=0.001$) and between progression and a lower P1NP concentration ($p=0.02$). Twelve patients did not show radiographic progression. These patients showed lower initial PASRI scores (5.35 vs 12.6, $p=0.001$; in the multivariate analysis: $p=0.03$; OR: 0.73, 95%CI: 0.55-0.98) and a lower P1NP concentration (38.7 vs 61.1; $p=0.006$; in the multivariate analysis: $p=0.01$; OR: 1.05, 95%CI: 1.008-1.096).
- ▶ **Conclusions:** As in patients with AS, male gender, smoking and the presence of initial damage were associated to a higher radiographic progression. These patients were associated to a higher rate of vertebral fracture and lower levels of P1NP. Radiographic progression was not associated to inflammatory parameters, peripheral manifestations or to the treatment used. 25% of the patients did not show radiographic progression

FRI0443

DOES THE CYTOKINE PATTERN, INCLUDING THE IL23 - IL17 IMMUNE AXIS, CHANGE IN PREGNANT WOMEN WITH PSORIATIC ARTHRITIS?

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- ▶ **Background:** During pregnancy, most patients with psoriatic arthritis (PsA) experience a natural improvement of their symptoms. This might be due to the immunological changes that occur in normal pregnancy to allow tolerance to the semiallogeneic fetus. Pregnancy induces a down-regulation of the adaptative immune system and generates a specific cytokine milieu. The balance between T helpers cells (Th), Th1/Th2/Th17, depends on the cytokine milieu and interleukin (IL) 23 promotes the expansion and survival of Th17 cells. The IL23-IL17 axis is up-regulated in PsA.
- ▶ **Objectives:** The aim of our study is to investigate changes of the cytokines pattern with focus on the IL23-IL17 immune axis during and after pregnancy in PsA patients compared with non-pregnant PsA patients and healthy controls (HC).
- ▶ **Methods:** Nineteen PsA patients (10 pregnant, 9 non-pregnant) and 19 HC (11 pregnant and 8 non-pregnant) were prospectively studied. Clinical assessment and blood sampling was done in pregnant women before, during and after pregnancy and once in the non-pregnant group. Sera were analyzed for levels of C reactive protein (CRP) and high sensitive CRP (hsCRP) by enzyme linked immunoassay. The following cytokines and regulatory molecules were measured by magnetic bead-based multiplex immunoassay: the activation marker soluble CD40 ligand (sCD40L), the Th1 cytokines tumor necrosis factor α (TNF α) and Interleukin (IL)-1 β , the Th2 cytokines IL-4, IL-10, IL-31, IL-33, IL-25 and the Th 23/17 pathway cytokines IL-6, IL-17A, IL-17F, IL-21, IL-22, IL23.
- ▶ **Results:** In the non-pregnant groups we observed that patients with PsA had higher levels of hsCRP, sCD40L, TNF α , IL-1 β , IL-33, IL-6 and IL-22 than HC.

Though pregnant PsA patients had inactive or mild disease activity with normal CRP levels, the hsCRP levels were higher than those of pregnant HC.

In the HC group, pregnant women at the third trimester showed higher levels of IL-10, IL-33 and TNF α than at the postpartum time point. Moreover, healthy women at the third trimester had higher levels of IL-1 β , IL-33 and IL-22 than age-matched non-pregnant women.

At the third trimester of pregnancy, patients with PsA displayed higher levels of hsCRP, sCD40L, TNF α and IL-6 than HC. Interestingly, pregnant PsA patients did not show any differences in the cytokine pattern compared to non-pregnant PsA patients.

Most differences appeared when comparing PsA and HC at the postpartum time point. Postpartal patients with PsA showed higher levels of sCD40L, TNF α , IL-1 β , IL-10, IL-33, IL-31, IL-6 and IL-22 compared to HC

- ▶ **Conclusions:** Pregnancy induces no predominance of circulating Th2 cytokines but rather a coexistence of Th1, Th2 and Th17 cytokines. Patients with PsA present a more pronounced inflammatory profile consisting of elevated hsCRP levels, Th1 and Th17 cytokines during pregnancy and postpartum. Thus, inactive disease in pregnant PsA patients was associated with persisting immunological activity including the IL-23 /Th17 immune axis.

FRI0457

RECOMMENDATIONS FOR THE MANAGEMENT OF COMORBIDITIES IN PSORIATIC DISEASE

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- ▶ **Objectives:** To establish recommendations for the management of comorbidities in patients with psoriatic disease (PsD).
- ▶ **Methods:** A multidisciplinary panel drafted the recommendations in a nominal group session. Evidence from four systematic reviews was added. Agreement was assessed by two-rounds Delphi technique. Recommendations with an agreement $\geq 7/10$ by at least 70% of participants were kept in.
- ▶ **Results:** A total of 19 recommendations on three key topics were issued: 1) screening of specific comorbidities, 2) specific preventive or therapeutic actions, and 3) general management.

- **Recommendations for the screening of specific comorbidities**
- CV disease and risk factors should be screened early and periodically; if present, they must be controlled. LE 3, A 9.8
- Adequate control of obesity and overweight should be a priority. LE 3, A 9.3
- Psycho-affective disorders should be investigated. LE 4, A 8.9
- Inquiring about sexual dysfunctions is recommended. LE 5, A 7.7
- Pts with ocular symptoms should be referred rapidly to ophthalmology. LE 5, A 8.8
- Uric acid and gouty symptoms should be periodically monitored. LE 4, A 8.8
- If new skin lesions, skin cancer should be screened, especially if pt. received PUVA, CsA or biological treatment. LE 5, A 8.5
- **Therapeutic and preventive actions**
- Drugs with potential negative effect on comorbidities should be avoided. LE 5, A 9.5
- Even in absence of risk factors, it is recommended to inform about CV risk. LE 5, A 8.4
- It is advisable to include dietary recommendations, adapted to pt preferences, to prevent overweight and obesity. LE 2, A 8.8
- Regular aerobic exercise should be recommended. LE 2, A 9.1
- Smoker pts should be encouraged to cease smoking on each visit. LE 3, A 9.8
- Pts should be encouraged to cease or reduce alcohol intake. LE 4, A 9.1
- It is advised to follow standard guidelines for the prevention of osteoporosis, especially in pts on chronic GC therapy. LE 5, A 8.8
- **Recommendations on the management of chronic patients with PD**
- The management of pts with PsD must be holistic; rheumatologists or dermatologists will play a key role coordinating with other specialists. LE 5, A 9.8
- For monitoring and control of comorbidities associated with PsD, it is essential to involve GPs and other specialists, as well as to promote pt empowerment. LE 5, A 9.3

Conclusions: Disease control coupled with the management of comorbidities is critical to ensure optimal patient care. These recommendations suggest actions on detection, management and integration

FRI0458

ASSESSMENT OF COMORBIDITY IN PSORIATIC DISEASE: HOW OFTEN SHOULD BE PERFORMED?

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- ▶ **Background:** Psoriatic disease (PsD) is associated with multiple comorbidities. When establishing management protocols, the periodicity for detection and evaluation of such comorbid conditions needs to be specified.
- ▶ **Objectives:** To establish guidelines for the follow-up of selected comorbidities in patients with PsD.
- ▶ **Methods:** An expert panel with specialists in Rheumatology, Internal Medicine, Dermatology and General Practitioners defined the comorbidities with higher impact on PsD based on the existing literature and their experience. The periodicity for detection and monitoring of comorbidities in the Rheumatology setting was established by consensus after iterations and systematic review.
- ▶ **Results:** The expert panel agreed to evaluate comorbidities as part of routine clinical practice at the time of diagnosis, upon changes in systemic treatment and at follow-up visits (evidence level 5, level of agreement 8.8). In any case, monitoring must be customized depending on the risk profile, morbidity, comorbidities and patient preferences. The following table shows the proposed periodicity for detection, assessment, and monitoring of the most important comorbidities in PsD.

At first visit	At all visits	Annually	Every 2 years	Before any change in treatment
Personal and family history Allergies List of treatments CV assessment and CV risk score. Screening of: Obesity and metabolic syndrome (waist circumference, BMI) Diabetes (blood glucose and HbA1c) HTN Dyslipidemia Smoking Cancer Alcoholism Depression Liver or kidney problems	Interrogation of new onset symptoms and corresponding examinations. Liver and kidney function.	CV risk SCORE: Total cholesterol, LDL and triglycerides Glucemia Smoking Blood pressure BMI Waist circumference lymphadenopathy screening Evaluation of the psycho-emotional state Questioning for addictions (alcohol / smoking)	Dermatology and Rheumatology recommendation: Dietary Exercise Check for lipid-lowering antihypertensive treatment if altered (by Dermatology, Rheumatology and GPT).	CV risk Infection risk Latent Tuberculosis Vaccinations Working and living conditions

Conclusions: This proposal for a periodic assessment of comorbidities in patients with PD allows systematic clinical monitoring of the patient by the Rheumatologist and Dermatologist, and can contribute to the early detection and management of these comorbidities

FRI0468

HIGH PREVALENCE OF US DETERMINED SUBCLINICAL SYNOVITIS IN EARLY PSORIATIC ARTHRITIS CORRELATES BETTER WITH THE SJC RATHER THAN TJC: RESULTS FROM THE LEEDS SPARRO COHORT

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- ▶ **Background:** Ultrasound (US) is known to be more sensitive than clinical examination in detecting synovitis in psoriatic arthritis (PsA). However, some studies found disparity between the US and clinical findings
- ▶ **Objectives:** To assess the prevalence of synovial involvement in early PsA using clinical and sonographic assessments.
- ▶ **Methods:** A total of 49 subjects with early PsA (CASPAR criteria) recruited in the Leeds Spondyloarthropathy Register for Research and Observation (SpARRO) study, a prospective longitudinal observational cohort, was assessed. The mean disease duration is 1.6 ±0.5 years; F:M ratio is 1.3; median SJC76 is 2 (1-2), median TJC78 is 6 (3-17); 90% of subjects had current skin psoriasis. Baseline US scan was performed on 1274 joints including bilateral wrists, MCP2-3, PIP2-3, elbows, knees, ankles & MTP 1-5. Grey Scale (GS) and Power Doppler (PD) were scored on a 0-3 semi-quantitative scale for each joint. Joints were considered clinically active if tender or swollen, and sonographically active if GS≥2 and/or PD≥1. We compared US active (yes/no) against tender (yes/no) and swollen (yes/no). The majority of the patients (88%) were DMARD naïve
- ▶ **Results:** US identified a higher proportion of subclinical synovitis among swollen rather than tender joints in subjects with early PsA. The agreement between clinical examination (tender & swollen) and US findings was high (73 & 87%) respectively. The most common sites for subclinical synovitis were MTP joints. In contrast, wrist tenderness and MTP2 swelling were the highest overestimated joints among the physical examination.
- ▶ **Conclusions:** The prevalence of subclinical synovitis is high in early PsA. Joint swelling is more likely to correlate with PD or GS in PsA when compared to joint tenderness. As opposed to RA, where clinical tenderness correlates with subclinical synovitis, the tender joint count may not be a reliable clinical measure to assess synovitis in PsA. Possible reasons for the over-estimation of TJC in clinical examination may be the concomitant occurrence of fibromyalgia. Larger studies are needed to confirm our results.

SAT0411

BIOLOGIC DISCONTINUATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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- ▶ **Background:** Over the past years, introduction of biologics for treatment of psoriatic arthritis (PsA) has improved the treatment responses in all clinical domains. However, little is known regarding the characteristics of patients who discontinue/switch biologics in non-clinical trial setting.
- ▶ **Objectives:** To characterize PsA patients who discontinue/switch the index biologic and evaluate the reasons for discontinuation in the Corrona PsA/Spondyloarthritis (SpA) registry, a large US national cohort of patients with PsA/SpA.
- ▶ **Methods:** PsA patients enrolled in the registry between 3/2013 and 7/2015, with a biologic at baseline (registry enrollment) and at least 2 follow-up visits were included. Two cohorts were identified: patients who discontinued/switched the index biologic (group 1) and those who stayed on the index biologic by the 2nd follow-up visit approximately 15 months after the enrollment (group 2). Descriptive analyses on patient demographics, clinical outcomes (eg. clinical disease activity index (CDAI), dactylitis, enthesitis), patient reported outcomes (eg. pain, fatigue, work productivity and activity impairment (WPAI)) and treatment at time of enrollment were examined. Chi-square tests and t-tests were used for continuous and categorical variables respectively to evaluate differences.
- ▶ **Results:** Of the 251 PsA patients meeting the inclusion criteria, 26% (n=65) discontinued/switched the index biologic and 74% (n=186) stayed on the index biologic by the 2nd follow-up visit. A significantly greater percent of females discontinued/switched the index biologic (56% vs 41%, p < 0.05). However both cohorts were similar in age (mean: 55 yrs vs 53 yrs), and disease duration (12 vs 12 yrs.). Group 1 patients reported significantly higher scores for pain (mean: 42 vs 27) and fatigue (mean: 48 vs 33) compared to Group 2 (p < .0001). Almost one-third of patients in Group 1 reported greater overall work impairment (mean: 30% vs 15%, p < 0.01) compared to Group 2. Patients in Group 1 were most likely to have higher disease activity (mean CDAI: 13 vs 9, p < 0.0001) and enthesitis (26% vs 15%, p < 0.05) vs. group 2. Overall a majority of patients had a history of prior biologic use (97%), with about 55% on current monotherapy. The major reason for discontinuing the index biologic was lack of efficacy (60%), followed by other reasons (16%) and side effects (12%).
- ▶ **Conclusions:** About a quarter of patients discontinued their index biologic over an average of 15 months follow up period. Those patients were more likely to have higher disease activity (CDAI) and poorer patient reported outcomes (pain, fatigue, WPAI) at enrollment. The most common reason for switching was lack of efficacy.

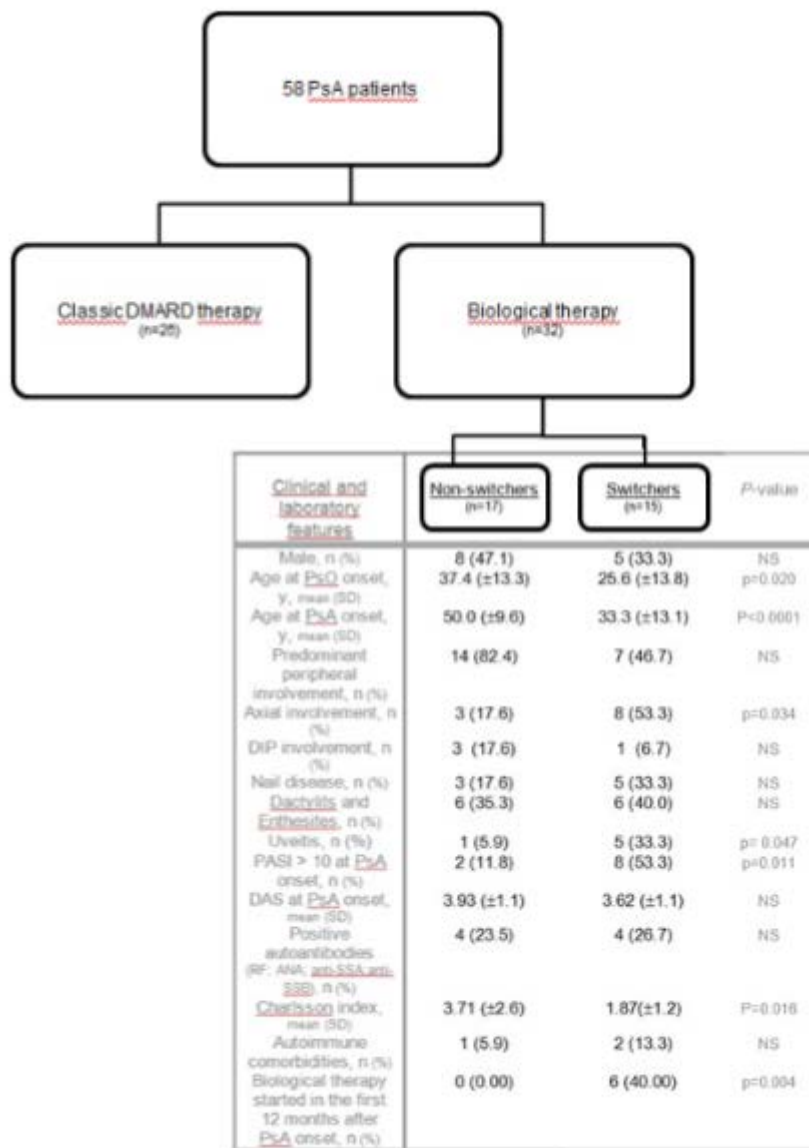
SAT0412

BIOLOGICAL THERAPY IN PSORIATIC ARTHRITIS (PSA): DIFFERENCES BETWEEN SWITCHERS AND NON-SWITCHERS

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- ▶ **Background:** Switching biological therapies is becoming increasingly common in routine management of PsA patients. However, evidence in this topic is still scarce. Predictive markers for an optimal approach to the sequential prescription of biologics are lacking.
- ▶ **Objectives:** In a population of PsA patients, we aimed to determine differences in baseline clinical and laboratory features between switchers and non-switchers.
- ▶ **Methods:** We conducted a retrospective analysis of the PsA patients followed at our outpatient clinic in the last 24 months. Demographic, clinical and laboratory data were collected. Severity of skin manifestations and peripheral arthritis at PsA onset were recorded using PASI and DAS28 score. Patients who changed biological therapies due to therapeutic failure (primary or secondary) or toxicity were defined as switchers.
- ▶ For comparison of clinical and laboratory features we used chi-square test for categorical variables and Mann-Whitney or T-Student test for continuous variables.
- ▶ **Results:** 58 PsA patients were included, 60.3% were women; the mean age at PsA and psoriasis (PsO) onset was 46.4(±15) and 34.8(±15) years, respectively. At PsA onset, 24.1% of patients had a PASI score>10 and a mean DAS of 3.76(±1.0). Laboratory features, arthritis and extra-articular manifestations were assessed (Image). 94.8% of patients were prescribed with non-biologic DMARD therapy and 55.2% with biological therapy, after failing to respond to a classic DMARD treatment alone. Median time from diagnosis until biological therapy prescription was 25.9(±56,5) months.
- ▶ Out of 32 patients prescribed with biologics, 15 (46.9%) switched to another biologic agent, mainly due to secondary failure (63.6%), primary failure (18.2%) and adverse events (13.6%). 15.65% and 3.1% of patients required 2 or 3 switches. Etanercept was the first line agent prescribed in the majority (78.8%) of patients. Adalimumab (73.3%) and ustekinumab (50.0%) were the most used agents as second and third line biological therapies, respectively.
- ▶ Switchers were significantly younger at psoriasis onset (25.6(±13.8) vs 37.4(±13.3) years, p=0.020) and also at PsA onset (33.3(±9.6) vs 50.0(±13.1) years, p<0.0001). They had higher PASI (p=0.011) levels comparing to non-switchers. Uveitis and axial involvement were significantly more common in switchers (p=0.047 and p=0.034, respectively). All patients starting biological therapy on the first 12 months after disease onset switched to another biological agent.



Conclusions:

Age at PsO and PsA onset is a well-established clinical factor with significant impact in disease severity and in skin and arthritis manifestations. Our work suggests that it might also play a role in first biological treatment failure determining a need to switch. Higher PASI score at PsA onset, axial involvement and uveitis also seem to be associated with more likelihood of switching. Our results should be considered exploratory. Larger studies are required to determine the role of these clinical features in predicting biological treatment switching.