

OP0028 LOW DOSE IL-2 THERAPY CAN RECOVERY TH17/TREG CELL BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Recent studies have shown that increased number of Th17 cells and decreased number of Treg cells in the peripheral blood contribute to ankylosing spondylitis (AS). However, current therapy for AS, including biological agents, immunosuppressant and glucocorticoid, can not correct the imbalance of Th17 and Regulatory T (Treg) cells in AS patients effectively. It has been reported that low dose IL-2 can selectively expand Treg cells and had a critical effect on homeostatic balance between the Th17 and Treg cells.

Objectives: The study is to explore the effect of low dose IL-2 therapy on the balance of Treg and Th17 cells in patients with AS and observe the efficiency and side effects of the therapy.

Methods: Seventeen patients, who met the 1984 modified New York criteria and had evidence of active inflammatory spondylitis (defined as Bath AS Disease Activity Index (BASDAI) score >4) despite of receiving standard therapy including glucocorticoid, immune-suppressants, biological agents or combination of them, were enrolled. These patients were not only given traditional treatment, but also injected subcutaneously low-dose IL-2 (50 WIU/day for 5 days). Clinical and laboratory indicators were compared before and after IL-2 treatment. The side effects were observed in the course of therapy.

Results: The number of Treg cells significantly increased after the treatment by 1 week (22.58±12.80 vs. 73.46±33.79, $p<0.001$). At the same time, there was a significantly decrease in the ratio of Th17/Treg cells (0.67±0.70 vs. 0.32±0.33, $p=0.068$). Besides, Th17 cells were also increased (12.83±9.24 vs. 19.26±13.24, $p=0.054$). Clinical manifestations were improved after the combination treatment of IL-2 and traditional drugs, especially BASDAI was decreased (4.57±0.61 vs. 1.98±0.83, $P<0.001$). No obvious adverse reactions were observed.

Conclusions: Low dose IL-2 therapy can restore and maintain the balance of Th17 and Treg cells in the active patients with AS. Manifestation improved after the combination therapy. The therapy is safe. Further research is needed to investigate long term benefits of low-dose IL-2 therapy.

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OP0029 EVALUATION OF THE EFFICIENCY OF SACROILIAC JOINTS CORTICOID INJECTIONS UNDER SCAN CONTROL AND ITS RELATIONSHIP WITH THE PRESENCE OR ABSENCE OF SACROILIITIS LESIONS SEEN ON MRI OF PATIENTS WITH SPONDYLOARTHRITIS

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Background: Sacroiliitis is a common symptom for patients suffering from axial and/or peripheral spondyloarthritis. Several studies have demonstrated that long standing corticosteroid injections of the sacroiliac joints can reduce significantly sacroiliitis pain. However, it is difficult to identify predictive factors of good response to the infiltration.

Objectives: Hence, our purposes were to evaluate the benefit from sacroiliac long standing corticosteroid injections and to determine if MRI sacroiliac images could predict infiltration's response.

Methods: This monocentric study was conducted in real-life circumstances between January 2013 and June 2016 from a standardized procedure. Thirty-one patients having inflammatory pain originating from the sacroiliac joints were infiltrated with a long acting corticosteroid (cortivazol) under CT scan guidance. Hence, 56 sacroiliac joints were injected. To be included, patients had to suffer mainly from low back and/or buttock region in the context of axial or peripheral spondyloarthritis defined by the 2009 ASAS criteria. A contrast enhanced MRI was performed if the last MRI dated more than six months before the infiltration. The main clinical outcome was a global benefit expressed by the patient at day 15 after the infiltration (D15), 1 month (M1), 3 months (M3) and 6 months (M6).

Results: 44.1% of patients had a global benefit of at least 50% at D15, 63.6% at M1, 48.3% at M3 and 35.7% at M6. Besides, there was a decrease of the spontaneous Visual Analog Scale for pain (VAS) of the sacroiliac joint at D15, M1 and M3. Likewise, there was a decrease of the provoked VAS of the sacroiliac

at D15, M1, M3 and M6. The decrease of the spontaneous VAS was at least of 50% for 35.2% of patients at D15, 41.5% at M1, 25.6% at M3 and 33.3% at M6. There was no decrease of the BASDAI, BASFI, ESR, CRP, ASDAS ESR and ASDAS CRP. Moreover, no relationship was found between the efficiency of sacroiliac infiltrations in terms of global benefit as well as of decrease of the VAS of at least 50% and the presence of sacroiliitis images on the MRI. Neither when looking at the different subtypes of sacroiliitis lesions (bone marrow oedema, synovitis, osteitis). Among the non active sacroiliitis structural lesions (erosions, subchondral sclerosis, bone bridges...), only fatty involution was statistically more present in the group with a global improvement or a VAS of less than 50%.

Conclusions: Long acting corticosteroid infiltrations of the sacroiliac joints are useful in patients suffering from inflammatory sacroiliitis pain. However, the majority of sacroiliac joints images found on a concomitant MRI does not predict the treatment response except fatty involution that seems to be associated with a lower response. Likewise, composite indexes/scores as well as parameters of systemic inflammation are not relevant for the patients follow up in that indication.

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OP0030 INEQUITY IN BIOLOGIC DMARD PRESCRIPTION FOR SPA ACROSS THE GLOBE. RESULTS FROM THE ASAS COMOSPA STUDY

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Background: The value of biologic DMARDs (bDMARDs) in SpA is well recognized but global access to these treatments can be limited due to high cost and other factors.

Objectives: This study explores variation in the use of bDMARDs in SpA across countries and to what extent socio-economic (SE) factors may explain variation.

Methods: Patients fulfilling the ASAS SpA criteria in the multi-national, cross-sectional ASAS COMOSPA study were studied. Multi-level logistic regression models with random intercept for country were constructed with current use of bDMARDs as the dependent variable. Contribution of socio-economic factors using country health expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) as independent country-level factors, was explored in models adjusted for socio-demographic as well as clinical variables known to determine bDMARD-use in SpA.

Results: In total, 3370 patients from 22 countries were included (mean [SD] age 43 [14] years; 66% male; 88% axial disease). Across countries, 1275 (38%) were bDMARD users. Crude mean bDMARD-use varied between 5% (China) to 74% (Belgium). After adjustment for relevant socio-demographic and clinical variables, important variation in bDMARD-use across countries remained (Figure, $p<0.001$). Country-level socio-economic factors, specifically higher health

Figure. bDMARD uptake (%) by country. Adjusted percentage use shown along with 95% CI, based on models with socio-economic, socio-demographic and clinical variables. Crude bDMARD uptake indicated by the orange squares.

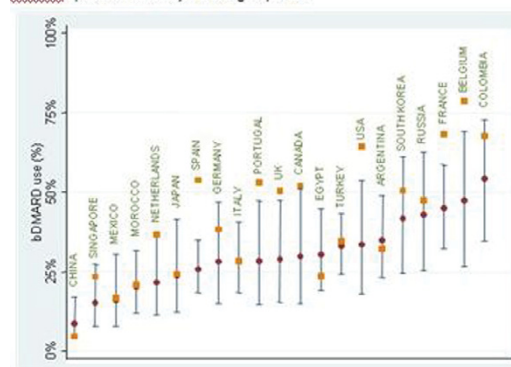


Table. Impact of country socio-economic factors on the use of bDMARDs in a model adjusting for socio-demographic and clinical variables (country included as random effects).

Independent predictors	bDMARD use OR (95% CI) (n=2758)
Country health expenditure (US dollars)	1.91(0.93,3.92)
Age (years)	1.00(0.99,1.01)
Male gender (vs females)	1.25(1.03,1.52)
Axial (vs peripheral) disease	1.55(1.09,2.22)
ASAS (CRP based)	0.80(0.73,0.87)
Sacroiliitis on X-ray	1.38(1.09,1.74)
History of extra-articular manifestations	1.36(1.13,1.65)
BMI (kg/m ²)	1.02(1.00,1.04)
Total NSAID score (0-100) in last 3 months	0.99(0.99,1.00)
Current csDMARD use	0.71(0.58,0.87)
Past csDMARD use	1.98(1.63,2.41)
Past bDMARD use	2.53(1.98,3.25)
Education (secondary/university vs primary)	0.75(0.51,1.10)

expenditures were related to higher bDMARD uptake (Table), though not meeting statistical significance (OR 1.91; 95% CI 0.93,3.92). Similar findings were found with country GDP (OR 1.72; 95% CI 0.83,3.57).

Conclusions: There remains important residual variation across countries in bDMARD uptake of patients with SpA followed in specialized SpA centers. This is despite adjustment of well-known factors for bDMARD use such as clinical and country-level socio-economic factors.

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Early diagnosis of systemic sclerosis and myositis: biomarkers and diagnostic tool

OP0031 DEVELOPMENT OF A NOVEL EPITOPE-BASED DIAGNOSTIC ASSAY FOR SYSTEMIC SCLEROSIS

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Background: We described the conformational PDGFR α epitope of V_HPAM-V κ 16F4 agonistic autoantibody¹, cloned from memory B cells of a SSc patient, that can induce fibrosis in vivo². We showed that peptides composing this epitope may be specifically recognized by serum IgG of patients with systemic sclerosis (SSc), but not of controls.

Objectives: i. To identify the immunodominant peptide within the discontinuous PDGFR α epitope of V_HPAM-V κ 16F4; ii. to identify other immunodominant epitopes recognized by agonistic autoantibodies; iii. to use these immunodominant peptides to develop an epitope-based assay for diagnosis of SSc and classification of SSc clinical subtypes.

Methods: i. The large PDGFR α peptide library used for epitope mapping of monoclonal anti-PDGFR α antibodies¹ was screened with 25 SSc (12 limited, 13 diffuse) and 25 healthy control (HC) serum samples. ii. A smaller PDGFR α peptide library containing only the top 20 conformational binders plus 20 linear and 20 conformational controls was synthesized. 60 conformational and linear peptides of a cognate protein forming a molecular complex with PDGFR α were included in the array. 20 scrambled peptides were added as negative controls. This library was screened with the same 50 serum samples. iii. A third library was synthesized, retaining the top cognate protein peptide binders, and 15 chimeric PDGFR α /cognate protein peptides, chosen among the best binders, with some nonbinding controls. This library was tested as before. Libraries were synthesized by Pepscan Presto, Netherlands. Statistical analysis was performed by Wilcoxon-Mann-Whitney test. Correlations between serological results and clinical status were made.

Results: i. An immunodominant peptide discriminating SSc from HC serum samples was identified in the first library. ii. This was confirmed by the second library, which highlighted also one immunodominant epitope from the cognate protein. Statistical analysis identified two cohorts of SSc samples (reactive vs nonreactive, the latter undistinguishable from HC) each composed by limited and diffuse SSc subtypes. iii. The third peptide library identified the chimeric peptide recognized exclusively by the reactive SSc serum samples, which were taken from patients with active, progressive disease regardless of limited vs diffuse classification, whereas the nonreactive SSc samples were taken from subjects with less active, non progressive disease.

Conclusions: We developed a conformational epitope-based assay detecting SSc-specific, agonistic, serum autoantibodies. The preliminary results suggest that this novel array may identify SSc patients with active disease, regardless of the canonical classification criteria. We propose this assay for prospective screening of large cohorts of patients affected by, or suspected for, SSc, to validate it as a tool for disease activity assessment and/or early diagnosis.

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OP0032 IS IMMUNOHISTOCHEMISTRY USEFUL TO PREDICT RESPONSE TO TREATMENT IN NECROTIZING MYOPATHIES?

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Background: Muscle biopsy is the gold standard for the diagnosis of inflammatory myopathies, but the role of immunohistochemistry in Necrotizing Myopathies (NM) has not been fully characterized yet.

Objectives: To determine if MHC-I expression and pattern of C5b-9 deposition in capillaries correlate with clinical phenotype and response to treatment in NM.

Methods: The Neuropathology Departmental database was searched to identify patients with a histological diagnosis of NM and follow up data for at least 6 months (30 patients). Electronic patient records were reviewed retrospectively to record demographics, autoantibodies, treatment, proximal muscle power at 3, 6 and 12 months by Manual Muscle Testing (MMT) (2), levels of CK and flares. Patients were classified as responders when there was improvement of MMT $\geq 20\%$ and non-responders when MMT improvement was $< 20\%$ (3). All biopsies were reviewed blindly by an experienced neuropathologist. MHC-I expression was classified as positive only if over expressed in all fibers. The patterns of C5b-9 deposition in endomysial capillaries were classified as specific (solid), non-specific (granular) or negative.

Results: MHC-I positive group (n=16/30) had a higher proportion of responders (62.5% vs 7.7%, p=0.002), higher number of patients with total recovery of muscle power (66.7 vs. 15.4%) and were more commonly positive for autoantibodies (75% vs. 35.7%, p=0.030) when compared to the MHC-I negative group (n=14). 17 patients were positive for auto-antibodies of which 9 were myositis specific antibodies [SRP (n=6), HMG-CoA reductase (n=1), Jo-1 (n=1), P155/140 (n=1)] and 4 were myositis associated antibodies [Ro-52 (n=2), Ku (n=1), Pm/Scl (n=1)]. 13/30 patients had C5b-9 deposition, with a specific pattern in 5 and non-specific in 8. The specific pattern group had a greater reduction of CK after 6 months compared to non-specific and negative respectively (98% vs. 77% vs. 56.8%, p=0.006), greater reduction in CK after 12 months (96.6% vs. 68.9% vs. 59.6%, p=0.024) and higher rates of responders (80% vs. 60% vs. 18.8%, p=0.001). Six patients were on immunosuppressants (azathioprine/hydroxychloroquine, n=2), steroids (n=3) or both (n=1) for a minimum of 4 weeks when the biopsy was performed. Differences in age, gender, clinical features or treatment were not found to be statistically significant.

Conclusions: Upregulation of MHC I and solid staining pattern of C5b-9 in the capillaries of NM patients appears to be associated with a better outcome.

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OP0033 SPECT- AND PET/CT IMAGING IN NEWLY ONSET IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Diagnosis of idiopathic inflammatory myopathies (IIMs) is challenging and so far no pathognomonic signs exist by imaging. Few radionuclide imaging techniques have been tested for this purpose, mainly ^{99m}Tc-pyrophosphate planar imaging and ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG-PET/CT). However, ^{99m}Tc-PYP uptake has been assessed visually and at best graded semi-quantitatively.

Objectives: We aimed for quantitative ^{99m}Tc-pyrophosphate single photon emission computed tomography/computed tomography (^{99m}Tc-PYP-SPECT/CT) as well as ¹⁸F-FDG-PET/CT imaging in a group of newly onset IIM patients.

Methods: Thirteen patients (mean age 62 years) with newly diagnosed, untreated IIM underwent ^{99m}Tc-PYP SPECT/CT of the thorax, pelvis, and thighs. Seven of the patients also had a whole-body ¹⁸F-FDG PET/CT scan. Forty-nine healthy controls (mean age 59 years) underwent ^{99m}Tc-PYP SPECT/CT and 26 healthy controls (mean age 57 years) had a ¹⁸F-FDG PET/CT scan done. Volumes of interest (VOIs) covering the right biceps, triceps, and quadriceps muscles were drawn manually on each series. Registered ^{99m}Tc-PYP counts, respectively standardized uptake values (SUVs) of ¹⁸F-FDG were obtained from all VOIs. Registered counts were decay- and attenuation-corrected and adjusted for body weight and administered dose of ^{99m}Tc-PYP, yielding a parameter similar to the SUV [g mL⁻¹].