Ab+ cases, 2 groups were found; one included TNF- α , MCP-1 and IP-10, and the other had IFN- γ as a sole component.

Conclusion: Cytokine profiles differ among subgroups in myositis. In anti-DDA5+ myositis, IL-15 and IFN- α with strong correlation and IL-6 were characteristic cytokines, while IFN- γ was a unique one in anti-ARS+ myositis

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SAT0282

EFFICACY AND SAFETY OF ORAL PROSTACYCLIN RECEPTOR AGONIST SELEXIPAG IN PATIENTS WITH SYSTEMIC SCLEROSIS -ASSOCIATED PULMONARY ARTERIAL HYPERTENSION IN DAILY CLINICAL PRACTICE, A CASE SERIES

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Background: Pulmonary arterial hypertension (PAH) is a frequent complication in systemic sclerosis (SSc) and a major cause of death despite the available treatments (1). Until the availability of the oral prostacyclin receptor agonist selexipag in 2016, parenteral medication targeting the prostacyclin pathway was often not feasible for patients with SSc-PAH due to practical barriers. Selexipag added to background therapy improves prognosis of PAH in the published pivotal trial (2). However, to date information on results of SSc-PAH patients treated with any combination of targeted therapies including selexipag in daily clinical practice are lacking.

Objectives: Evaluation of the efficacy and safety of selexipag in SSc-PAH patients in a real life case series.

Methods: All patients with SSc associated PAH (WHO group 1) diagnosed by right heart catheterization who started with selexipag between 09-2016 and 06-2018 from two PAH expert centres were included. Data on demographics, concurrent medication, functional class, 6 minute walking distance and NT-pro-BNP level were recorded at baseline and during follow-up. Every 12 weeks we recorded the opinion of the treating expert team, resulting in a conclusion "improvement", "stabilization" or "deterioration". Additionally treatment effect was assessed according to the abbreviated risk assessment described by Boucly (3). Side effects and adverse events were registered and evaluated.

Results: We included 13 SSc-PAH patients, all classified as limited cutaneous SSc. Ten patients were female. Median age was 68 years (IQR 58-75), median SSc disease duration 7.4 years (IQR 4.7-13.5) and median PAH duration 4 years (IQR 2.5-7.5). All patients were on double background therapy. At baseline 1 patient had two low risk criteria, 1 patient had one low risk criterion, the other patients had no low risk criteria. Two patients discontinued selexipag within 4 weeks due to side effects. The eleven patients reaching maintenance dosage had a median follow up of 48 weeks (IQR 24-72). At the end of follow up, 2/11 patients improved, 4/11 stabilized, and 5/11 deteriorated as evaluated by their expert team. Two of these deteriorated patients died due to right ventricular failure and gastro-intestinal bleeding respectively. Of the patients deteriorating, 3 initially stabilized for a period of 24 to 60 weeks. None of the patients achieved 3 low risk criteria, three patients achieved 1 low risk criterion. No unknown side effects were reported.

Conclusion: Adding selexipag to double background therapy in a high risk cohort stabilized symptoms in the majority of these patients with an acceptable safety profile. Sustained improvement of PAH symptoms is reached in only a minority of our SSc-PAH patients. Further research examining multiple target therapy, including selexipag, in patients with early SSc-associated PAH is warranted.

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SAT0283

CLINICAL AND SEROLOGICAL FEATURES OF SYSTEMIC SCLEROSIS IN ITALIAN AND EGYPTIAN PATIENTS

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Background: Clinical and serological variations exist in the severity of Systemic Sclerosis (SSc) patients, according to different geographic areas.

Objectives: To evaluate clinical and serological features in 2 cohorts of Italian and Egyptian SSc patients and to identify factors associated with Interstitial lung disease (ILD), a leading cause of mortality, by using multivariate logistic regression analysis.

Methods: An Italian center and 3 Egyptian centers participated in SSc patient recruitment in 2017. The cross-sectional demographic, clinical, and laboratory data were collected and defined according to severity score and activity index, previously developed [1, 2]. The database included 152 consecutive Italian patients, 135 women (88.8%) and 17 men (11.2%) and 197 consecutive Egyptian SSc patients, 177 women (89.8%) and 20 men (10.2%), all of whom fulfilled the classification criteria proposed by LeRoy and Medsger [3].

Results: We found that Egyptians SSc patients were younger (41.18±12.5 vs 58.59±12.6 yrs), had an earlier onset of the first non Raynaud's Phenomenon symptom (7.28±5.89 vs 14.99±11.11) and a more severe Modified Rodnan Skin Score (MRSS>14) (79.27% vs 13.6%). A greater percentage of Egyptian patients presented the active form of the disease (53.3% vs 15.5%) and had a Pulmonary Arterial Pressure (PAPs) estimated by echocardiography ≥ 40 mmHg (37.5% vs 10.6%), than Italian patients. Furthermore, Egyptian patients affected from the limited form of the disease (lcSSc), presented a higher MRSS (67.2% vs 2.6%), higher PAPs levels (34.5% vs 9.2%), an active form (41.7% vs 7.8%) and history of past/current ulcers (62.2% vs 30.6%) than Italian lcSSc patients. Severity score was higher in Egyptian patients than in the Italians (General: 22.9% vs 6.2%, Peripheral vascular: 48.2% vs 23.9%, skin: 19.8% vs 3.6%, joint/tendon: 19.9% vs 8.5%, muscle: 8.1% vs 2.6%, lung: 41.1% vs 25.3%, heart: 11.2% vs 4.1%). Kidney involvement was more severe in the diffuse cutaneous form (dcSSc) of the disease in Egyptians patients than Italians (2% vs 0.4%). In the multivariate analysis, PAPs ≥ 40 mmHg (OR: 2.622, 95%CI:1.031-6.660, p=0.043), past/current ulcers (OR:3.450, 95%CI:1.265-9.409, p=0.016), presence of anticentromere (ACA) (OR:3.846, 95%CI:1.488-9.940, p=0.005) and anti-topoisomerase I (SCL70) (OR:5.012, 95%CI:1.740-14.441, p=0.003) antibodies and heart involvement (OR:3.018, 95%CI:1.448-6.288, p=0.003) were associated with ILD in the Egyptian database, suggesting a potential role as predictive biomarkers. Advanced age (OR:1.036, 95%CI:1.009-1.063, p=0.008), dcSSc (OR:4.726, 95%CI:2.021-11.049, p=0.001) and joint involvement (OR:1.695, 95%CI:1.094-2.627, p=0.018) were independently associated with ILD in the Italian patients.

Conclusion: This cross-sectional study analyzed the demographic, clinical and laboratoristic variations in Egyptians and Italian patients and their association with ILD, suggesting possible differences to be further investigated in adequately powered studies.

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SAT0284 CD123+ PLASMACYTOID DENDRITIC CELLS (PDCS) FROM SYSTEMIC SCLEROSIS PATIENTS ARE SUSCEPTIBLE TO THE CYTOTOXIC ACTIVITY OF TAGRAXOFUSP, A CD123-TARGETED THERAPY

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Background: Tagraxofusp is a novel targeted therapy directed to the interleukin-3 receptor (CD123). Tagraxofusp is comprised of human IL-3 recombinantly fused to a truncated diphtheria toxin (DT) payload engineered such that IL-3 replaces the native DT receptor-binding domain. In this way, the IL-3 domain of tagraxofusp directs the cytotoxic DT payload to cells expressing CD123. Upon internalization, tagraxofusp irreversibly inhibits protein synthesis and induces apoptosis of the target cell. Tagraxofusp was recently approved by the FDA for the treatment of patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), a malignancy derived from the plasmacytoid dendritic cell (pDC) precursor. pDCs are immune cells that express CD123, secrete IFN- α , and play a role in inflammation and disease pathogenesis observed in systemic sclerosis (SSc) patients^{1,2}. Therapeutic depletion of pDCs or attenuation of pDC function may represent a novel approach to treating SSc patients.

Objectives: To assess the ability of tagraxofusp to selectively deplete pDCs from SSc patients *ex vivo*.

Methods: Patients fulfilled the 2013 ACR/EULAR classification criteria for SSc³. PBMCs from either SSc patients or healthy volunteers (HV) were prepared using Ficoll-Paque density gradient from fresh blood. pDCs were isolated from PBMCs as previously described and used to enrich the frequency of pDCs in an additional draw of PBMCs⁴. pDC-enriched PBMCs (3-6% pDCs) were cultured at 2×10^5 cells per well in the presence or absence of CpG-274 (0.5 μ M) to activate pDCs and then incubated with tagraxofusp (0.01-100 ng/ml, 0.17 pM-1.7 nM) at 37°C, 5% CO₂, and 95% humidity. After 24 h of culture, pDC survival was assessed by flow cytometry (CD14-, CD3- BDCA4+ CD123+), and supernatants were collected for cytokine quantification by a multiplexed Luminex assay. Changes in gene expression were measured by PCR on 10 μ g cDNA,

and calculated based on relative threshold cycle and expression of a ubiquitin housekeeping gene.

Results: Tagraxofusp was cytotoxic towards pDCs from both HV (n=5) and SSc donors (n=5) to a similar extent. The ED₅₀ of tagraxofusp in pDCs from HV and SSc was 4.3 and 3.2 ng/ml (74.4 and 55.4 pM), respectively; no effect was observed on B or T cells across the tagraxofusp dose range tested (Fig.1A). Tagraxofusp-mediated pDC depletion was further accompanied by a 68-fold reduction in secreted IFN- α and a 3-fold downregulation of GBP, a type 1 IFN-induced gene (Fig. 1B).

Conclusion: Tagraxofusp is a novel CD123-targeted therapy that is cytotoxic towards pDCs from SSc patients. These data present a novel approach of targeting pDCs in the treatment of SSc, and a clinical trial is under design.

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SAT0285 EVALUATION OF CHRONIC PAIN IN PATIENTS WITH SYSTEMIC SCLEROSIS COMPARED TO THOSE WITH CHRONIC HEADACHE AND RHEUMATOID ARTHRITIS

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Background: Systemic Sclerosis (SSc) is a chronic systemic disease frequently leading to disability and low quality of life. Chronic pain (CP), due to severe disease complications and internal organs involvement, is often underestimated. Based on available data around a 60-70% of patient with SSc suffer of chronic pain but we still lacking of fine tools to better evaluate it and follow up patients

Objectives: Evaluate pain in SSc patients, in terms of its intensity, sensory and affective components, the interference with physical and social activities, impact on quality of life and correlation with main SSc clinical manifestations.

Methods: From January 2013 to January 2018 we retrospectively evaluated 98 patients with a diagnosis of SSc [F/M=87/11; Limited/Diffuse SSc 63/35 anti-Scl70/ACA/ANA nucleolar positivity 45/39/14; mean age 55.6 ± 12.6 DS; mean disease duration 9.9 ± 7.6 DS] according to 2013 ACR/EULAR criteria; 47 patients with a diagnosis of chronic headache (CH) as defined by the International Classification for Headache Disorders, Third Edition beta version (ICHD-3 beta) criteria [F/M 37/10; mean age 52.6 ± 14.2 DS; mean disease duration: 7 ± 2 yrs DS] and 46 patients with Rheumatoid Arthritis [F/M 36/10, mean age 61 ± 13 , mean disease duration 10 ± 2 yrs, DS]. All patients fulfilled self-completing questionnaires for the evaluation of pain and quality of life: Visual Analogic Scale (VAS), Numeric Rating Scale (NRS), Short Form-McGill Pain Questionnaire (SF-MPQ), Brief Pain Inventory Score (BPI) e Health Assessment Questionnaire (HAQ).