FRI0447

WORLDWIDE EXPERT AGREEMENT ON UPDATED EULAR/EUSTAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC SCLEROSIS

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Background: In 2017, updated EULAR/EUSTAR recommendations for treatment of Systemic sclerosis (SSc) were published.¹ Implementation in clinical practice of these recommendations might be dependent on agreement and local drug availability.

Objectives: To evaluate worldwide agreement of the updated recommendations for treatment of SSc among SSc experts. To determine factors that might influence agreement.

Methods: An online survey was set out (June – September 2017), containing the 17 EULAR/EUSTAR updated recommendations. Levels of agreement were determined for each item on a 10-point scale (0=not at all; 10=completely agree). Local drug availability was assessed (yes/no). An e-mail containing a web link to the survey was sent out to international SSc-networks (EUSTAR, Scleroderma Clinical Trials Consortium, Australian Scleroderma Interest Groups, International Systemic Sclerosis Inception Cohort) and to 54 additional SSc-experts representing South-America and Asia. Levels of agreement were compared between subgroups stratified for EUSTAR membership, geographical area, drug availability, and years of experience.

Results: In total 269 responders participated, of whom n=209 completed each single item. The majority are rheumatologists (n=200, 83%), currently working in Europe (n=185; 71%); 65% (n=156) are EUSTAR member, and have >10 years of experience in the SSc field (n=150; 63%). Other geographical areas are also represented (Africa n=2, 1%; Asia n=18,7%; Australia n=13,5%; North-America n=27,10%; South-America n=17,6%). Mean level of agreement was high (8.0; standard deviation [SD, 2.5], with top-3 highest mean agreement for ACE-inhibitors for scleroderma renal crisis (9.2 [2.1]), blood pressure control in case of corticosteroids (9.0 [2.2]) and treatment with protonpump inhibitors to prevent reflux complications (9.0 [2.2]). Top 3 of lowest mean agreement included fluoxetine for Raynauds phenomenon (RP) (4.6 [2.8]), hematopoietic stem cell transplantation (HSCT) for severe SSc (7.1 [2.9]) and methotrexate for skin involvement in early diffuse SSc (7.4 [2.8]). When comparing Europe to other regions agreement differed significantly (p<0.05) for the following recommendations: iloprost for RP, iloprost and bosentan for digital ulcers, methotrexate for early diffuse SSc, cyclophosphamide for SSc-related lung disease, and HSCT for severe SSc. Comparison of agreement between responders stratified for EUSTAR membership (yes/no), years of clinical experience (<or>10 years) and local availability of the drug/treatment option (yes/no) showed that in case of iloprost, bosentan and HSCT availability of drug/treatment option contributed to differences in agreement. Neither EUSTAR membership nor years of experience could explain these differences.

Conclusions: In general, worldwide agreement on recently updated recommendations for treatment of SSc is high. Differences in agreement are partially explained by geographical area and local drug availability. Future evaluations should focus on implementation of published recommendations and take drug availability into account to further improve guideline-development.

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FRI0448

MDA5 ANTIBODY POSITIVE CLINICAL AMYOPATHIC DERMATOMYOSITIS (CADM): A SINGLE TERTIARY CENTRE CASE SERIES OF 13 PATIENTS

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Background: Positive anti-melanoma differentiation-associated gene 5 (MDA5) antibody has been reported in 50%–73% of patients with clinical amyopathic dermatomyositis (CADM)¹. About half of MDA5 +CADM patients die of rapid

progressive interstitial lung disease (RP-ILD), defined as worsening dyspnea within 1 month that required high-flow oxygen therapy or ventilator support in previously stable patients.

Objectives: This descriptive study aims to systematically characterise the clinical features, treatment and outcome of 13 cases of MDA5 +CADM patients at a single referral centre.

Methods: Myositis antibody testing became available at Vancouver Coastal Health, Canada since 2014. We retrospectively reviewed clinical presentations, laboratories, imaging studies, treatment and outcome of patients with MDA5 antibody. The data is presented descriptively.

Results: Total 13 cases (4 male and 9 female) of MDA5 +CADM were identified (2014–2017). Mean age was 49.9±11.5. Ten were Asian descent (8 Chinese, 1 Philippine, and 1 Indo-Mauritian) and 3 Caucasians. All 13 patients had typical DM rash (heliotope, Gottron's, mechanic's hands, periungual erythema). Cutaneous ulcers over the extensor surfaces of joints were seen in 7/13 and palmar papules in 4/13, both of which were characteristic for MDA5 +CADM. Only 3/13 patients had CK elevation with little muscle weakness; all others had normal CK and no detectable weakness.

ILD was present in all 13 patients. 7/13 (53.8%) patients had RP-ILD and 4/13 (30.7%) died within 3 months of onset of worsening dyspnea, despite steroid, cyclophosphamide, Rituximab, cyclosporine and IVIG; 3 survived after receiving lung transplant. 6/13 (46.2%) patients had stable ILD and are still alive. 5/7 patients with RP-ILD (71.4%) had coexisting Ro52 antibody whereas only 1/6 patients with stable ILD (16.7%) had Ro52. Of the 6 patients with stable ILD, one had worsening cutaneous ulceration and ILD that required IV cyclophosphamide; one had refractory dermatitis and recurrent pneumomediastinum eventually stabilised on rituximab; one responded to tacrolimus with improving respiratory symptoms; one had panniculitis refractory to IVIg, hydroxychloroquine, azathioprine and tofacitinib, and ultimately responded to IV cyclophosphamide; one had mild ILD but severe cutaneous disease who eventually agreed to rituximab, and the last patient went with traditional Chinese medicine and lost follow up. None had underlying malignancy.

Conclusions: In this case series of 13 patients with MDA5 +CADM, 54% were Chinese, a finding similar to previous reported higher incidence in Asians. It is important to recognise the characteristic cutaneous and pulmonary features of this entity early on as mortality is high. Refractory panniculitis can be found in MDA5 +CADM. All patients had ILD with 54% RP-ILD and 31% mortality within 3 months. Coexisting Ro52 may be predictive of worse prognosis. Early intensive immunosuppression is instrumental for refractory cutaneous manifestation and/or progressive ILD. As lung transplantation became more available, three patients with RP-ILD in this series received lung transplant successfully and they were maintained on mycophenolate and tacrolimus after transplant.

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FRI0449

OVERLAP MYOSITIS AND PRIMARY MYOSITIS: CLINICAL OUTCOMES AND PROGNOSIS

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Background: Among the subtypes of idiopathic inflammatory myopathy (IIM), it has been recognised that primary polymyositis (PM) and primary dermatomyositis

(DM) have a worse prognosis than overlap syndrome (OM). However, the benign course of OM has not been confirmed in other studies. The identification of specific characteristics that could allow a correct classification may be important for its prognosis.

Objectives: To analyse clinical characteristics and survival of patients diagnosed with OM, and to compare if there are differences with other IIM subgroups in a multicentric cohort.

Methods: Retrospective, multicentric longitudinal observational study of a cohort of patients followed between January 1980 and December 2014, with a diagnosis of MII. The patients were divided into 2 groups: OM and primary idiopathic inflammatory myositis (PIIM), which included PM and DM. Patients classified as OM had to meet IIM criteria and criteria for rheumatoid arthritis (RA), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) or primary Sjögren's syndrome (SS).

Results: The present study included a total of 348 patients (98 OM, 250 PIIM). The connective tissue diseases associated with OM were: MCTD in 32 (32.7%), SSc in 29 (29.6%), SLE in 21 (21.4%), RA in 8 (8.2%) and SS in 8 (8.2%). Patients with OM showed remarkable differences compared to PIIM. In general, OM exhibited more extramuscular involvement and more complications, with more serious infections (41% vs. 24%, $p < 0.001$) and higher mortality (31% vs. 20%, $p = 0.043$). In the multivariate study of mortality prognostic factors, the overlap syndrome contributed significantly to a higher mortality (OR 5.56 (95%CI 2.32–13.23); $p < 0.0001$).

Conclusions: In the REMICAM registry of 348 inflammatory myopathies, 98 cases of myositis with overlap syndrome have been included, presenting with more extramuscular complications, more severe infections and higher mortality than other myopathies. It would be important to identify these patients at the onset of the disease, in order to closely monitor for development of possible complications.

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FRI0450

ASSOCIATIONS OF ALTERATIONS OF PERIPHERAL REGULATORY T AND TH17 ABSOLUTE CELL NUMBERS WITH CLINICAL FEATURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic inflammatory disease with complex pathogenesis. The role of regulatory T cells (Tregs) in the development of SSc has started being studied during the last decade with new aspects being disclosed continuously. Although there is a general agreement in the medical literature regarding the decreased functional capacity of circulating Tregs in SSc, the alteration of absolute number of Treg and Th17 cells as well as their associations with clinical characteristics of SSc are still unclear.

Objectives: The aim of the present study was to explore the relationship between absolute reduction of peripheral CD4 + regulatory T and Th17 cell subset and clinical characteristics in SSc patients.

Methods: The peripheral CD4 + T subsets from 54 patients with SSc and 30 healthy control subjects were analysed. The patients were divided into the untreated group (n=29) and treated group (n=25). The patients were also divided into group 1 (n=9) for the prominent pulmonary lesions, group 2 (n=5) for prominent esophageal involvement, group 3 (n=8) for both lung lesions and esophageal involvement, and group 4 (n=10) who had fingers swelling, sclerosis, ulceration prominent. Directly using the results from flow cytometry combined with internal standard beads, absolute number of peripheral Th17 and Treg cells from the subjects in each group were calculated.

Abstract FRI0450 – Figure 1. Comparison of the levels of CD4+T lymphocyte subgroups among different groups. (A) The percentage of Th2 cells were significantly increased in untreated group compared with healthy controls. (B) The number of CD4+CD25+FOXP3+Treg cells decreased in patients with prominent pulmonary lesions. (C) The ratio of Th1/Th2 cells was not found to be significantly decreased in each group. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Abstract FRI0450 – Figure 2. Comparison of absolute number of Treg and Th17 cells in each group with different clinical manifestations. (A) The number of Th17 cells were significantly increased in group 4 compared with group 1 and group 2. (B) The number of CD4+CD25+FOXP3+Treg cells decreased in patients with SSc. (C) The ratio of Th17/Treg cells was no statistically significant different in each group. * $P < 0.1$; ** $P < 0.01$; *** $P < 0.001$.

Results: Although there were some changes among CD4 + T cell subsets in peripheral blood from these SSc patients, the major alteration was the reductions of Treg cell absolute number. Compared with the normal controls, the number of CD4+CD25+FOXP3+Treg cells were significantly decreased in untreated group ($p = 0.029$), in group 1 ($p = 0.014$) and in group 2 ($p = 0.073$) as compared with healthy controls. Interestingly, Tregs in group 2 were significantly lower than those in group 1 ($p = 0.006$), in group 3 ($p = 0.098$) and in group 4 ($p = 0.034$). In addition, the number of Th17 cells were significantly higher in group 3 ($p = 0.003$) and 4 ($p < 0.001$) when compared with the normal controls, as well as in group 4 was significantly higher than that in group 1 ($p = 0.044$), in group 2 ($p = 0.016$), moreover, the number of Th17 cells in group 3 was significantly higher than that in group 2 ($p = 0.017$).

Conclusions: The absolute number of peripheral CD4 + CD25+FOXP3+Treg cells decreased in untreated patients, indicating that this reduction arising from the disease itself. Our findings suggest that the severity of clinical manifestations in patients with SSc is related to the absolute decrease of peripheral Treg cells. Although there was no statistically significant different, absolute number of the Treg cells trended to decrease in patients who had more severe clinical manifestations. With the involvement of vital organs, the absolute number of Treg cells decreased more significantly. Moreover, in patients with relatively mild clinical manifestations, the increase in the absolute number of Th17 cells is even more obvious, suggesting that Th17 also plays an important role in early and intermediate stages.

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