Methods: Subjects who completed the double-blind placebo-controlled (DBPC) part of JBT101-DM-001 with 12 weeks of active dosing and 4 weeks of safety follow-up were eligible to receive lenabasum 20 mg BID in an open-label extension (OLE). Safety and efficacy evaluations were done at Week 4 after the start of OLE, then every 8 weeks thereafter.

Results: 20/22 (91%) eligible subjects enrolled in the OLE and 17/20 (85%) were on baseline immunosuppressive drugs. There was a mean interval of 31 weeks (range 4–92 weeks) from the end of active DBPC dosing and the start of the OLE, during which time subjects remained on background medications prior to adding lenabasum in the OLE. At the time of OLE data cut-off, no subjects had discontinued, all 20 subjects in the OLE completed visits through Week 12 and 11 subjects completed visits through Week 28. During the 28 weeks of OLE dosing, adverse events (AEs, n=30) occurred in 14/20 (70%) subjects. Only 1 subject had a moderate AE, all other AEs were mild. Four (20%) subjects had AEs considered related to lenabasum. The only AE that occurred in more than 1 subject was DM flare (n=2, 10%). During the OLE, there was improvement from the beginning of the OLE dosing and from the study start in Cutaneous Dermatomyositis Activity and Severity Index (CDASI) Activity score and physician Likert assessments of global disease activity, skin disease activity and extramuscular disease activity. Similarly, there were improvements in multiple patient-reported outcomes, including patient 10 cm VAS scores of global disease activity, skin disease activity, itch and pain, as well as the Skin-dex-29 symptoms domain and PROMIS-29 physical function, fatigue, pain interference, and anxiety domains. Selected efficacy outcomes are shown in figure 1 as change from study start during two periods: 1) "off treatment" from the end of active DBPC dosing to the start of OLE, dotted line; and 2) OLE dosing, solid line.

Abstract SAT0512 – Figure 1. Mean change from Baseline±SE in Selected Efficacy Outcomes

Conclusions: Lenabasum continues to have a favourable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no severe or serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved from study start and start of the OLE, although open-label nature of dosing with lenabasum is acknowledged. These data support further testing of lenabasum for the treatment of DM.

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SAT0513

PROGRESSIVE SKIN FIBROSIS IS ASSOCIATED WITH A DECLINE IN LUNG FUNCTION AND POORER SURVIVAL IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) ANALYSIS

W. Wu¹, S. Jordan¹, N. Graf², J. Pena³, J. Curram⁴, Y. Allamore⁵, M. Matucci-Cerinic⁶, J.E. Pope⁷, C. Denton⁸, D. Khanna⁹, O. Distler¹ on behalf of EUSTAR coauthors. ¹University Hospital Zurich, Zurich, Switzerland; ²Graf Biostatistics, Winterthur, Switzerland; ³Bayer US LLC, Parsippany, NJ, USA; ⁴Bayer Plc, Reading, UK; ⁵Cochin Hospital, Paris Descartes University, Paris, France; ⁶University of Florence, Florence, Italy; ⁷University of Western Ontario, St. Joseph's Health Care, London, ON, Canada; ⁸University College London, Royal Free Hospital, London, UK; ⁹University of Michigan, Ann Arbor, MI, USA

Background: Short disease duration and low baseline modified Rodnan skin score (mRSS) have been identified as independent predictors of progressive skin fibrosis in patients with diffuse cutaneous systemic sclerosis (dcSSc) using the EUSTAR database.¹ However, whether worsening of skin fibrosis is an appropriate surrogate marker for new-onset or deterioration of visceral organ disease and overall survival in dcSSc has been questioned.

Objectives: To determine whether progressive skin fibrosis is associated with visceral organ progression and mortality in dcSSc patients during follow-up.

Methods: We performed a survival analysis of the EUSTAR database including patients with dcSSc, fulfilling the ACR 1980² criteria, with baseline mRSS ≥ 7 in 2009 or later, valid mRSS at 12±3 months after baseline and ≥ 1 available annual follow-up visit. Progressive skin fibrosis was defined as an increase in mRSS >5 units and ≥ 25% from baseline to 12±3 months later. Disease outcome was defined as occurrence of one of the following new events during follow-up based on expert group consensus: relative decrease in forced vital capacity (FVC) ≥ 10%; left ventricular ejection fraction (LVEF) <45% or relative decrease in LVEF >10% for patients with baseline LVEF <45%; pulmonary hypertension globally judged on echocardiography by the treating physician; renal crisis; all-cause death. The association between skin progression and disease outcomes over follow-up was evaluated by Kaplan–Meier analysis, log-rank test and multivariate Cox regression. Multiple imputation was used to handle missing values.

Results: Among 1021 eligible dcSSc patients, 78 (7.6%) had progressive skin fibrosis within 1 year (defined as progressors). The median follow-up period was 3.4 years. Survival analyses indicated that skin progressors had a significantly higher probability of FVC decline ≥ 10% (53.6% vs 34.4%; p<0.001) and all-cause death (15.4% vs 7.3%; p=0.003) than non-progressors (figure 1). These significant associations between skin progression and FVC decline and all-cause death were also observed in the subgroup of patients with either baseline mRSS ≤ 22/51 or disease duration ≤ 15 months. Multivariate Cox regression confirmed that skin progression was independently associated with FVC decline ≥ 10% (HR 1.79, 95% CI 1.20 to 2.65) and all-cause death (HR 2.58, 95% CI 1.31 to 5.09).

Abstract SAT0513 – Figure 1. Kaplan-Meier survival plots for A) pulmonary progression and B) all-cause death during follow-up for skin progressors and non-progressors

Conclusions: In patients with dcSSc, progressive skin fibrosis within 1 year is associated with a decline in lung function and worse survival over follow-up. This evidence-based finding is helpful for cohort enrichment in clinical trials for both skin and lung fibrosis, and for risk stratification in clinical practice.

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SAT0514

MRI – GUIDED THERAPY FOR SYSTEMIC SCLEROSIS ASSOCIATED MYOSITIS

Y. Braun-Moscovici¹, D. Militianu², N. Puchkov², D. Markovits¹, M. Braun³, M. A. Nahir¹, A. Balbir-Gurman¹. ¹Rheumatology department, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion; ²Department of Medical Imaging, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, Haifa; ³Liver Institute, Beilinson Hospital, Sackler School of Medicine, Tel Aviv University, Petach Tikva, Israel

Background: Muscle involvement in systemic sclerosis (SSc) has a significant impact on morbidity, functional capacity, and mortality. The muscle histopathology is heterogeneous including inflammatory and fibrotic changes. Currently there are no satisfactory means to diagnose inflammatory myopathy in SSc pts with normal creatine kinase (CK) and to assess the response to therapy.

Objectives: Our aim was to evaluate whether muscle magnetic resonance imaging (MRI) might be a tool to diagnose inflammatory myopathy in SSc patients (pts) and to assess the effect of muscle oriented- immunomodulatory therapy.

Methods: We retrospectively analysed the clinical data of 290 consecutive SSc pts seen at our centre between the years 2012–2017. Our cohort is part of the EUSTAR registry (centre 042). Pts with muscle weakness as defined by the Medsger muscle severity score of ≥ 1 and at least one MRI study were included. Clinical data analysis included SSc subtype, disease duration, modified Rodnan skin score (mRSS), Medsger muscle severity score, CK, autoantibody profile, MRI and immunomodulatory treatment.

Results: 26 pts with muscle weakness answered the criteria of Medsger muscle severity score of ≥ 1 MRI data were available, in 17 of the pts. Muscle oedema and fasciitis were seen in MRI in 13 pts (10 diffuse subset, median: age 40, disease duration 1.25 years, mRSS 13.5). MRI was normal in 4 pts (2 diffuse SSc, median: age 50 years, disease duration 6 years, mRSS 4). CK was normal in 10 pts with pathologic MRI. Anti-topoisomerase was positive in 6 pts, RNA polymerase 3 – in 3 pts, anti-centromere – in 2 pts and 6 pts were only ANA positive. Muscle biopsy results were available in 4 pts: Biopsy was compatible with myositis in 3 pts with pathologic MRI and revealed fibrosis in 1 pt with normal MRI. 14 pts received immunomodulatory treatment: rituximab (3 pts), rituximab and intravenous immunoglobulins (IVIG) (3 pts), IVIG and methotrexate/azathioprine/mycophenolate mofetil.⁸ A second MRI was performed in 6 pts with first pathologic MRI, after 12 months of treatment. Significant regression of muscle oedema and per fasciitis was observed in 5 pts and correlated with clinical amelioration, with improvement of muscle strength. No clinical and imaging improvement occurred in one patient, despite the treatment. No change in muscle strength was seen in the patient with normal MRI and evidence of fibrosis on muscle biopsy, although the skin score improved.

Conclusions: MRI might serve as a non-invasive tool for diagnosis of inflammatory myopathy in SSc pts with early disease, Medsger muscle severity score of ≥ 1 and normal CK and for assessment of treatment efficacy.

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SAT0515

CLINICAL CHARACTERISTICS OF PATIENTS WITH CANCER-ASSOCIATED MYOSITIS COMPLICATED BY INTERSTITIAL LUNG DISEASE

Y. Kaneko¹, T. Nunokawa², Y. Taniguchi³, Y. Yamaguchi⁴, T. Gono⁵, K. Masui⁶, A. Kawakami⁷, Y. Kawaguchi⁸, S. Sato⁹, M. Kuwana¹⁰ on behalf of JAMI investigators. ¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine; ²Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo; ³Department of Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi Medical School Hospital, Kochi; ⁴Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Kanagawa; ⁵Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo; ⁶Department of Anesthesiology, National Defense Medical College School of Medicine, Saitama; ⁷Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki; ⁸Institute of Rheumatology, Tokyo Women's Medical University, Tokyo; ⁹Division of Rheumatology, Department of Internal Medicine, Tokai University School of Medicine, Kanagawa, Japan

Background: Cancer-associated myositis (CAM) is believed to be rarely complicated by interstitial lung disease (ILD), and, thus, detailed clinical characteristics of CAM in patients with polymyositis (PM)/dermatomyositis (DM)-associated ILD are not well known.

Objectives: To clarify the incidence, risk factors, and impact on survival of malignancy in patients with PM/DM-associated ILD, using a large cohort data.

Methods: We used 497 patients with PM/DM-associated ILD enrolled in a multi-centre retrospective cohort of incident cases from 44 institutions across Japan (JAMI). CAM was defined as malignancy diagnosed within 3 years before or after PM/DM diagnosis. Demographic data and clinical characteristics were recorded at the time of diagnosis, and follow-up survival and malignancy data were collected prospectively.

Results: Thirty-two patients with CAM (6.4%) were identified. Patients in the CAM group were older (64.3 vs 55.1 years, $p < 0.001$), had shorter disease duration at onset (4.1 vs 7.0 months, $p = 0.01$), and presented with arthritis less frequently (24.1 vs 48.5%, $p = 0.01$), in comparison with those with non-CAM group. All patients with CAM were older than 40 years, and the proportion of CAM increased along with the age. Patients who were ≥ 59 years at diagnosis and lacked arthritis were at 12 times higher risk for concomitant malignancy than those without such features (figure 1). Frequencies of autoantibodies, including anti-MDA5, anti-ARS, and anti-TIF1gamma, were not different between the groups. In 19 patients (59%), malignancy was diagnosed within 3 months before or after PM/DM diagnosis. Eleven CAM patients were died, and cause of deaths included ILD in 6 and malignancy in 5. Survival analysis by Kaplan-Miier method demonstrated that CAM patients had a poorer survival than did non-CAM patients ($p = 0.016$).

Conclusions: In patients with PM/DM-associated ILD, older age at diagnosis and lack of arthritis are predictors for concomitant malignancy, which leads to a reduced survival.

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Vasculitis

SAT0516

TWO DISTINCT SUBSETS OF LOW DENSITY GRANULOCYTES IN ANCA ASSOCIATED VASCULITIS

A. Endo, Y. Komagata, K. Yamagishi, N. Ikegaya, K. Fukuoka, M. Karube, Y. Arimura, S. Kaname. Division of Nephrology and Rheumatology, First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan

Background: Low density granulocyte (LDG), a proinflammatory population of neutrophils, was first described in systemic lupus erythematosus (SLE) and has