SAT0510

CUTANEOUS MANIFESTATIONS IN IDIOPATHIC INFLAMMATORY MYOPATHIES: FACTORS ASSOCIATED WITH CALCINOSIS

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Background: Calcinosis is a cutaneous manifestation that produces disability and complications in patients with idiopathic inflammatory myopathies (IIM). Studies about associated factors are limited.

Objectives: To investigate cutaneous manifestations and factors associated with calcinosis in patients with IIM from the REMICAM registry.

Methods: A multicenter retrospective study (1980–2014) was performed. Patients were classified as primary dermatomyositis (DM), primary polymyositis (PM), cancer associated myositis (CAM), overlap myositis (OM), inclusion body myositis, immune-mediated necrotising myopathy (IMNM) and juvenile myositis (JuM). A description of the cutaneous manifestations in each subgroup of IIM was done. The associations between calcinosis and demographic data, clinical characteristics, antibodies and treatments were analysed independently for JuM and adult IIM.

Results: 479 patients were included, of whom 49 (10%) had calcinosis with the following distribution: 27 JuM (55%), 9 DM (18%), 9 OM (18%), 3 PM (6%) and 1 IMNM (2%). Non-characteristic cutaneous manifestations were more prevalent in DM, OM, CAM and IMNM. At multivariate analysis, disease duration (OR=2; p=0.016), immunoglobulin treatment (OR=5.68; p=0.036) and immunosuppressants (OR=8.94; p=0.01) were associated with calcinosis in JuM. In addition, dysphagia (OR=21.3; p=0.008), positivity for anti-PM-Scl (OR=34.1; p=0.01), baseline ESR (OR=1.05; p=0.04) and interstitial lung disease (OR=10.2; p=0.039) were associated with calcinosis in adult.

Conclusions: Our results suggest that factors associated with calcinosis might be different in adult and juvenile myositis, but in both cases, they are related to more severe disease.

Disclosure of Interest: None declared

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SAT0511

PRACTICAL SUGGESTIONS ON INTRAVENOUS ILOPROST IN RAYNAUD'S PHENOMENON AND DIGITAL ULCER SECONDARY TO SYSTEMIC SCLEROSIS: SYSTEMATIC LITERATURE REVIEW AND EXPERT CONSENSUS

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Background: Raynaud's phenomenon (RP) and digital ulcer (DU) are prominent features of SSc. According to the 2017 EULAR recommendations, intravenous (IV) iloprost (ILO) may be used for RP and DU after failure of oral therapies. Where available, IV ILO is indicated in RP secondary to systemic sclerosis (SSc) for 3–5 days with no other advice about the regimen (dosage, duration and frequency).

Objectives: To provide a systematic review focused on IV ILO use in SSc RP and DU and to perform a meta-analysis. In the case of lack of data, a Delphi consensus was performed to provide practical suggestions about ILO usage in SSc RP and DU and to propose a research agenda for future studies.

Methods: The systematic review of the literature on IV ILO in SSc patients complicated by DU and RP was performed according to PRISMA guidelines and the meta-analysis to the GRADE system. A three-step web-based Delphi consensus was designed if not enough data were available from the literature.

Results: The review flow process is outlined in figure 1. The meta-analysis could not be performed due to insufficient literature data about dosage, regimen and frequency of IV ILO. Therefore, a three-round Delphi exercise was performed to

identify and establish a consensus about IV ILO use in SSc RP and DU. Expert consensus was reached at the third step for the following items:

- Severe or refractory to oral therapy RP, IV ILO 0.5 and 2.0 ng/kg/min, 1–3 days monthly.
- DU healing, IV ILO 0.5 and 2.0 ng/kg/min up to the maximum tolerated dose the first day of therapy, 1–3 days monthly.
- DU prevention, IV ILO 0.5 and 2.0 ng/kg/min, 1 day monthly.
- Research agenda: trials for head-to-head comparison and for regimen assessment.

Conclusions: IV ILO is currently available in some countries with the approved indication only for RP-SSc for 3–5 days. Our data, based on expert consensus, suggest a 1–3 days monthly regimen for RP and DU healing and 1 day monthly for DU prevention. These suggestions may allow clinicians to decide how to personalise the IV ILO therapy according to patients' needs. Although these suggestions are intended for clinical setting use, it will be necessary to formally validate the present suggestions in future clinical trials.

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SAT0512

SAFETY AND EFFICACY OF LENABASUM IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS SUBJECTS TREATED IN AN OPEN LABEL EXTENSION OF TRIAL JBT101-DM-001

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Background: Lenabasum (aka anabasum, JBT-101) is a selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. It is a synthetic, oral, non-immunosuppressive small molecule. Lenabasum showed acceptable safety and tolerability and evidence of clinical benefit in 22 subjects with refractory, skin-predominant dermatomyositis (DM) in Phase 2 trial JBT101-DM-001 (NCT02466243).

Objectives: This study evaluated safety and efficacy of open-label dosing of lenabasum in moderately-to-severely active skin-predominant DM in subjects who were refractory to or intolerant of hydroxychloroquine treatment.

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

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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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