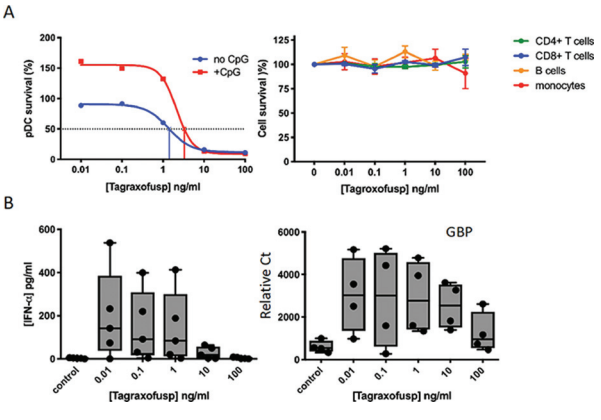
REFERENCES
[1] Valentini, et al. Ann Rheum Dis 2001
[2] Medsger TA Clin Exp 2003
[3] LeRoy EC, et al. J Rheumatol. 1988 Feb

Disclosure of Interests: Vasiliki Liakouli Grant/research support from: PFIZER, Speakers bureau: SANOFI, Hesham Hamoud: None declared, Piero Ruscitti Grant/research support from: Pfizer, Speakers bureau: MSD, BMS, Lilly, Sobi, Mahmoud Ibrahim Risha: None declared, Mohamed Elsayed Hanafy: None declared, khaled elnoafly: None declared, Rasha Ali: None declared, Gihan Omar: None declared, Adel Elsayed Grant/research support from: This study was funded by EVAPHARMA., Abdelazeim Elhefny: None declared, Mervat Abogabal: None declared, Sameh Mobasher: None declared, Paola Cipriani Speakers bureau: ACTELION, PFIZER, Roberto Giacomelli Grant/research support from: Pfizer, Actelion, Speakers bureau: Actelion, Bristol-Myers Squibb, Merck Sharp & Dohme, Abbvie, Pfizer, Sobi, Roche
DOI: 10.1136/annrheumdis-2019-eular.4935

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

Ross Lindsay[1], Janice Chen[1], Robert Spiera[2], Jessica Gordon[2], Marie Dominique Ah Kioon[2], Franck Barrat[2], Christopher Brooks[1]. [1]*Stemline Therapeutics, Research and Development, New York, United States of America*; [2]*Hospital for Special Surgery, New York, United States of America*

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 SSc[3]. 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 PBMCs[4]. pDC-enriched PBMCs (3-6% pDCs) were cultured at $2x10^5$ cells per well in the presence or absence of CpG-274 (0.5 μM) to activate pDCs and then incubated with tagraxofusp (0.01-100 ng/ml, 0.17 pM-1.7 nM) at 37°C, 5% CO_2, 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 μg 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 ED_{50} 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.



REFERENCES
[1] Ah Kioon MD, Tripodo C, Fernandez D, et al. Plasmacytoid dendritic cells promote systemic sclerosis with a key role for TLR8. Sci Transl Med. 2018 Jan 10;10(423).
[2] van Bon L, Affandi AJ, Broen J, et al. Proteome-wide analysis and CXCL4 as a biomarker in systemic sclerosis. N Engl J Med. 2014 Jan 30;370 (5):433-43.
[3] van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: An American College of Rheumatology/European League against rheumatism collaborative initiative. Ann Rheum Dis. 2013 Nov;72(11):1747-55.
[4] Guiducci C, Ott G, Chan JH, et al. Properties regulating the nature of the plasmacytoid dendritic cell response to Toll-like receptor 9 activation. J Exp Med. 2006 Aug 7;203(8):1999-2008.

Disclosure of Interests: Ross Lindsay Shareholder of: Stemline Therapeutics stock, Grant/research support from: Stemline, Employee of: Stemline, Janice Chen Shareholder of: stemline stock, Grant/research support from: stemline, Employee of: stemline, Robert Spiera Grant/research support from: Roche-Genentech, GlaxoSmithKline, Bristol-Myers Squibb, Boehringer Ingelheim, Cytori, Chemocentryx, Corbux, Consultant for: Roche-Genentech, GlaxoSmithKline, CSL Behring, Sanofi Aventis, Jessica Gordon Grant/research support from: Corbus Pharmaceuticals
Cumberland Pharmaceuticals
, Marie Dominique Ah Kioon Grant/research support from: stemline, Franck Barrat Grant/research support from: stemline, Christopher Brooks Shareholder of: Stemline stock, Grant/research support from: stemline, Employee of: stemline
DOI: 10.1136/annrheumdis-2019-eular.2102

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

Luca Magnani[1], Federica Lumetti[2], Emanuele Cocchiara[2], Amelia Spinella[2], Carlo Baraldi[2], Luigialberto Pini[2], Lanfranco Pellesi[2], Gianluigi Baiocchi[1], Carlo Salvarani[1], Dilia Giuggioli[2]. [1]*IRCC Santa Maria Nuova Reggio Emilia, Reggio Emilia, Italy*; [2]*University Of Modena and Reggio Emilia, MOdena, Italy*

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-complying 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).

Results: SSc patients started to suffer of CP in younger ages compared to AR/CH cohort but patients suffering of CH have higher mean scores in all questionnaires compared to AR/SSc. CH patients, have higher mean score in SFMPQ-sensory and affectory. Hundred percent (100%) of AR patients suffered of chronic pain. They, generally, had higher scores than SSc patients with a prevalence of the affectory component. The 83.9% (67/75 pts) of SSc patients experienced chronic pain [SF-MPQ PRI: 6.25±8.34DS; SF-MPQ PPI: 1.69±1.34DS; BPI-fattore1: 13.37 ±11.26DS; VAS: 40.7±29.6DS; NRS: 4.08±2.98DS] and in a great majority (84%) that pain interfered with their working activities and social lifes. Fortyeight percent of SSc patients had digital ulcers and 41.3% had musculoskeletal involvement. Pain used to correlate with both of them [p=0.004; p=0.041]. In patients with DUs, affectory component of pain overuled on the sensory one

Conclusion: SSc patients frequently experience chronic pain and particularly those who have a history of active DUs and musculoskeletal involvement. By the way, it seems that the BPI questionnaire could be more suitable than VAS or NRS in assessing DUs' pain. Furthermore it provides useful information on the impact of CP on social life and work impairment. Otherwise, SF_MPQ allows clinicians to better discriminate affective or sensory components of pain.

REFERENCES

[1] The impact of systemic sclerosis on health-related quality of life assessed by SF-36: A systematic review and meta-analysis. Li L, et al.; Int J Rheum Dis. 2018 Nov;21(11):1884-1893.

Disclosure of Interests: Luca Magnani: None declared, Federica Lumetti: None declared, Emanuele Cocchiara: None declared, Amelia Spinella: None declared, CArlo Baraldi: None declared, Luigialberto Pini: None declared, Lanfranco Pellesi: None declared, Gianluigi Baiocchi: None declared, Carlo Salvarani Grant/research support from: Roche, Consultant for: Eli Lilly and Company, Roche, Abbvie, Dilia Giuggioli: None declared
DOI: 10.1136/annrheumdis-2019-eular.8105

SAT0286 EVALUATION OF SWALLOWING ALTERATIONS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Emiliano Marasco[1], Giulia Bertino[2], Ludovico De Stefano[1], Lorenzo Volpiano[1], Pietro Canzi[2], Marco Benazzo[2], Carlomaurizio Montecucco[1], Lorenzo Cavagna[1]. *[1]Rheumatology Department, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy; [2]Otorinolaringoiatria, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy*

Background: Dysphagia represents a frequent and disabling symptom in patients with Idiopathic Inflammatory Myopathies (IIMs) and it has been recently included in the new ACR/EULAR classification criteria for IIMs. Despite the clinical relevance, dysphagia assessment in IIMs is not currently standardized and evaluation tools are highly variable between different centers. Functional Endoscopic Evaluation of Swallowing (FESS) is an exam that allows, by using nasal endoscopy, the direct evaluation of anatomic structures and swallowing abilities in different swallowing phase. In fact, FESS could help the identification of different problems leading to dysphagia occurrence and to related dysphagia problems. Thanks to these characteristics, FESS for ENT specialists is the gold standard technique for evaluating swallowing functions. However, no studies so far have investigated the role of FESS in the assessment of IIMs and we are completely lacking a semeiotic description of FESS findings in these patients.

Objectives: To provide the first semeiotic description of swallowing alterations evidenced by FEES in a cohort of IIMs patients.

Methods: We retrospectively reviewed the FEES findings of IIMs patients performed at our hospital.

Results: We enrolled 19 patients with a diagnosis of IIMs (10 patients were positive for a myositis specific antibody), of these 16 (84%) reported symptomatic dysphagia. We divided patients into 3 groups based on levels of peripheral muscle strength. Six patients (32%) had no clinical sign of active muscle disease (MRC scale 5, median CK 51 mU/ml, IQR 35-235), 5 patients (26%) had a mild reduction in muscle strength (MRC scale 4, median CK 76, IQR 54-220) and 8 patients (42%) showed a moderate-severe reduction in muscle strength (MRC scale ≤3, media CK 1440, IQR 628-6180). The 67% of patients without muscle disease activity showed an impairment in the oral phase of swallowing for solids and the 33% for fluids; 33% had a reduction in the activation of the pharyngeal phase of swallowing for both fluids and solids; only 17% of patients showed any sign of penetration, aspiration or pharyngeal residue for both solids and fluids. In the group of patients with moderate muscle activity, 80% of patients showed impairment in the oral phase of swallowing for solids and 40% for fluids; 60% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 40% for fluids; 40% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. Finally, in the group of patients with severe muscle disease activity, 88% of patients showed an impairment in the oral phase of swallowing for solids and 50% for fluids; 63% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 50% for fluids; 75% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. The 15% of all patients (3 cases, 1 from each group of muscle activity) showed a dysfunction in the upper esophageal sphincter. Of note, 3 patients (15%; 1 with moderate and 2 with severe muscle disease activity) required nutrition through nasogastric tube.

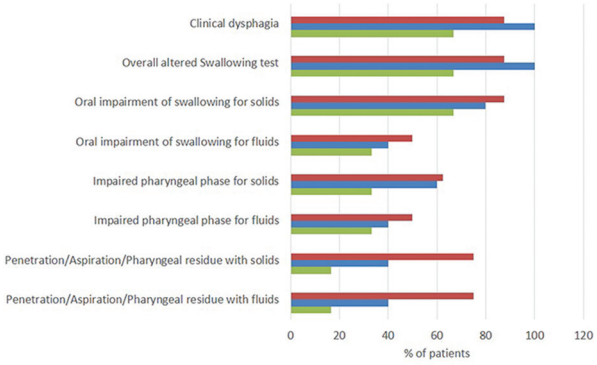


Figure 1: swallowing alteration for solids and fluids in patients divided by muscle disease activity: no signs of muscle disease activity (green), moderate muscle disease activity (blue) and severe muscle disease activity (red).

Conclusion: We showed that FESS study identified swallowing dysfunctions in both the oral and pharyngeal phases of swallowing. Swallowing dysfunctions were more prevalent in patients with greater muscle involvement; however, alterations were not rare also in patients with no clinical signs of muscle activity and, in particular, in the few patients without reported symptoms of dysphagia. FEES appears as a useful tool for the evaluation of dysphagia in IIMs.

REFERENCE

[1] Brady S, Otolaryngol Clin North Am. 2013 Dec;46(6):1009-22

Disclosure of Interests: Emiliano Marasco: None declared, Giulia Bertino: None declared, Ludovico De Stefano: None declared, Lorenzo Volpiano: None declared, Pietro Canzi: None declared, Marco Benazzo: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Lorenzo Cavagna: None declared
DOI: 10.1136/annrheumdis-2019-eular.7384

SAT0287 SERUM CYTOKINE PROFILE IDENTIFIES PATHOMECHANISM AND EFFICIENT BIOMARKERS OF DISEASE ACTIVITY AND PROGNOSIS IN INTERSTITIAL PNEUMONIA COMBINED WITH POLYMYOSITIS/ DERMATOMYOSITIS

Shogo Matsuda[1], Takuya Kotani[1], Takaaki Ishida[1], Youhei Fujiki[1], Takayasu Suzuka[1], Koji Nagai[1], Kenichiro Hata[1], Takeshi Shoda[2], Kentaro Isoda[2], Shigeki Makino[1], Tohru Takeuchi[1], Shigeki Arawaka[1]. *[1]Osaka Medical College, Internal Medicine (IV), Takatsuki, Japan; [2]Yodogawa Christian Hospital, Rheumatology, Osaka, Japan*

Background: Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies that mainly involve the muscles, skin, lungs, and heart. PM/DM are frequently complicated by interstitial lung disease (ILD) that causes increased mortality. Anti-aminoacyl tRNA synthetase (ARS) antibody and anti-melanoma differentiation-associated gene 5 (MDA5) antibody are associated with complications of ILD. Anti-ARS antibody-positive PM/DM-ILD responds well to immunosuppressive therapy and has a good short-term prognosis but a high rate of relapse over the long term. In contrast, anti-MDA5 antibody-positive PM/DM-ILD responds poorly to immunosuppressive therapy, and its prognosis is poor. Recently, a number of cytokines have been implicated in the pathomechanism and