with hypotonic oesophagus presented a reduced FVC ($84.63\% \pm 22.86\%$ vs $102.93 \pm 21.40\%$, $p < 0.0001$), TLC ($79.85\% \pm 19.62\%$ vs 95.29 ± 19.80 , $p < 0.0001$) and DLCO ($42.88\% \pm 20.00\%$ vs $59.89 \pm 20.78\%$, $p < 0.0001$) at baseline and to a faster deterioration of DLCO median values ($5.10\% \pm 20.61\%$ vs $-4.77 \pm 14.23\%$, $p = 0.012$) at follow-up. Patients with hypotonic oesophagus have an higher prevalence of diffuse skin disease and ongoing immunosuppressive treatment, but were comparable in term of age, sex, BMI, smoking habits, disease duration and prevalence of autoantibodies to the patients without this alteration.

Conclusions: The esophagogram is wide available, well tolerated and inexpensive tool to assess upper gastro-intestinal tract involvement and its abnormalities are associated to SSc-ILD severity. Because of a faster deterioration of lung function is associated to esophagogram abnormalities, a complete gastro-intestinal evaluation in ILD-SSc patients is mandatory.

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THU0405

THE ASSOCIATION BETWEEN BASELINE SERUM RESISTIN LEVELS AND THE DEVELOPMENT OF NEW DIGITAL ULCERS IN PATIENTS AFFECTED BY SYSTEMIC SCLEROSIS

F. Pignataro¹, D.P.E. Margiotta¹, G. Sambataro¹, L. Navarini¹, A. Gigante², E. Rosato², A. Afeltra¹. ¹Unit of Allergy, Clinical Immunology and Rheumatology, Campus Bio-Medico University; ²Department of Clinical Medicine, Sapienza University, Rome, Italy

Background: Resistin is a soluble factor produced by adipose tissue, implicated in the regulation of inflammatory processes and in microvascular damage.¹ When incubated with resistin, endothelial cells respond by a greater production of endothelin-1, a potent endothelium-derived vasoactive factor that engenders endothelial dysfunction (ED) in many cardiovascular and autoimmune diseases, such as Systemic Sclerosis (SSc).² SSc is a complex connective tissue disease, whose pathogenesis results from the variable interaction of three main processes: microvascular damage, autoimmunity-mediated inflammation and fibroblast activation.³ ED is at the base of the development of painful ischaemic events due to chronic hypoxia, namely digital ulcers (DUs),⁴ considered a prognostic marker of disease severity.⁵

Objectives: To evaluate the association between baseline serum resistin levels and the development of new DUs in a cohort of patients with SSc.

Methods: We conducted a one-year prospective cohort study. Patients with SSc and healthy controls (HC) were consecutively enrolled. Baseline serum resistin was assessed by commercial ELISA kit. The development of new DUs was prospectively evaluated during the follow-up after the cross-sectional point in which the resistin levels were measured.

Results: We enrolled 70 SSc patients and 26 HC matched by gender and vital parameters. Mean basal resistin levels were increased in SSc patients compared to HC (6.58 ± 5.48 vs 2.56 ± 0.95 , $p = 0.0004$). In SSc group, resistin was higher among patients with active DUs ($p = 0.0007$), infected DUs ($p = 0.0009$) and active pattern at nailfold videocapillaroscopy ($p = 0.01$). During one-year follow-up, 27 (38%) SSc patients presented new skin ulcers. Baseline resistin was increased in patients who developed new DUs (8.4 ± 6.4 vs 5.4 ± 4.5 , $p = 0.026$). In multiple logistic regression, the development of new DUs was associated to basal serum resistin concentration (OR 2.1, 95% CI 1.1–3.9), to the presence of active DUs at

baseline (OR 3.4, 95% CI 1.0–11.9), and to basal Disease Activity Score (DAI) according to European Scleroderma Study Group⁶ (OR 1.3, 95% CI 1.0–1.6). In proportional Cox regression, the time to new DUs was associated to basal resistin concentration (HR 1.7, 95% CI 1.1–2.8) and DAI (HR 1.2, 95% CI 1.0–1.4).

Conclusions: Serum resistin seems to be associated to the presence and to the development of DUs, suggesting a possible involvement in micro-vascular dysfunction in patients affected by SSc.

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THU0406

IV CYCLOPHOSPHAMIDE VS. RITUXIMAB FOR THE TREATMENT OF EARLY DIFFUSE SCLERODERMA LUNG DISEASE: OPEN LABEL, RANDOMISED, CONTROLLED TRIAL

G. Sircar¹, R.P. Goswami², D. Sircar³, D. Rath¹, S. Mondal², P.S. Mahapatra¹, A. Ghosh², P. Ghosh¹. ¹Rheumatology; ²IPGME and R, Kolkata, India; ³Nephrology, IPGME and R, Kolkata, India

Background: Systemic sclerosis is characterised by fibrotic changes in the skin and lung, and the mainstay of treatment has been cyclophosphamide. B cell involvement suggests that rituximab may also be of therapeutic benefit. In this study, we compared the safety and efficacy of rituximab compared to cyclophosphamide in the treatment of skin and lung manifestations of systemic sclerosis.

Objectives: The aims of the study were to assess the efficacy and safety of IV Rituximab compared to IV cyclophosphamide in the primary therapy of systemic sclerosis, with particular emphasis on pulmonary and dermatological manifestations.

Methods: We randomly assigned 60 patients of systemic sclerosis, age 18–70 years with skin and lung involvement, to monthly pulses of cyclophosphamide 500 mg/sq. m or rituximab 1000 mg x 2 doses at 0, 15 days. Primary outcomes were forced vital capacity (FVC) percent predicted at six months. Secondary outcomes were: absolute change in litres (FVC-L) at six months; modified Rodnan Skin Scores at 6 months, six-minute walk test (6MWT), and Medsger's score

Results: The FVC (%mean $\pm$ SD) in Rituximab group improved from 61.30 (± 11.28) to 67.52 (± 13.59) while in Cyclophosphamide group, it declined from 59.25 (± 12.96) to 58.06 (± 11.23) at 6 months ($p = 0.003$). The change of FVC was 1.51 (± 0.45) L to 1.65 (± 0.47) L in Rituximab group compared to 1.42 (± 0.49) to 1.42 (± 0.46) L in Cyclophosphamide group. The mRSS changed from 21.77 (± 9.86) to 12.10 (± 10.14) in RTX group and 23.83 (± 9.28) to 18.33 (± 7.69) in Cyclophosphamide group after 6 months. Serious adverse events were more common in the cyclophosphamide group.

	Rituximab (n=30)			Cyclophosphamide (n=30)			Difference at 6 months Mean (95% CI)	p-value
	Baseline (mean (SD))	6 months (mean (SD))	p-value	Baseline (mean (SD))	6 months (mean (SD))	p-value		
Forced vital capacity (%)	61.30 (11.28)	67.52 (13.59)	0.002 ^a	59.25 (12.96)	58.06 (11.23)	0.496 ^a	9.46 (3.01 to 15.90)*	0.003 ^b
Forced vital capacity (L)	1.51 (0.45)	1.65 (0.47)	<0.001	1.42 (0.49)	1.42 (0.46)	0.356	0.23 (-0.013 to 0.47)**	0.091 ^b
Modified Rodnan Skin Score at baseline	21.77 (9.86)	12.10 (10.14)	<0.001	23.83 (9.28)	18.33 (7.69)	<0.001	-6.23 (-10.88 to -1.58)***	0.001 ^b
Medsgers Severity Scale	8.33 (3.04)	4.67 (2.35)	<0.001	9.60 (2.44)	5.96 (2.81)	<0.001	-1.30 (-2.64 to 0.04)#	0.036 ^b
6 min walking test (metres)	359.63 (65.95)	409.60 (69.29)	<0.001	335.90 (89.30)	349.14 (99.75)	0.428	60.46 (16.07 to 104.84)	0.001 ^b
Pulmonary hypertension present	4 (13%)	5 (16%)		5 (16%)	5 (16%)		####	

a Statistical comparison for FVC (%) before and after therapy for each group were done with paired-t test. For all other outcome variables same analysis was run with Wilcoxon signed rank test and reported p-values are 2-tailed only.

b Denoted comparison of outcome variables at 6 month between the two treatment groups i.e., rituximab versus cyclophosphamide. P-values were calculated by Mann-Whitney U test and reported p-values are 2-tailed only.

* $p = 0.005$ ** $p = 0.063$ *** $p = 0.01$ **** $p = 0.008$ # $p = 0.057$ ## $p = 1$