Total Collagen/Length	PBS 5mU/ml		Bleomycin 5mU/ml		PBS 10mU/ml		Bleomycin 10mU/ml	
	Day1	Day3	Day1	Day3	Day1	Day3	Day1	Day3
M1	26.62221	8.075801	13.65193	2.020586	7.889791	4.814997	33.09294	6.023478
M2	20.72036	6.119037	17.93023	10.1741	1.852593	20.07658	44.17843	81.4925
M3	8.364862	8.10193	29.75995	16.07763	13.43434	19.56702	24.42635	23.34717
Average	18.56914	7.432256	20.44737	9.424107	7.725576	14.81953	33.89924	36.95438

Abstract THU0356 – Figure 2. Total collagen content

	Value	Sample1	Sample2	Sample3	Average
ADSC Absolute Cell Count on Day1	PBS 5mU	23446.8	4709.1	7657.2	11937.7
	Bleomycin 5mU	7985.04	5680.08	12243.6	8636.24
	PBS 10mU	10209.06	16826.4	16199.16	14411.54
	Bleomycin 10mU	4349.34	2640.96	5853.12	4281.14
ADSC Absolute Cell Count On Day 3	PBS 5mU	214.272	381.264	609.96	401.832
	Bleomycin 5mU	474.24	234.396	236.232	314.956
	PBS 10mU	185.328	449.064	506.88	380.424
	Bleomycin 10mU	349.272	85.86	292.032	242.388

Abstract THU0356 – Figure 3. ADSC cell count measured by flow cytometry

Disclosure of Interests: None declared

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THU0337 COMPARISON OF THE EFFICACY OF TWO RITUXIMAB REGIMENS IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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Background: Rituximab (RTM) is considered as a promising therapeutic agent for treatment of interstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, the limited number of RTM-treated patients, heterogeneity of the studies in relation to main parameters, considerably different dose regimens, cumulative doses, and observation periods does not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc. The question whether to combine RTM with immunosuppressants (IS) or it is possible to use it as a single-agent therapy in the patients with SSc associated with ILD is still relevant.

Objectives: To compare the time courses of pulmonary function parameters and dermal fibrosis parameters during the use of RTM in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD in the open-label prospective non-randomized study.

Methods: 90 patients with the confirmed SSc diagnosis and ILD evidence based on HRCT findings were enrolled into the study. All patients received low-dose and moderate-dose prednisolone regimens. **Group A** (n=45) received a total RTM dose 3.1±1.2 g in combination with IS

(27/60% mycophenolate mofetyl, 16/35.6% cyclophosphamide, 2/4.4% methotrexate; the patient's average age was 47.4±11.6 years, with female proportion 82%; SSc duration 4.6±3.5 years; diffused/localized forms 1.3/1). **Group B** (n=45) received RTM as a single therapy agent in a total dose 2.7±1 g (average age 45.0±15 years, female proportion 82%, SSc duration 6.7±5.6 years, diffused/localized forms 1.5/1). The age, gender proportion, SSc form, FVC and DLCO, and RTM cumulative doses were similar in the both groups. The follow-up period was 42 months. The time courses of FVC, DLCO, modified skin count (mRss, points), activity index (EScSG, points) were assessed in the study.

Results: In Groups A and B during the therapy significant decrease in mRss (p=0.00034 and 0.000002 respectively) and EScSG (p=0.00011 and 0.000000 respectively), FVC increase (p=0.00017 and 0.00001, respectively), and stabilization of the DLCO were observed.

The treatment groups did not differ significantly in the median FVC increment, clinically meaningful FVC and DLCO increments of decrements, and EScSG and mRss time courses.

Parameters	Group A	Group B
EScSG 1	3.2±1.9*	2.7±1.6*
M ± SD		
EScSG 2	1.6±1.3*	1.2±0.98*
M ± SD		
mRss 1	11.0±9.3 *	11.5±9.3*
M ± SD		
mRss 2	7.2±5.6 *	5.6±4.2*
M ± SD		
FVC 1 M ± SD	76±20.3*	77.8±19.7 *
FVC 2 M ± SD	82.7±22.5*	86.8±19.7*
Δ FVC%	5.7	8.3
	[0; 11.2]	[1.1; 15.4]
FVC increment by ≥10%, n/%	14/31	17/37.8
FVC decrement by ≥10% n/%	2/4.4	2/4.4
DLCO 1 M ± SD	44.5±19	47.8±17.1
DLCO 2 M ± SD	45.4±16.8	50.4±16.9
Δ DLCO%	1.3	2.1
	[-1.6; 6.9]	[-1.41; 7.1]
DLCO increment by ≥10%, n/%	3/6.7	5/11
DLCO decrement by ≥10% n/%	5/11	4/8.9

Notes: in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the values measured before and after the treatment

Conclusion: RTM administration both in combination with IS and as a single agent therapy in the patients with SSc associated with ILD effectively alleviated skin induration and EScSG, improved or stabilized the pulmonary function parameters. The absence of statistically significant difference in the time course of evaluated parameters between the groups substantiate potential RTM use as a single-agent therapy that, this is most important for the patients with poor tolerability or contraindications to IS administration.

Disclosure of Interests: None declared

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THU0338 SIMVASTATIN-CONJUGATED NANOPARTICLE ENHANCES THE THERAPEUTIC EFFECT OF ADIPOSE-DERIVED STEM CELLS ON INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) associated with connective tissue disease is a life-threatening pathological condition that causes respiratory failure when it progresses. Lung inflammation is treated with corticosteroids and immunosuppressants, and pulmonary fibrosis is treated with anti-fibrosis agents such as pirfenidone and nintedanib. However, many cases are treatment-resistant and the outcome is poor. Moreover, adverse effects such as infections resulting from immunosuppressive therapy are problematic. The development of new treatments is thus required for ILD from the viewpoint of the poor effect and adverse effects of the currently available treatments. Research and development with adipose-derived stem cells (AdSCs) in immunosuppressive therapy have progressed for autoimmune diseases, and favorable outcomes have been reported. In recent years, the effectiveness of AdSCs in ILD model mice has been demonstrated (ref). The statin preparation has not only an angiogenesis promoting action, an immunosuppressive action, an anti-fibrotic action but also an action of promoting a cellular function including a migratory ability.

Objectives: We have investigated the hypothesis that statin, an agent with pleiotropic effects, could augment the therapeutic potential of AdSCs. **Methods:** ILD was induced by bleomycin (BLM) in C57BL/6 mouse, and the mice were assigned in the following groups: 1) Control, 2) NP-AdSCs (2.5×10^4 cells), and 3) STNP-AdSCs (2.5×10^4 cells).

Results: Simvastatin-conjugated nanoparticles (STNP) significantly promoted the migration activity and cell survival without changing the proliferation activity, and up-regulated transforming growth factor (TGF) β -1 in vitro assays. Lung inflammation and fibrosis assessed were significantly suppressed at 4 weeks after starting BLM administration in STNP-AdSCs group (Figure). The levels of IL-4, IFN- γ , TNF- α , COL1A1, and TIMP1 mRNA expression at 28 days after BLM administration were significantly lower in STNP-AdSCs group compared with that in other groups.

Conclusion: Simvastatin-conjugated nanoparticles enhanced the therapeutic effect of a small number of AdSCs transplantation.

Abstract THU0338 – Figure 1

REFERENCE:

[1] Sci Rep 6; 7 (1): 14608, 2017.

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THU0339 PULMONARY INVOLVEMENT AND OUTCOME IN SYSTEMIC SCLEROSIS (SSC) – ILD-PH AS AN IMPORTANT SUBSET

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Background: Pulmonary involvement is the leading cause of death in SSC and can manifest as interstitial lung disease (ILD), pulmonary

hypertension (PAH) or a combination (ILD-PH). Aim of this analysis was to determine prevalence, clinical characteristics and outcomes of different forms within the German SSC Network.

Objectives:

Methods: SSC patients were analyzed for pulmonary involvement, clinical characteristics and outcome.

Results: There were 3699 pts in 42 centers with a mean follow up time of 34.4 ± 12.6 months. At baseline, ILD was frequent (29.5%), while ILD-PH and PAH had lower prevalences (7.5%, 6.1%). At the end of follow up, 32% of SSC pts had ILD, 13% ILD-PH and 7% PAH. ILD and ILD-PH were more frequent in the diffuse form (47%, 12%), while PAH did not differ between subforms. Significant differences in baseline characteristics between PAH vs. ILD-PH vs. ILD were found for age (62, 59, 54 years), sex (males: 15%, 22%, 24%) and smoking prevalence (non-smokers 49%, 63%, 57%). Mean DLCO and FVC were 56%/93% for PAH, 49%/78% for ILD-PH and 56%/81% for ILD. Significant decreases for DLCO ($\geq 15\%$) and FVC ($\geq 10\%$) were found in 45%/26% in PAH, 45%/26% for ILD-PH and 36%/16% in ILD. All-cause mortality was 8.1% for the total cohort and differed significantly between patients without pulmonary involvement (4%), ILD (7.8%), PAH (14.2%), and ILD-PH (21%, $p < 0.001$).

Conclusion: ILD is the most prevalent pulmonary involvement in SSC, while PH-ILD is associated with the most detrimental survival. Significant differences in baseline characteristics of types of pulmonary SSC involvement may help to identify patients at risk in the future.

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