Results: Among 72 (66 female) patients, mean (SD) age was 57.1 (11.1) years, modified Rodnan skin score 10.6 (10.5), SHAQ 0.64 (0.61) and 6MWT distance 473.5 (95.5) m. Mean BHT time was 35.05 (14.90) sec at the first time, 38.92 (16.14) sec at the second time, and 41.11 (17.71) sec at the third time. The BHT time showed a statistically significant negative correlation with Borg scale (pre-test, $r = -0.336$, $p = 0.002$; post-test, $r = -0.252$, $p = 0.034$; Figure 1 and Table 1), while 6MWT showed a negative correlation with only post-test Borg scale (pre-test, $r = -0.113$, $p = 0.343$; post-test, $r = -0.351$, $p = 0.002$; Table 1). The BHT time was positively correlated with DLCO (%), $r = 0.409$, $p < 0.001$ and FVC (liters, $r = 0.402$, $p < 0.001$) (Table 1). We also found a statistically significant correlation between BHT time and SHAQ score ($r = -0.451$, $p < 0.001$; Table 1). However, EF and PASP by TTE showed no significant relationship with BHT time (EF, $r = -0.108$, $p = 0.374$; PASP, $r = -0.246$, $p = 0.054$; Table 1).

Figure 1. Association of Borg dyspnea scale with breath-holding time.

Table 1. Pearson's correlation coefficients (r) for the relation between BHT and clinical parameters in comparison to 6MWT.

	Pre-test Borg scale	Post-test Borg scale	DLCO (%)	FVC (L)	FVC (%)	FVC /DLCO (%)	EF (%)	PASP (mm Hg)	SHAQ (score)
BHT (sec)	-0.366**	-0.252*	0.409***	0.402***	0.191	-0.244***	-0.108	-0.246	-0.451***
6MWT (m)	-0.113	-0.351**	0.297*	0.321**	0.063	-0.250*	0.137	-0.354**	-0.531***

BHT, breath-holding test; 6MWT, 6-minute-walk test; DLCO, diffusing capacity for carbon monoxide; FVC, forced vital capacity; EF, ejection fraction estimated by transthoracic echocardiography; SHAQ, Scleroderma Health Assessment Questionnaire.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Conclusion: The BHT is a simple, safe, and less time-consuming test, reflective of pulmonary parameters and SHAQ, as compared with 6MWT. Our results suggest that the BHT might be a useful surrogate marker of cardiopulmonary capacity in SSc patients.

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POS0857

IMMUNOSUPPRESSANTS (CYCLOPHOSPHAMIDE AND MYCOPHENOLATE MOFETIL) VERSUS RITUXIMAB A SINGLE-AGENT THERAPY IN SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE: REAL CLINICAL PRACTICE

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Background: Although interstitial lung disease (ILD) occurs in the majority of patients with systemic sclerosis (SSc), treatment options for this manifestation is empirical and at present consists of Cyclophosphamide (CyP) or Mycophenolate Mofetil (MMF). However, the immunosuppressants (IS) use leads to rather limited improvement of ILD and is associated with many adverse reactions. The search for novel, more efficacious agents has been continued, such as attracting much attention RTM. However, the limited number of RTM-treated patients, 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.

Objectives: To compare the impact of IS and RTM a single-agent therapy on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.

Methods: 116 patients with the confirmed SSc diagnosis and ILD evidence based on MSCT findings were enrolled into the study. All patients received low and moderate-dose glucocorticoids regimens. Group A (n=35) received RTM as a single therapy agent for 13.3±2.3 months at total dose 1.35±0.5g (the patient's average age was 45.0±15 years, with female proportion 80%; SSc duration 6.3±2.3 years; diffused/localized forms 1.3/1). Group B (n=36) received parenteral CyP for 12±6 months at total dose 10.6±5g (the average age 47±12 years, females 92%, SSc duration 5.0±4.8 years, diffused/localized forms 1.6/1). Group C (n=45) received MMF for 12±6 months at a dose of 2 grams per day (the average age 49±13 years, females 91%, SSc duration 7.1±5 years, diffused/localized forms 1/1.3). The time courses of FVC, modified skin count (mRss, points), activity index (EScSG, points) were assessed into the study.

Results: In Groups A, B and C the therapy was associated with significant decrease in mRss ($p=0.02$, 0.008, 0.007, respectively) and EScSG ($p=0.00017$, 0.000165, 0.01, respectively).

Evaluation of FVC time course revealed significant FVC increase only in Groups A ($p=0.002$) and B ($p=0.034$), with median increment about 5%.

In Groups A and B 10% FVC increase was found in the third of the patients thus exceeding respective parameter twice in Group C ($p=0.15$ and 0.008, respectively). The patient percentage with FVC decrease by ≥10% did not differ significantly between groups.

The therapy was better tolerated in RTM-treated group: during RTM therapy adverse reactions emerged in lower proportion of the patients (4/11%) compared with CyP (19/53%, $p=0.0000$) and MMF-treated group (12/27%, $p=0.5$).

Parameters	Group A	Group B	Group C
Activity Index 1	2.8±1.4*	3.2±1.9*	1.9±1.5*
M ± SD			
Activity Index 2	1.4±1.2*	1.4±1.2*	1.2±0.9*
M ± SD			
Skin count 1	11.5±9.5 *	11.2±7.9 *	7.5±6.9 *
M ± SD			
Skin count 2	8.2±6.2 *	7.9±6.8 *	4.8±3.9 *
M ± SD			
FVC 1 M ± SD	78.7±20.0 *	80.5±20.1*	90.3±20.8
FVC 2 M ± SD	84.2±20.0*	85.8±20.4*	92.2±21.0
Δ FVC %	5.3	5.7	1.9
	[0.8; 11.1]	[0; 11.2]	[-3.5; 6.0]
FVC increment by ≥10%, n/%	9/26	14/31	6/13.3
FVC decrement by ≥10% n/%	2/5.7	2/4.4	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: All agents effectively alleviated skin induration and EScSG, but only RTM and CyP significantly improved FVC. The RTM single therapy was better tolerated compared to IS. The study findings substantiate potential use an RTM single therapy both as a first-line agent for ILD treatment in the patients with a progressive course of ILD damage SSc, and in the event of CyP inefficacy of poor tolerability. The MMF use is more preferable in patients with less pronounced ILD.

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POS0858

POTENTIAL EFFICACY PREDICTORS OF ANTI-B-CELL THERAPY 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 With Interstitial Lung Disease (ILD) in the patients with systemic sclerosis (SSc). However, the limited number of RTM-treated patients, considerably

varying dose regimens, cumulative doses and observation periods, lack of data on potential predictors of RTM therapy response do not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc.

Objectives: The study of potential efficacy predictors of anti-B-cell therapy in the patients with SSc associated with ILD.

Methods: 90 patients with SSc-ILD verified by multispiral computed tomography were enrolled to the study and received RTM therapy for 12-42 months at cumulative dose 2.9 ± 1.1 grams (disease duration 5.9 ± 4.8 years, diffused/limited SSc 1.3/1, average age 47 ± 13.6 years, females 83%). All patients received low or moderate dose glucocorticoids. 45 patients received RTM in addition to immunosuppressive therapy (cyclophosphamide and mycophenolate mofetil) because of inadequate efficacy of immunosuppressants. After evaluation of FVC trends in the patients receiving RTM the overall study population was divided into two patient groups for the analysis: group A ($n=35$) comprised the patients with $\geq 10\%$ FVC increase (disease duration 6.1 ± 5.8 years, diffused/limited SSc 1.3/1, average age 50 ± 12 years, females 86%, cumulative RTM dose 3.2 ± 1.24 grams), and group B ($n=11$) comprised the patients with $\geq 5\%$ FVC decrease (disease duration 5.2 ± 4 , diffused/limited SSc 0.8/1, average age 43 ± 16 , females 72%, cumulative RTM dose 2.5 ± 0.99 grams). Subsequently correlation analysis was made to clarify the association between delta FVC and a number of clinical (age, gender, duration and form of SSc, modified skin count, presence of gastroesophageal reflux, mPAP, SSc activity (EScSG, points), cumulative RTM dose, immunosuppressive therapy) and laboratory parameters (ESR, ANA-HEP-2, a-Scl-70, CRP, B cell count).

Results: In the overall patient population RTM therapy was associated with significant FVC increase from $77.0 \pm 19.9\%$ to $84.7 \pm 20.9\%$ ($p=0.000000$), with median FVC increment 6.6% [0;14.1].

In group A FVC increased from 75.3 ± 19.9 to 94.3 ± 20.4 ($p=0.000000$), with median FVC increment 16.3 [12.6; 24.7].

In group B FVC decreased from 82.5 ± 23.2 to 72.3 ± 19.4 ($p=0.000176$), with median FVC decrement 10.4% [-13.4; -6].

Correlation analysis in groups A and B showed significant association of between delta FVC and the patient age ($R=0.36$), cumulative RTM dose ($R=0.34$) and EScSG during the last examination ($1.2 \pm .0$ and 3.1 ± 1.4 in groups A and B, respectively; $R=-0.42$). No significant correlation between delta FVC and any other tested parameters was found.

Conclusion: Therefore, older patients who received the cumulative rituximab dose more than 3 grams with suppressed SSc activity achieved greater FVC increase at the background of therapy. These data allow to consider the above parameters as potential predictors of response to anti-B-cell therapy in the patients with SSc-ILD.

Disclosure of Interests: None declared

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POS0859 DEEP PHENOTYPING OF DERMATOMYOSITIS BASED ON LIPID FERROPTOSIS-RELATED GENES BY MACHINE LEARNING

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Background: Dermatomyositis (DM) is an idiopathic inflammatory myopathy with heterogeneous clinical manifestation that raise challenges regarding diagnosis and therapy¹. Ferroptosis is a newly discovered form of regulated cell death that is the nexus between metabolism, redox biology, and rheumatic immune diseases². However, how ferroptosis maintains the balance of lymphocyte T cells and affect disease activity in DM is unclear.

Objectives: To investigate an ferroptosis-related multiple gene expression signature for classification by assessing the global gene expression profile, and calculate the lymphocyte T cells status in the different subsets.

Methods: Gene expression profiles of skeletal muscle from DM samples were acquired from GEO database. GSE143323 (30 patients and 20 HCs) was selected as the training set. The GSE3307 contained 21 DM patients and was selected as the validation set. The 60 ferroptosis genes were obtained from previous literature³. The intersection of the global gene and ferroptosis genes was considered the set of significant G-Ferroptosis genes for further analysis. The "NMF" (R-package) was applied as an unsupervised clustering method for sample classification by using G-Ferroptosis genes expression microarray data from the training datasets. An ferroptosis score model was constructed. The performance of the ferroptosis genes-based risk score model constructed by the DM training set was validated in the batch-1 and batch-2 DM sets. Normalized ferroptosis genes training data was used to compare the ssGSEA scores of gene sets between the high risk and low risk group. The statistical software package R (version 4.0.3) was used for all analyses. P value < 0.05 were considered statistically significant.

Results: We selected 54 significant G-Ferroptosis genes for further analysis in training set. There were 2 distinct subtypes (high-ferroptosis-score groups and low-ferroptosis-score groups) identified in G-Ferroptosis genes cohort which were also identified in validation datasets (Fig.1A, C, D). Metallothionein 1G (MT1G) was a characteristic gene of low-ferroptosis-score group. The characteristic genes of high-ferroptosis-score group were acyl-CoA synthetase family member 2 (ACSF2) and aconitase 1 (ACO1) (Fig.1B). Patients in high-ferroptosis-score group had a lower level of Tregs compared with that of low-ferroptosis-score patients in both training and validation set ($P < 0.05$, Fig.1E).

Conclusion: The biological process of ferroptosis is associated with the lever of Tregs, suggesting the process of ferroptosis may be involved in the disease progression of DM. Identifying ferroptosis-related features for DM might provide a new idea for clinical treatment.

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Figure : (A and B) Molecular typing of patients with DM based on ferroptosis-related gene expression profiles consensus clustering of GEO samples by NMF. Comparison of ferroptosis score levels between the two subgroups of the training set (C) and the validation set (D). (E) Comparison of the ssGSEA scores between different score groups. The scores of 22 immune cells are displayed in boxplots. ns $P > 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

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POS0860 EFFICACY AND SAFETY OF TWO COURSES OF RITUXIMAB BIOSIMILAR ACELLBIA IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS: A PROSPECTIVE OBSERVATIONAL STUDY

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