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 ≥10% FVC increase at the background of therapy. These data allow to consider the above 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±19.9 % to 84.7±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 (12±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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POSS859 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 identified in G-Ferroptosis genes cohort which was 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.

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). Metabolomicin 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.

References:

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POSS860 EFFICACY AND SAFETY OF TWO COURSES OF RITUXIMAB BIOSIMILAR ACELBIA IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS: A PROSPECTIVE OBSERVATIONAL STUDY

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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 were displayed in boxplots. *P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.

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