AN EXTENT OF INTERSTITIAL LUNG DISEASE IS A POTENTIAL PREDICTOR OF RESPONSE TO A-B-CELL THERAPY IN THE PATIENTS WITH SYSTEMIC SCLEROSIS

O. Koneva, O. Desinova, O. Ovasyannikova, L. Garzanova, M. Starovoytova, L. Ananieva

Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background

Systemic sclerosis (SSc) is a connective tissue disease associated with chronic polyclonal B-lymphocytic activation and immunological tolerance disturbance. Several research and clinical studies showed that B-cell depletion is potentially efficacious in SSc treatment. However, neither strong evidence of Rituximab (RTX) efficacy for treatment of interstitial lung disease (ILD) associated withSSc, no potential predictor of response to a-B-cell therapy.

Objectives

To evaluate rituximab (RTX) therapy efficacy in the patients with systemic scleroderma (SSc) differing in extent of interstitial lung disease (ILD) based on miltispiral computed tomography (MSCT) findings.

Materials and methods

42 patients (average age 48±2 years; male/female 1/6, diffuse/limited disease 1.5/1 (25 and 17), disease duration since the first non-Raynaud syndrome – 6.6±5.9 years) with definitely diagnosed SSc and ILD signs evidenced by MSCT were enrolled into the study. During the observation period 29±15.3 months the patients received RTX total dose of 2.5±1.3 grams in combination with glucocorticoids at average dose of 11.7±3.9 mg. 10 (24%) patients concurrently took immunosuppresants. The therapy efficacy was evaluated both in the general study population and in the patient subgroups with interstitial lesion extent up to 20% (Group A, n=13) and greater than 20% (Group B, n=29) of total pulmonary tissue area [1].

ITEMS	VALUE
SSc duration since the first non-Raynaud syndrome, M±δ, years	6.6±5.9
male/female ratio	1/6
Age, M±δ, years	48±2
diffused/limited disease ratio	1.5/1
follow-up duration since the first examination, M±δ, month	29±15.3
average RTX dose at the time of the last examination, M±δ, g	2.5±1.3
average glucocorticoids dose, M±δ, mg	2.5±1.3
interstitial lesion extent up to 20% (Group A), N	13
interstitial lesion extent greater than 20% (Group B), N	29

Table 1. Characteristics of group (n=42)

Results

In the general patient population significant FVC increase from 73.2±18.8% to 82±21.8% (p=0.000031) and stabilization of diffusing lung capacity (42.6±15.7% vs 44.7±14.6%. p=0.2) were observed. Median FVC increment was 6% (25th%–3,3%; 75th%–16%). FVC-based parameters increased by ≥10% in 16 (38%) patients and decreased in 3 (7%) patients.

Average FVC values in Group A were significantly higher compared with Group B both at the baseline (88.8±18.6% vs 65.4±14.5%, p=0.0002) and after the treatment (103.3±15.9% vs 74.1±18.5%, p=0.0009) with statistically significant FVC increase in both groups during the treatment period (p=0.016 and p=0.0014, respectively). Median FVC increment in Group A and Group B was 10.2% (25th%–4.7%; 75th%–21.9%) and 5.9% (25th%–2.75%; 75th%–14.7%), p>0.05, respectively. FVC-based parameters increased by ≥ 10% in 6(46%) patients in Group A, and in 10 (34%) patients in Group B, and decreased in 1 (8%) and 2(7%) patients, respectively. Average DLCO values were also significantly higher in Group A compared to Group B both before and after treatment (58.4±16.4% vs 36.3±10.1%. p=0.025; 59.3±15.2% vs 38.9±9.7%. p=0.005); DLCO values did not change over time during RTX therapy.

Median FVC increment in Group A and Group B was 10.2% (25th%–4.7%; 75th%–21.9%) and 5.9% (25th%-2.75%; 75th%-14.7%), p>0.05, respectively. FVC-based parameters increased by ≥10% in 6(46%) patients in Group A, and in 10 (34%) patients in Group B, and decreased in 1 (8%) and 2(7%) patients, respectively.

Average DLCO values were also significantly higher in Group A compared to Group B both before and after treatment (58.4±16.4% vs 36.3±10.1%. p=0.025; 59.3±15.2% vs 38.9±9.7%. p=0.005); DLCO values did not change over time during RTX therapy.

Fig. 1. Dynamics of FVC during RTX-therapy

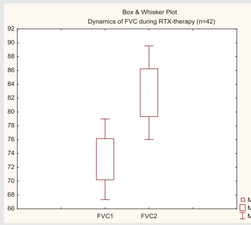


Fig. 2. Delta of FVC in groups A and B during RTX-therapy

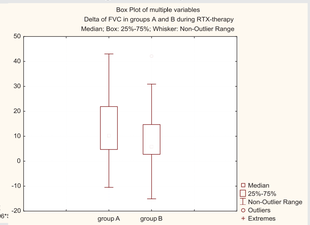
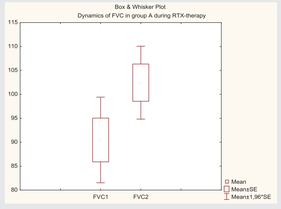


Fig. 3. Dynamics of FVC in groups A and B during RTX-therapy



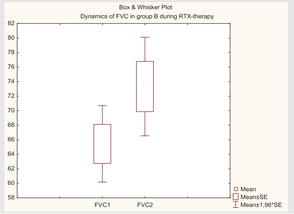
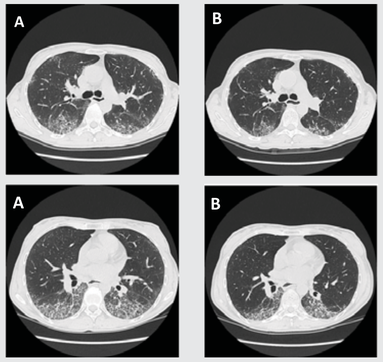


Fig 4 Reduction in the severity of interstitial changes during RTX-therapy

The patient Sh., 59 years: group B, the duration of the SSc-5 years Prednisolone 10 mg (3 years), Mycophenolate Mofetil 2gr. (1 year)



A – year 2012 , before RTX-therapy FVC – 70,8%, DLCO -38% average CT-score-24

B - year 2014, after RTX-therapy (cumulative dose – 3 gramms) FVC-88,8%%, DLCO-45% average CT-score -18

Conclusion

RTX-therapy resulted in significant FVC increase. FVC increment in the patient group with ILD extent up to 20% achieved significance in contrast to the patients with ILD extent greater than 20%, where FVC increment was 5.9%. Obtained data suggest that initial lung lesion area is a potential predictor of response to a-B-cell therapy in the patients with SSc.

1. Goh NS, Desai SR, Veeraraghavan S, et al. Interstitial lung disease: a simple staging system. Am J Respir Crit Care Med. 2008 Jun 1; 177(11):1248-1254.