Efficacy of rituximab in treatment naive PSS related ILD patients needs to be studied.

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AB0634 RITUXIMAB IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE, A CASE SERIES OF 18 PATIENTS

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Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc). Immunosuppressives such as cyclophosphamide (CYC) and mycophenolate mophetil (MMF) are used in its treatment with no proven efficacy (1). Rituximab (RTX) appears to be an emerging agent according to case series.

Objectives: This retrospective study aims to evaluate the efficacy of RTX on SSc-ILD in a group of patients followed in our center.

Methods: A chart review revealed 18 patients (16 women, 2 men; mean age 50.3±12.1 SD years (range 30–72), mean disease duration 8.3±9.3 SD years) with SSc who have been diagnosed as having ILD (confirmed by high-resolution thorax computed tomography and pulmonary function tests) and have been treated with one or more cycles of RTX. Efficacy was evaluated according to the criteria of the American Thoracic Society: improvement= an increase in FVC≥10% or DLCO≥15%; worsening= a decrease in FVC≥10% or DLCO≥15%; stabilization= changes in FVC less than 10% or DLCO less then 15% (2).

Results:

Table 1 Demographic findings of the patients and their response to RTX treatment

	Group 1 (ILD with short duration and naive to treatment)	Group 2 (ILD with long duration and previous IS therapy)	All patients
Number of patients	4 (22.2%)	14 (77.7%)	18
Sex (F/M)	3/1	13/1	16/2
Mean disease duration	2±0.8 SD years	10.2±9.8 SD years	8.3±9.3 SD years
Follow-up time after initiation of RTX	12.2±6.8 SD months	21±12.4 SD months	19±11.8 SD months
Baseline FVC%	69.2±20.9	65.1±14	
Last FVC%	66.7±13	61.6±19.6	
Baseline DLCO%	57.7±24.1	43.5±12.2	
Last DLCO%	52±18	41.2±21.8	
Outcome: Stable/ Improvement (n)	2	7	9
Worsening (n)	2	5	7
Death	0	1	1
Unable to do PFT (n)	0	1	1

Four patients were treatment naive for ILD when they received RTX (Group 1). The mean duration between the diagnosis of ILD and RTX treatment in Group 1 was 3.5 months (range 0–14 months). The average RTX cycle in this group was 2 with 1 patient also receiving mycophenolate mophetil in combination with RTX. The mean follow-up time after the initiation of RTX in this group was 12.2±6.8 SD months (range 7–22 months). FVC/DLCO was stable or improved in 2/4 compared to baseline and worsened in 2/4 at the end of follow-up at group 1.

Fourteen patients had a 10.2 years-history of SSc and have been treated with immunosuppressives (cyclophosphamide, azathioprine, methotrexate, MMF) for ILD before RTX (Group 2). The mean duration between the diagnosis of ILD and RTX treatment in Group 2 was 71.2 months (range 5–246 months). These patients received a mean of 3 cycles of RTX with 5 receiving MMF (n=3) or AZA (n=2) in addition to RTX. One patient died after 3 months following the first RTX cycle (unknown reason) and 1 was unsuitable for spirometry because of microstomia. Of the remaining 12 patients in Group 2, improvement or stabilisation was seen in 7 and worsening was seen in the remaining 5 patients.

Conclusions: RTX appears to be modestly effective for ILD of SSc. The duration of ILD as well as the presence or absence of previous immunosuppressive therapy do not appear as playing a role in response.

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AB0635 THE CLINICAL FEATURES AND PROGNOSIS OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SCLERODERMA AND OTHER CONNECTIVE TISSUE DISEASE DURING THE MODERN MEDICAL ERA IN JAPAN

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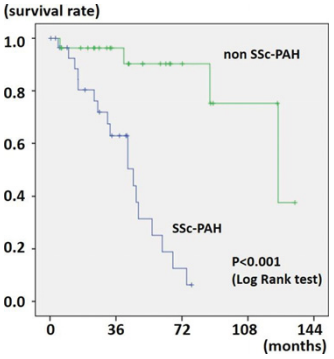
Background: Due to the recent progress of vasodilators for pulmonary arterial hypertension (PAH), the prognosis of PAH has been getting better for the past 10 years. Among them, idiopathic PAH (IPAH) well improved but PAH associated with connective tissue disease (CTD-PAH) especially scleroderma (SSc-PAH) have poorer prognosis than IPAH.

Objectives: This study intended to clarify the clinical features and prognosis of CTD-PAH in modern era when multiple PAH drugs are available, in addition, compare between SSc-PAH and PAH associated with other CTD-PAH (non SSc-PAH).

Methods: Fifty-seven consecutive CTD-PAH patients were enrolled to this study, who received hemodynamic examination with right heart catheterization between 2004 and 2016. Thirty of 57 patients were SSc-PAH patients and other 27 patients were non SSc-PAH patients (11 mixed connective tissue disease, 8 systemic lupus erythematosus, 5 primary sjogren syndrome, 1 polymyositis, 1 rheumatoid arthritis and 1 Still's disease were included). We retrospectively analyzed the relationship between clinical parameters at baseline and the prognosis of CTD-PAH patients.

Results: Mean age at entry were 65.3±10.3 and 48.3±15.5 years old each other (SSc-PAH vs non SSc-PAH $P<0.001$). Twenty-eight SSc-PAH (93%) and 26 non SSc-PAH patients (96%) took at least one vasodilator, among them, 18 SSc-PAH (60%) and 13 non-SSc-PAH (48%) patients took multiple vasodilators at the end of follow-up period. Comparing the baseline clinical parameters between two groups, vital capacity and diffusing capacity of the lung for carbon monoxide (DLCO) were significantly lower in SSc-PAH patients than non SSc-PAH patients and brain natriuretic peptide and creatinine level were higher in SSc-PAH patients than non SSc-PAH patients ($P<0.05$). However, there were no significant differences in hemodynamic indices between two groups. During a mean follow-up period of 42.5±31.5 months, 22 patients (18 SSc-PAH and 4 non SSc-PAH) died or received lung transplantation. The SSc-PAH patients had worse prognosis than non SSc-PAH patients (figure: $P<0.001$). Only 6 of 18 SSc-PAH patients and 1 of 4 non SSc-PAH patient died of PH related cardiovascular event and other principal causes of death included interstitial lung disease (ILD), neoplasm and infection. Applying multivariate Cox-proportional hazard regression, mean pulmonary arterial pressure, right atrial pressure, creatinine level and %DLCO were extracted as the independent risk for all-cause mortality.



Conclusions: SSc-PAH patients had poor prognosis among CTD-PAH patients despite the progression of PAH drugs. As well as the report from REVEAL registry, not only PAH severity but also respiratory dysfunction may predict the prognosis of CTD-PAH patient. Scleroderma is multiorgan disease affected by complex pathology of vasoconstriction (ischemia), proliferation, inflammation, autoimmune disorder and fibrosis. Our data suggest that vasodilator alone is not enough to improve the prognosis of CTD-PAH patients. Comprehensive therapeutic strategy for scleroderma is needed.

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