year). The hazard ratio (HR) was 0.57 (95% CI, 0.32-0.99) after adjustment of initial dose of CS and other concomitant medications. Subgroup analysis showed that CNI were more effective for AOSD patients with high ALT levels (≥ 80 IU/L) and/or severe complications such as HPS and DIC. The persistency rate of CNI was 71% at 5th year. Adverse events occurred more frequently in the CNI+ group than in the CNI- group (18% versus 8%, p = 0.04); however, serious adverse events did not increase in the CNI+ group (3% versus 2%). AOSD-related mortality had never been found in the observation period. One patient had a fatal course due to septic shock in the CNI+ group.
Conclusion: Our retrospective analysis suggested that CNI could be an additional option for treating AOSD with acceptable safety.

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OP0167 B LYMPHOCYTES DIRECTLY CONTRIBUTE TO TISSUE FIBROSIS IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is a fibro-inflammatory condition marked by rapid clinical improvement after selective depletion of B lymphocytes with rituximab. This feature suggests that B cells might participate in fibrogenesis and wound healing (1-3).
Objectives: In the present work we aimed to demonstrate that B lymphocytes contribute directly to tissue fibrosis in IgG4-RD.
Methods: Total circulating CD19+ B-lymphocytes, naïve B cells, memory B cells, or plasmablasts from IgG4-RD patients were cultivated with human fibroblasts. Pro-fibrotic soluble factors and collagen production in the co-cultures were assessed by ELISA and Luminex assays. RNA-sequencing and quantitative RT-PCR were used to assess fibroblast activation in the presence of B cells, as well as the induction of pro-fibrotic pathways in B cell subsets. Relevant pro-fibrotic and inflammatory molecules were confirmed in vitro by functional experiments and on IgG4-RD tissue sections by multi-color immunofluorescence studies.
Results: B cells from IgG4-RD patients (i) produced the pro-fibrotic molecule PDGF-B and stimulated collagen production by fibroblasts; (ii) expressed enzymes implicated in extracellular matrix remodeling such as LOXL2; (iii) produced the chemotactic factors CCL-4, CCL-5, and CCL-11; and (iv) induced the production of these same chemokines by activated fibroblasts. Plasmablasts expressed sets of genes implicated in fibroblast activation and proliferation, and therefore represent cells with intrinsic pro-fibrotic properties
Conclusion: We have demonstrated that B cells, contribute directly to tissue fibrosis in IgG4-RD. These unanticipated pro-fibrotic properties of B lymphocytes, particularly of plasmablasts, might be relevant for fibrogenesis in other fibro-inflammatory disorders and for wound healing processes in physiological conditions.

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OP0168 DERIVATION AND VALIDATION OF A NEW STILL ACTIVITY SCORE (SAS)

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Background: Adult-onset Still's disease (AOSD) is a rare, chronic, multisystem and auto-inflammatory disorder. Although several classification criteria exist for the diagnosis of AOSD, there is no valid method for the assessment of disease activity for these patients.
Objectives: To determine a simple method for the assessment of AOSD activity.
Methods: We conducted a cross-sectional, multicenter study for assessment of disease activity in AOSD patients. All AOSD patients were fulfilled the Yamaguchi criteria. Age, sex, disease duration and current symptoms were recorded. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), leukocyte count, and ferritin levels were also recorded. Visual analog scale (VAS) (0–10 cm) and likert scale (as remission, low, moderate, severe, and more severe disease activity) were used for physician's (PhGA) and patient's (PtGA) global assessment of disease activity. Patients were enrolled to ''derivation cohort'' (n=125) and subsequently ''validation cohort'' (n=72). Ordinal logistic regression model was used to derive Still Activity score (SAS).
Results: Overall, 197 (66.5% female) AOSD patients were enrolled. Mean age was 39 (13) years and median disease duration was 2 (0–30) years. Cross-sectional frequency of AOSD findings were as follow; fever 69 (35%), rash 55 (27.9%), arthritis 57 (28.9%), arthralgia 112 (56.9%), sore throat 58 (29.4), myalgia 80 (40.6), lymphadenopathy 25 (12.7%), splenomegaly 37 (18.8%), hepatomegaly 23 (11.7%), abdominal pain 8 (4.1%), pleuritic pain 8 (4.1%), pericarditis 4 (2%), hemophagocytic syndrome 4 (2%). Mean (SD) ESR (mm/h), CRP (mg/dl), ferritin and leukocyte count were 32.5 (31), 43.4 (65.3), 1169 (3088) and 10356 (4821), respectively. Mean PtGA and PhGA was 3.86 (3.29), and 3.05 (3.06). SAS derived for the assessment of AOSD disease activity is given in Table 1.

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SAS were correlated with the PtGA of disease activity as 83% for the derivation cohort and 75% for the validation cohort, also, correlation of this score and patient's global VAS assessments were 79% and 73%, respectively. Sensitivity and specificity of SAS equal and/or higher than 4 to predict '' active (severe) and highly active (more severe) AOSD activity'' are 100% and 82.6%, respectively (Figure 1).

Conclusion: In this study, we created a Still activity score (SAS) with the routine clinical and laboratory features of patients. This score can detect patients who have high likelihood of being in active disease status. In the future perspective, SAS should be assessed in the clinical trials and routine practice.

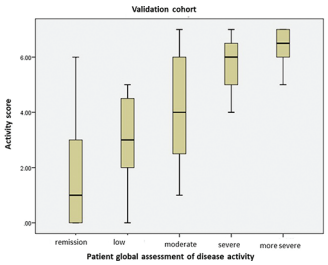

Figure 1. Boxplot of SAS and patients' global assessment of disease activity

Table 1. Still activity score (SAS)

	0 point	1 point	2 points
Fever	Absent		Present
Arthralgia	Absent		Present *
Neutrophilia% ≥65	No	Yes	
Ferritin ≥ 350 ng/ml	No	Yes	

*If number of swollen joints ≥2, add 1 point.

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OP0169

LONG-TERM SURVIVAL IN LUNG TRANSPLANTATION FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONECTIVE TISSUE DISEASES. STUDY OF 26 CASES OF A SINGLE CENTER

D. Prieto-Peña, Monica Calderón-Goercke, Amaya Martínez-Meñaca, Victor Manuel Mora-Cuesta, Sonia Fernández-Rozas, David Iturbe-Fernández, Jose Manuel Cifrián-Martínez, Miguel A González-Gay, Ricardo Blanco. *Marqués de Valdecilla University Hospital, Santander, Spain*

Background: Interstitial lung disease (ILD) is one of the most serious complications associated with connective tissue diseases (CTD). Patients with ILD have increased mortality and limited treatment options. Lung transplant has been recognized as an option for patients with end-stage CTD-ILD. However, rheumatic diseases are still sometimes considered a contraindication for lung transplant because of concerns for worse outcomes.

Objectives: Our aims were to: **a)** assess long-term post-transplant survival in patients with CTD-ILD and **b)** compare post post-transplant survival of patients with CTD-ILD with patients with idiopathic pulmonary fibrosis (IPF).

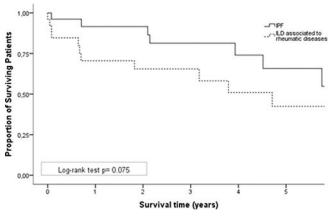
Methods: Single center study in a referral center for lung transplant of all patients who underwent lung transplantation for CTD-ILD between 1998 and 2017. This cohort was compared with patients with IPF (group-matched for age, transplant year and basiliximab induction). Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test.

Results: We studied 26 patients with CTD-ILD matched to 26 patients with IPF. The underlying diseases of patients with CTD-ILD were: Rheumatoid arthritis (n=9), Scleroderma (n=6), Sjögren syndrome (n= 4), ANCA-vasculitis (n=3), Anti synthetase syndrome (n=2), Dermatomyositis (n=1), Systemic lupus erythematosus (n=1). The comparative study of baseline characteristics between both groups is shown in the TABLE. All of RA patients undergoing transplantation in our study had the histologic subtype of usual interstitial pneumonia (UIP) whereas non-specific interstitial pneumonia (NSIP) was the most common histologic subtype of ILD associated with the rest of CTD. Cumulative survival rates at 5 year post-transplant did no differ significantly between CTD-ILD and IFP [42.4% vs 65.8% (p=0.075)] (FIGURE 1).

TABLE

	IPF (n=26)	CTD-ILD (n=26)	P
Age *(years)*, mean ± SD	60.4 ± 5.3	56.5 ± 8.3	0.06
Sex *(women), n (%)*	6 (23.1)	18 (69.2)	0.001
Time on waiting list (*days*), median [IQR]	86.0 [35.5-268.3]	82.0 [37.0-212.3]	0.78
Smokers, n (%)	19 (73.1)	11 (42.3)	0.07
Type of transplant (*bilateral*), n (%)	8 (30.8)	13 (50.0)	0.16
Donor CMV + and recipient CMV -, n (%)	4 (15.3)	2 (7.7)	0.72
Basiliximab induction, n (%)	9 (34.6)	9 (34.6)	0.99
Variables at transplant			
FEV 1 (%), median [IQR]	57 [35.5-71.3]	50 [41.0-60.0]	0.34
FVC (%), median [IQR]	54 [36.0-65.8]	51 [44.0-61.0]	0.55
FEV1/FVC, median [IQR]	82 [75.9-88.5]	80 [72.0-89.1]	0.52
DLCO	24 [18.7-42.0]	30 [23.0-43.5]	0.49
KCO	66 [49.5-82.5]	68 [42.9-78.0]	0.54
Serum creatinine (*mg/dL*), mean ± SD	0.78 ± 0.14	0.80 ± 0.31	0.74
Right catheterization, n (%)	11 (42.3)	16 (61.5)	0.07
mPAP (*mm Hg*), mean ± SD	23.3 ± 3.8	26.5 ± 8.6	0.15
PCP (*mm Hg*), mean ± SD	13.3 ± 2.7	12.0 ± 4.7	0.44
Treatment pre-transplant			
Glucocorticoids, n (%)	20 (76.9)	23 (88.5)	0.22
Immunosuppressive drugs, n (%)	7 (26.9)	21 (80.8)	0.001
Allograft dysfunction			
Acute rejection	15 (62.5)	8 (32.0)	0.032
Chronic rejection	2 (8.3)	5 (20.0)	0.417

CTD-ILD: interstitial lung disease related with connective tissue diseases; DLCO: diffusing capacity of lung for carbon monoxide; IFP: idiopathic pulmonary fibrosis; KCO: transfer coefficient of the lung for carbon monoxide; RA-ILD: interstitial lung disease related with rheumatoid arthritis; mPAP: mean pulmonary arterial pressure; PCP: pulmonary capillary pressure.



Conclusion: Our retrospective analysis showed a trend to lower long-term post-transplant survival than in those with IPF, however no statistical differences were found in cumulative survival rates at 5-years post-transplant. These data support that lung transplantation should be considered in patients with end-stage CTD-ILD.

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