Figure 1.

Conclusion: Brentuximab vedotin already achieved the primary endpoint at 24 weeks, after half of the intended recruitment sample reached this landmark. A comparison with CSRG controls showed that mRSS only decreased significantly in patients treated with brentuximab. This interim report suggests that brentuximab vedotin might effectively improve skin involvement in patients with diffuse SSc and severe skin involvement.

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OP0173

REDUCTION OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS ON RITUXIMAB TREATMENT. LONG-TERM FOLLOW-UP

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Background: A sound experience has been accumulated up to date with the use of rituximab (RTX) for treatment of systemic sclerosis (SSc). Some studies reported improvement of skin fibrosis following treatment with RTX, but long-term follow-ups are really few.

Objectives: to evaluate the effect of RTX on the manifestations of skin fibrosis in patients (pts) with SSc in the long-term follow-up.

Methods: This prospective study included 71 pts aged 46 years (17-66) on average, 59 (83%) pts were females, mean disease duration was 5,6±4,4 years, and mean follow-up - 42 months (12-72) (mo). Diffuse SSc was established in 42 (59%) pts. All pts received glucocorticoids in low doses. 45% of pts were receiving immunosuppressants at study entry. The following parameters were evaluated: Rodnan skin score (mRSS), interdigital space (IDS) (the distance between the tips of 1 and 5 fingers at maximum extension), oral aperture (OAp) and activity index (EScSG-AI) over the periods: 12-18 mo, 24-30 mo, 36-42 mo, 48-54 mo and 60-72 mo after initiation of RTX therapy. The results are presented as: mean values, delta (Δ), median, upper and lower quartiles.

Results: RTX therapy resulted in significant decrease of disease activity index, which statistically significantly correlated with decrease of mRSS - the main indicator of the severity of skin fibrosis ($r=0,39$; $p=0,001$). Changes in parameters by follow-up periods are presented in the Table 1.

Table 1. Changes in clinical and instrumental parameters at RTX treatment (delta; median; lower quartile; upper quartile).

Parameters	12-18 mo (n=71)	24-30 mo (n=55)	36-42 mo (n=36)	48-54 mo (n=24)	60-72 mo (n=17)
ΔmRSS	3,32 [3,3; 0; 8] $p=0,001$	5,4 [3; 0; 10] $p=0,001$	5,1 [3,5; 0; 9] $p=0,001$	5,3 [3; 0; 10] $p=0,001$	7,3 [5; 1; 14] $p=0,001$
ΔOAp, cm	0,24 [0,1; 0; 0,5] $p=0,0009$	0,26 [0,1; 0; 0,6] $p=0,0006$	0,39 [0,2; 0; 0,8] $p=0,004$	0,31 [0,3; 0; 0,7] $p=0,006$	0,36 [0,2; 0; 0,8] $p=0,009$
ΔActivity index (EScSG-AI)	1,49 [1,5; 0; 2,5] $p=0,001$	1,64 [1,5; 0; 2,5] $p=0,001$	1,11 [1; 0; 2] $p=0,0001$	2 [2; 1; 3] $p=0,0001$	2,17 [2; 1,5; 2] $p=0,0001$
Cumulative dose of RTX, g	1,43±0,6	2,97±0,8	3,45±1,3	3,96±1,1	5,15±1,7

Decreasing of mRSS statistically significantly correlated with increasing cumulative dose of RTX ($r=0,29$; $p=0,01$). Decreasing disease activity index correlated with increasing cumulative dose of RTX ($r=-0,37$; $p=0,01$). IDS improvement was documented at all assessment time periods, although statistically insignificant.

Conclusion: The results of this study confirm reported positive effect of RTX on the reduction of skin fibrosis in SSc. Long-term follow-up demonstrated steadily decreasing skin fibrosis and improvement of microstomia with increasing oral aperture in parallel with a decrease of the disease activity index and increasing cumulative dose of RTX.

Disclosure of Interests: None declared

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OP0174

SUBCLINICAL INTERSTITIAL LUNG DISEASE IS FREQUENT AND PROGRESSES ACROSS DIFFERENT CONNECTIVE TISSUE DISEASES

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Background: Based on the argument that symptoms define disease, physicians commonly apply the terms "preclinical" or "subclinical" disease to describe patients with disease-related findings but no accompanying symptoms for connective tissue disease associated interstitial lung disease (CTD-ILD). The term subclinical frequently applies to patients with mild ILD changes on high resolution chest tomography (HRCT), normal forced vital capacity (FVC), and without respiratory symptoms. Previous work in systemic sclerosis (SSc)-ILD did show that patients with even minor extent of ILD at baseline often progressed and had increased mortality risk, suggesting that it is not appropriate to define these patients as "subclinical".

Objectives: To identify the prevalence of subclinical ILD across CTD diagnoses, and assess the rate of progression of lung fibrosis compared to CTD without ILD and with clinical ILD.

Methods: All CTD patients, including SSc, anti-synthetase syndrome (ASS) and mixed connective tissue disease (MCTD) from the Oslo University Hospital diagnosed before 2015 and assessed for the presence of ILD by HRCT were included. The year 2015 was chosen to secure an observation time of at least five years from ILD diagnosis to study end on 01.01.2021 or time of death. All patients fulfilled the respective CTD classification criteria. Subclinical ILD was defined as an ILD extent <5% by semi-quantitative assessment of baseline HRCT, preserved lung function with FVC >80% predicted and without respiratory symptoms. Clinical ILD was defined as >5% extent of ILD or <5% extent of ILD on HRCT with respiratory symptoms or FVC <80%. The outcome was ILD progression, defined as increasing extent of ILD from baseline to follow-up HRCT by semi-quantitative assessment. Vital status was available in all patients and mortality was evaluated. Descriptive statistical analyses were conducted and time to ILD progression determined by Kaplan-Meier estimates.

Results: We identified 525 CTD patients, including 296 with SSc, 135 with MCTD and 94 with ASS who had conducted a baseline HRCT. Of these, 227 (43%) had no ILD, 67 (13%) subclinical and 231 (44%) clinical ILD (Table). Of the 67 subclinical ILD patients, 45 (15%) had SSc, 13 (10%) MCTD and 9 (10%) ASS of these specific cohorts. Over a median time of 4.5 years between baseline and follow-up HRCT, 95/395 (24%) showed progression of ILD, including 72 (26%) SSc and 23 (19%) MCTD patients. Disease progression frequently occurred in both subclinical ILD (38%) and clinical ILD (51%) patients (Figure). Age, gender, underlying CTD, and baseline lung function were not predictive for the progression of lung fibrosis. Progression was too infrequent to allow for meaningful multivariable regression analyses. After a median observation period of 12 years, 153 (29%) of the patients died. The 1-, 5- and 10-year survival rates in those without ILD, subclinical and clinical ILD were 97%/97%/99%, 88%/91%/82%, and 82%/85%/68% ($p<0.001$), respectively.

Table 1. Clinical characteristics, demographics and outcome

	No ILD (n=227)	Subclinical ILD (n=67)	Clinical ILD (n=231)
Age, y (SD)	50 (15.4)	51 (14.4)	52 (15.3)
Male sex, n (%)	89 (39)	22 (33)	111 (48)
Deceased, n (%)	50 (22)	12 (18)	91 (39)
Observation period, y median (range)	13.7 (18.6)	13.9 (17.9)	11.5 (17.1)
FVC% (SD)	97 (18.6)	99 (17.9)	81 (20.9)
FVC decline% (SD)	-0.70 (11.1)	-0.81 (16.5)	-1.61 (15.9)
DLCO% (SD)	73 (19.4)	73 (16.9)	55 (17.4)
Extent of ILD% (SD)	0 (0)	2.3 (1.5)	19.3 (16.8)
ILD progression% (SD)	0.08 (1.0)	3.1 (6.2)	3.6 (9.9)
ILD progressors, n (%)	3 (2)	20 (38)	72 (51)

Figure 1. Time to ILD progression in CTD without ILD, with subclinical and clinical ILD

Conclusion: Subclinical ILD is frequently present across CTDs and progresses over time in a substantial subgroup of patients, comparable to patients with clinical ILD. Our findings question the terms sub- and preclinical ILD, which may potentially lead to a suboptimal “watchful waiting management strategy”. Monitoring all CTD patients with any ILD is of high importance to identify disease progression early.

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OP0175 INTERNATIONAL MULTICENTRIC PROSPECTIVE STUDY ON PREGNANCY IN SYSTEMIC SCLEROSIS (IMPRESS-2)

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Background: Data about the obstetric outcomes of pregnant women with Systemic Sclerosis (SSc) mainly derive from retrospective studies. Moreover, little evidence is available to define if pregnancy impacts on SSc course and if children of SSc mothers have a normal post-natal development.

Objectives: To assessed the obstetric, pediatric and rheumatologic outcomes of SSc pregnancies in a prospective controlled study

Methods: Prospective recruitment of three cohorts.

1) 110 pregnant women with SSc.

2) 218 control pregnancies without systemic autoimmune diseases

3) 78 non-pregnant control SSc with a matching subject in cohort-1.

SSc was characterized for disease activity, severity, cutaneous/organ involvement and therapy. Women and their offspring were followed until 21 months after enrollment (ie, 12 months after expected delivery).

Results: Gestational and neonatal outcomes

Miscarriages and fetal death occurred in 7% and 5% of SSc pregnancies. Compared to control pregnancies, SSc pregnancies had higher rates of gestational hypertension (12% Vs 4%, p=0.004), pre-eclampsia (9% Vs 1%, p=0.002), fetal growth-restriction (13% Vs 4%, p=0.004), prematurity (26% Vs 7%, p<0.001) and cesarean section (52% Vs 4%, p=0.002). Newborns from SSc mothers weighted less (2773 Vs 3243g, p<0.001), were more frequently small for gestational age (SGA, 18% Vs 12%, p=0.05) and required neonatal-intensive care unit (ICU) more frequently (12% Vs 1%, p<0.001). Rates of newborn malformation/death, and one year-pediatric outcomes were similar.

Univariate and multivariate analyses were performed for relevant outcomes. For example, pre-eclampsia positively associated with baseline skin score and its evolution during pregnancy (p=0.015 and 0.013), immunosuppressive agents, bosentan and iloprost at baseline (p=0.001, 0.041 and 0.007), and twin pregnancy (p=0.006). Multivariate logistic regression for pre-eclampsia in SSc identified baseline arterial hypertension, immunosuppressive agents or of iloprost, twin pregnancy and assisted conception as risk factors (p=0.000, 0.002, 0.0025, 0.000 and 0.027), and baseline calcium channel blockers as protective factors (p=0.001).

SSc course during pregnancy

As compared to matched non-pregnant SSc, SSc pregnant women had lower Medsger disease severity index (0.6 +/-0.9 Vs 1.0 +/-1.1, p=0.022), health assessment questionnaire (HAQ, 0.21 +/-0.38 Vs 0.40 +/-0.55, p=0.026), and lower rate of iv iloprost (21% Vs 42%, p=0.006). Pregnant and non-pregnant SSc women had a similar disease course during the 21 months of follow-up, despite a lower use of immunosuppressive agents (17% Vs 36%, p=0.014). Two scleroderma-renal-crises (SRC) occurred during pregnancy (one was a relapse of a previous SRC; the other occurred at week 33, and resolved after premature delivery of a SGA newborn and ACE-inhibitors, preventing differentiation from pre-eclampsia).

Conclusion: SSc pregnancies have generally a favorable obstetric/pediatric outcome, albeit at a higher risk of gestational hypertension, pre-eclampsia, fetal growth restriction, prematurity, delivery of SGA newborn and requirement of neonatal-ICU. Pregnancy does not impact on SSc course, although SRC during late pregnancy and pre-eclampsia might be hardly discriminated.

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OP0176 ULTRASOUND (US) EVALUATION OF BOWEL VASCULOPATHY IN SYSTEMIC SCLEROSIS (SSC)

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Background: Gastrointestinal involvement is one of the most frequent features of SSc, affecting nearly 90% of patients, with a great impact on quality of life and morbidity. One of the key pathological factors of SSc bowel involvement is vasculopathy (1), although little is known about its pathophysiology and no treatments are currently available.

Objectives: To assess with abdominal US the superior mesenteric artery (SMA) and the inferior mesenteric artery (IMA) vessel characteristics and blood flow in SSc, compared to healthy controls (HC).

Methods: we performed fasting abdominal US in SSc patients fulfilling the ACR/EULAR 2013 classification criteria and HC. Patients with a history of peripheral / coronary arterial disease were excluded. For both SMA and IMA, caliber (mm), Peak Systolic Velocity – PSV (cm/sec), Reverse Velocity – RV (cm/sec), End-Diastolic Velocity – EDV (cm/sec), Mean Velocity – mV (cm/sec), Blood-flow (cm/sec), Resistive Index – RI and Pulsatility Index – PI were measured.

Results: 28 SSc patients [25 females (89.3%), mean age 48.75 ± 12.39 years; 6 (22.22%) anti-centromere and 19 (70.37%) positive for anti-topoisomerase I antibodies] and 28 HC [18 females (64.3%), mean age 36.25 ± 12.08 years] were evaluated. In SSc, the SMA caliber was significantly smaller than in HC (5.75 ± 0.62 vs. 6.45 ± 0.60 mm, p<0.0001), while IMA dimensions did not differ.

The SMA study revealed SSc patients had a significant reduction of RV (7.25 ± 6.37 vs. 18.52 ± 6.16 cm/sec, p<0.0001) and PI (3.33 ± 0.75 vs. 4.53 ± 1.03, p<0.0001) when compared to HC. In addition, in SSc the mV of SMA was significantly lower than in HC (38.03 ± 13.90 vs. 28.32 ± 9.25 cm/sec, p=0.0035), as well as the RI (0.88 ± 0.04 vs. 0.91 ± 0.03, p=0.0034); EDV was significantly increased (16.34 ± 7.03 vs. 12.64 ± 5.46 cm/sec, p=0.0321). Similarly to SMA, also in IMA RV and PI were significantly lower than controls (RV: 2.69 ± 6.10 vs. 17.06 ± 5.75 cm/sec, p<0.0001; PI: 3.54 ± 0.95 vs. 6.08 ± 1.53, p<0.0001). Moreover SSc patients presented a significant reduction of PSV and RI of IMA (PSV: 72.27 ± 27.23 vs. 93.81 ± 25.73 cm/sec, p=0.0084; RI: 0.88 ± 0.04 vs. 0.91 ± 0.03, p=0.0132) when compared to HC. Although the HC group was significantly younger than the SSc group (p=0.0003), all the results were confirmed after adjustment for age (Table 1).