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Table 1. The frequencies of non-vascular pulmonary manifestations in patients with Takayasu' arteritis

n (%)	All Patients n=197	Patients with PAH n=22	p
Symptoms	24 (12.2)	3 (13.6)	0.049
Cough/Dyspnea	4 (2)	3 (13.6)	0.000
Hemoptysis			
Pulmonary involvement in CT	10 (5.1)	5 (22.7)	0.000
	4 (2)	1 (4.5)	0.000
Pulmonary infiltrates	1 (0.5)	1 (4.5)	0.000
Nodules/cavities	1 (0.5)	1 (4.5)	0.000
Pulmonary hemorrhage	5 (2.5)	2 (9.1)	0.000
Pleural effusion			

(PAH: pulmonary arterial hypertension, CT: computed tomography)

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Scleroderma, myositis and related syndromes

FRI0300 IMPACT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS IN A COMPLETE, NATIONWIDE COHORT

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Background: Interstitial lung disease (ILD) represents a clinical challenge in systemic sclerosis (SSc) and associates with high mortality. The presence of severe lung fibrosis is a strong predictor for early mortality. There is substantial progress in SSc-ILD research, but precise, population-based data on cumulative incidence, range of severity and predictive value of clinical risk factors are lacking. Such data are vital for clinical decision making, and highly warranted as background information for appropriate development of screening and management strategies for SSc-ILD.

Objectives: To assess cumulative incidence of ILD, range of ILD severity and mortality risk predicted by baseline pulmonary function tests (PFT) and ILD extent by CT in a complete, nationwide SSc cohort.

Methods: The Norwegian SSc cohort study (Nor-SSc) includes all the 630 incident and 185 prevalent SSc patients from 2000-2012 meeting SSc classification criteria. A baseline PFT was recorded in 703 (86%) patients, and 650 (80%) had high resolution computed tomography (HRCT) images available for analyses. Extent of fibrosis was scored on 10 sections from every HRCT and expressed as percentage of total lung volumes. For the survival and mortality analyses, all Nor-SSc patients diagnosed from 2000-2012 (the 630 incident cases) were included and compared with 15 age- and gender matched controls per patient drawn from the national population registry. Vital status was available for all patients and controls at study end (January 2018). Descriptive statistics and standardized mortality rates (SMR) were estimated.

Results: Of the 815 patients in the total Nor-SSc cohort, 682 (84%) were female and 629 (77%) had limited cutaneous SSc. Mean age at SSc diagnosis was 53 yrs, with mean time from SSc onset to diagnosis of 3.8 yrs. We observed ILD on HRCT in 324/650 patients (50%), and the majority of these had <5% lung fibrosis (Figure 1A). Mean FVC at baseline was 94% of expected value, and nearly half of the patients (42%) had an FVC>100% (Figure 1B). Proportionate distribution of FVC

values in patients with no lung fibrosis, <10% lung fibrosis of total lung volume and >10% lung fibrosis is shown in Figure 1C. During the mean 8.6 yrs observation period of this study, 148 of the 630 incident SSc patients died, corresponding to an overall SMR of 2.4. Separate analyses of the 650 patients with baseline HRCT data showed that the SMR correlated with presence and extent of lung fibrosis, from SMR 2.2 in patients with no fibrosis to SMR 8 in patients with >25% lung fibrosis (Figure 1D). Correspondingly, we found that the SMR changed across patient groups stratified by baseline FVC%, with increased mortality evident already in the FVC 90-100% group (Figure 1E).

Conclusion: The results from this population based SSc cohort study provide new, unbiased data regarding the impact of ILD. Our results indicate a dose-response relationship between lung fibrosis extent and SMR; and between FVC% and SMR. Importantly, this relationship was evident even in groups with limited lung fibrosis and groups with normal range FVC%, strongly suggesting that all SSc patients should be screened with PFT and HRCT at baseline, to diagnose ILD early and tailor further management.

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FRI0301 GASTROINTESTINAL ADVERSE EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) TREATED WITH NINTEDANIB: DATA FROM THE SENSICIS TRIAL

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Background: In patients with idiopathic pulmonary fibrosis (IPF), nintedanib has a manageable adverse event (AE) profile characterised predominantly by gastrointestinal (GI) events. The efficacy and safety of

nintedanib versus placebo in patients with SSc-ILD were investigated in the SENSICIS trial (NCT02597933).

Objectives: To characterise GI AEs associated with nintedanib therapy in the SENSICIS trial.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years were randomised to receive nintedanib 150 mg bid or placebo double-blind. Dose reductions to 100 mg bid and treatment interruptions were allowed to manage adverse events. AEs reported over 52 weeks of treatment were coded using preferred terms in the Medical Dictionary for Regulatory Activities and analysed descriptively. A questionnaire was used to collect additional information on diarrhoea AEs.

Results: A total of 576 patients (288 per group) received ≥ 1 dose of nintedanib or placebo. Over 52 weeks, 13.9% and 7.3% of patients treated with nintedanib and placebo discontinued study treatment due to AEs. The most frequent AEs in patients treated with nintedanib were diarrhoea (75.7% vs 31.6%), nausea (31.6% vs 13.5%) and vomiting (24.7% vs 10.4%). Serious diarrhoea AEs were reported in 2 patients (0.7%) in each group, and serious vomiting AEs were reported in 2 patients (0.7%) in the placebo group and none in the nintedanib group. Of the 218 nintedanib-treated patients who experienced a diarrhoea AE, most experienced events that were at worst of mild (49.5%) or moderate (45.0%) intensity, most (70.2%) experienced 1 or 2 events, and the duration of diarrhoea AEs was ≤ 9 days for 50% of the events reported over 52 weeks. Among nintedanib-treated patients who experienced ≥ 1 diarrhoea AE, 26.1% had a permanent dose reduction and 9.2% discontinued study drug due to the AE. Among the 91 patients in the placebo group who experienced ≥ 1 diarrhoea AE, the duration of diarrhoea AEs was ≤ 3 days for 50% of the events reported over 52 weeks, 2.2% had a permanent dose reduction and 1.1% discontinued study drug due to the AE.

Conclusion: In patients with SSc-ILD, the gastrointestinal AEs associated with nintedanib were manageable for most patients and consistent with its known safety and tolerability profile in patients with IPF.

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FR10302

SAFETY AND EFFICACY OF RITUXIMAB BIOSIMILAR IN SYSTEMIC SCLEROSIS: AN ITALIAN MULTICENTER STUDY

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Background: recent data support the use of rituximab(RTX) in Systemic Sclerosis(SSc). RTX biosimilar(RTX-B) offers a more affordable option but its efficacy and safety have not yet been evaluated.

Objectives: To assess the safety and efficacy of RTX-B in SSc.

Methods: Data about SSc patients treated with RTX-B(1gr repeated after 2 weeks) and with a follow-up ≥ 6 months were retrospectively collected from 5 Italian centres. Both SSc patients naïve to RTX(RTX-Bn) or already treated with ≥ 1 course of RTX originator(RTX-O) and switched to RTX-B(RTX-Bs) were considered. A comprehensive assessment of disease features and organ involvement was available at baseline and at final follow-up for all patients. Non parametric tests were used.

Results: Data of 21 SSc patients(20 female, mean age 50.5 $\pm$ 11.8 years) were collected;mean disease duration at RTX-B therapy was 7.6 $\pm$ 4.8 yrs. Eleven patients(52%) had diffuse cutaneous SSc(dcSSc), 12(57%) were anti-topoisomerase+, 5 anti-RNA-polymeraseIII+ and 4 anti-centromere+. Twelve patients(57%) were RTX-Bn and 9 RTX-Bs(43%). In RTX-Bs patients, the median number of previous RTX-O courses was 3(range 1 – 8). RTX was decided because of skin progression in 11(52%), interstitial lung disease(ILD) worsening in 9(43%), arthritis in 6(29%), myocarditis and myositis in 1 patient each. All patients had been previously treated with immunosuppressants: mycophenolate mofetil(MMF) 14(67%), methotrexate(MTX) 7(33%), cyclophosphamide 6(29%), azathioprine 4(19%), tocilizumab and etanercept 1(5%) patient each. At RTX-B introduction, 14 (67%) patients were on concomitant immunosuppressant: 10(48%) MMF and 4(19%) MTX; 15 patients(71%) were also on steroids(mean dose:3.1 $\pm$ 2.1mg/day). At 6 months after RTX-B treatment, a significant reduction of the modified Rodnan skin score(mRSS), DAS28 and erythrocyte sedimentation rate(ESR) was observed in the entire cohort (p<0.001,p<0.028, p<0.003, respectively); mRSS was significantly reduced also in RTX-Bn (p<0.011) and RTX-Bs patients(p<0.046)(Table 1). No significant changes were observed for lung function tests. Only 1 RTX-Bs patient experienced a transient neutropenia 3 months after the 2nd RTX-B infusion whilst also on MTX.

Conclusion: in agreement with previous data published on RTX-O, also RTX-B seem efficient in improving skin and joint involvement and in stabilizing lung function, either in RTX-Bn and in RTX-Bs SSc patients.

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