Background: Gastroesophageal reflux disease (GERD) occurs frequently in patients with systemic sclerosis (SSc) and SSc-associated interstitial lung disease (SSc-ILD). PPI use has to be shown to improve survival in patients with idiopathic pulmonary fibrosis, whereas to date there are no data on the use of PPI in SSc-ILD.

Objectives: This study was aimed to assess whether use of PPI is associated with progression of SSc-ILD and survival.

Methods: We retrospectively analysed 1931 patients with SSc and SSc-ILD from the German Network for Systemic Sclerosis (DNSS) database (2003 onwards). Kaplan–Meier analysis compared overall survival (OS) and progression-free survival (PFS) in patients with vs. without GERD (SSc and SSc-ILD) and PPI vs. no PPI use (SSc-ILD only). Progression was defined as a decrease in either % predicted forced vital capacity ≥10% or single-breath diffusing capacity for carbon monoxide ≥15%.

Results: GERD was not associated with decreased OS or PFS in patients with either SSc or SSc-ILD. In patients with SSc-ILD, PPI use was associated with improved OS vs. no PPI use after 1 year (98.4% [95% confidence interval: 97.6–99.3%]; n=760 vs. 90.8% [87.9–93.8%]; n=290) and after 5 years (91.4% [89.2–93.8%]; n=357 vs. 70.9% [65.2–77.1%]; n=106; p<0.0001). PPI use was also associated with improved PFS vs. no PPI use after 1 year (95.9% [94.6–97.3%]; n=745 vs. 86.4% [82.9–90.1%]; n=278) and after 5 years (86.8% [83.0–90.6%]; n=286 vs. 45.9% [39.6–53.2%]; n=69; p<0.0001).

Conclusion: GERD had no effect on survival in SSc or SSc-ILD. PPIs improved survival in patients with SSc-ILD; however, controlled, prospective trials are needed to confirm this finding.

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Background: In the randomized SENSCIS trial in subjects with SSc-ILD, nintedanib reduced the rate of decline in FVC over 52 weeks (mL/year) by 44% compared to placebo. Healthy individuals have varied FVC depending on age, sex, ethnicity and height; expected values can be determined using internationally recognized reference equations.

Objectives: To provide further context to the FVC declines observed in the SENSCIS trial, we compared the decline in FVC observed in subjects with SSc-ILD in the SENSCIS trial with the decline in FVC that would be expected in hypothetical subjects without ILD matched for age, sex, ethnicity and height.

Methods: The SENSCIS trial enrolled subjects with SSc-ILD aged ≥18 years with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT, FVC ≥40% predicted and DLco 30–89% predicted. Baseline FVC (mL) and changes in FVC (mL) at week 52 were assessed in the nintedanib and placebo groups, with missing values at week 52 imputed using predictions from the primary analysis model (random slope and intercept model). Changes in FVC in the SENSCIS trial were compared to values in hypothetical healthy reference subjects matched to the SENSCIS subjects for age, sex, ethnicity and height. FVC values in these healthy reference subjects were derived from the equations published by the European Respiratory Society Global Lung Function Initiative in 2012, which were derived from data from over 70,000 subjects.

Results: In the nintedanib and placebo groups of the SENSCIS trial, respectively, mean (SD) time since onset of first non-Raynaud symptom was 3.5 (1.6) and 3.5 (1.8) years. In the nintedanib group, mean (SD) FVC at baseline was 2490 (737) mL, compared with 3403 (787) mL in the healthy reference subjects. In the placebo group, mean (SD) FVC at baseline was 2544 (817) mL compared with 3516 (887) mL in the healthy reference subjects. The difference in the change from baseline in FVC at week 52 between the nintedanib-treated subjects in the SENSCIS trial (n=287) and the healthy reference subjects was 26.6 mL ([95% CI: 12.1, 52.9]; p=0.04). The difference in the change from baseline in FVC at week 52 between the placebo-treated subjects in the SENSCIS trial (n=286) and the reference subjects was 77.5 mL ([95% CI: 51.4, 103.7]; p<0.001) (Figure 1).

Conclusion: Subjects with SSc-ILD who participated in the SENSCIS trial had marked lung function impairment at baseline compared with healthy matched reference subjects, despite a mean duration of SSc of 3.5 years. Over 52 weeks, the decline in FVC in subjects with SSc-ILD who received placebo was 4-fold greater than in healthy reference subjects. Subjects with SSc-ILD who were treated with nintedanib had a decline in FVC that was only slightly greater than the decline observed in the matched healthy subjects. These data support the clinical relevance of the reduction in the rate of FVC decline provided by nintedanib in patients with SSc-ILD.
Background: Systemic sclerosis (SSc) can impact multiple areas of the heart through fibrotic and vascular processes; leading to variable cardiac involvement including electrocardiogram (ECG) abnormalities. Conduction and rhythm disorders are associated with worse prognosis in patients with SSc. (1, 2)

Objectives: To study the incidence, risk factors and outcomes of conduction and rhythm disorders in a US population-based cohort of patients with SSc and non-SSc comparators from the same geographic area.

Methods: A previously identified incident cohort of SSc patients (1980-2016) in a well-defined geographic area was compared to a randomly selected 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base. Demographics, disease characteristics, cardiovascular risk factors and laboratory tests were abstracted by manual record review of ECGs and Holter ECGs were reviewed to determine the occurrence of any conduction or rhythm abnormalities. The need for cardiac interventions was also abstracted.

Results: 78 incident SSc cases and 156 non-SSc comparators were identified [age 56 years ± 15.9, 91% female]. Prevalence of any conduction disorders before SSc diagnosis compared to non-SSc comparators was 15% vs. 7% (p = 0.06), and any rhythm disorder was 18% vs. 13% (p = 0.33). During a median follow-up of 10.5 years in patients with SSc and 13.0 years in non-SSc comparators, conduction disorders developed in 25 SSc patients with a cumulative incidence (ci) of 20.5% (95% CI: 12.4-34.1%) compared to 28 non-SSc patients with ci of 10.4% (95% CI: 6.2-17.4%) (HR = 2.57; 95% CI: 1.48-4.45), while rhythm disorders developed in 27 SSc patients with ci of 27.3% (95% CI: 17.3-41.6%) vs 43 non-SSc patients with ci of 18.0% (95% CI: 12.3-26.4%) (HR = 1.62; 95% CI: 1.00-2.64) (Figure 1).

The need for cardiac interventions was also abstracted. Conduction disorders in patients with SSc during follow up included: 1st-degree atrioventricular block (AVB) (n=12), 2nd-degree AVB (n=1), 3rd-degree AVB (n=1), right bundle branch block (n=10), left bundle branch block (n=4), bifascicular block (n=6), and prolonged QT (n=13). Rhythm disorders included: atrial fibrillation (n=10), atrial flutter (n=4), supraventricular tachycardia (n=4), ventricular tachycardia (n=1), and premature ventricular contractions (n=16).

Pulmonary hypertension (PH) was the only significant risk factor identified for development of both conduction and rhythm disorders (HR = 8.38, 95% CI: 1.32-53.40 and HR = 8.07, 95% CI: 1.60-40.74, respectively). Current smoking significantly increased the risk for development of rhythm disorders (HR = 2.91, 95% CI: 1.62; 95% CI: 1.62-10.42, respectively, after adjusting for age, sex and calendar year of diagnosis).

Conclusion: Patients with SSc have a significantly higher prevalence of conduction disorders at disease onset than non-SSc comparators. During the course of their disease, their risk of developing conduction disorders is 2.6-fold, and risk of rhythm disorders is 1.8-fold increased, compared to non-SSc subjects.

PHT was significantly associated with increased risk of developing conduction and rhythm disorders among patients with SSc, a finding that should warrant increased vigilance and screening for ECG abnormalities in this population.

REFERENCES:

Figure 1. Cumulative incidence of any conduction or any rhythm disorder in SSc (solid line) vs non-SSc comparators (dashed line).

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