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Correlation between progression of skin fibrosis and progression of interstitial lung disease in patients with SSc-ILD: data from the SENSCIS® trial

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Introduction

- In the SENSCIS trial in patients with systemic sclerosis-associated ILD (SSc-ILD):[1]
  - Nintedanib slowed the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% versus placebo.
  - There was no significant difference between treatment groups in the progression of skin fibrosis measured using the modified Rodnan skin score (mRSS).
- In an analysis of patients with diffuse cutaneous SSc in the EUSTAR database, progression of skin fibrosis was associated with later (but not concurrent) decline in FVC.[2]

Aim

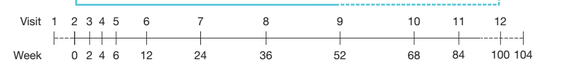
- To assess correlation between progression of skin fibrosis and progression of SSc-ILD in the SENSCIS trial.

Methods

Trial design

- Eligibility criteria included SSc with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on a high-resolution computed tomography (HRCT) scan, FVC ≥40% predicted and diffusion capacity of the lung for carbon monoxide (DLco) 30–89% predicted.
- Patients taking prednisone ≤10 mg/day or equivalent and/or stable therapy with mycophenolate or methotrexate for ≥6 months were allowed to participate.
- Patients were randomised to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks.

SENSCIS trial



R, randomisation.

- FVC was measured at baseline, weeks 2, 4, 6, 12, 24, 36, and 52, and, where patients remained in the trial, weeks 68, 84 and 100.
- mRSS was measured at baseline, weeks 12, 24, 36, and 52, and, where patients remained in the trial, weeks 68, 84 and 100.

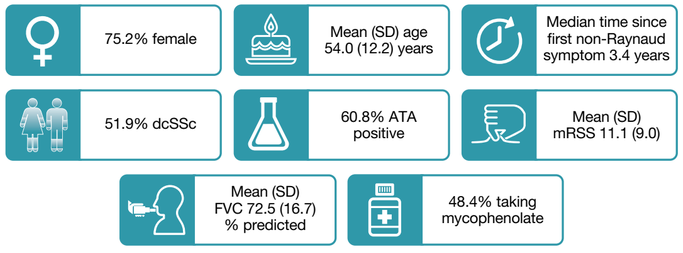
Analyses

- We calculated Spearman correlation coefficients between:
  - FVC (mL) at baseline and changes from baseline in mRSS over 100 weeks.
  - mRSS at baseline and changes from baseline in FVC (mL) over 100 weeks.
  - changes from baseline in mRSS and FVC (mL) over 100 weeks.
- We also assessed the rate of decline in FVC (mL/year) over 52 weeks considering mRSS at baseline as a continuous variable, using a random coefficient regression model.

Results

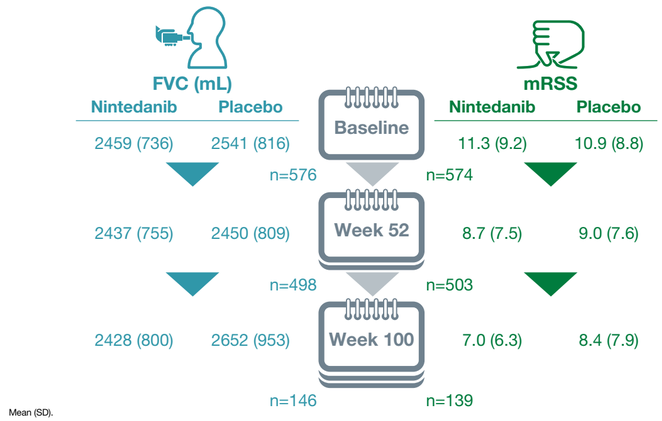
Patients

Baseline characteristics of patients in the SENSCIS trial (n=576)



ATA, anti-topoisomerase I antibody.

FVC and mRSS over 100 weeks

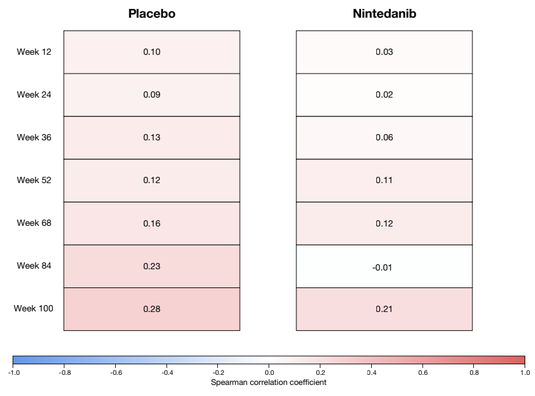


Mean (SD).

Relationships between FVC and mRSS

- No meaningful correlations were observed between FVC (mL) at baseline and changes from baseline in mRSS over 100 weeks.

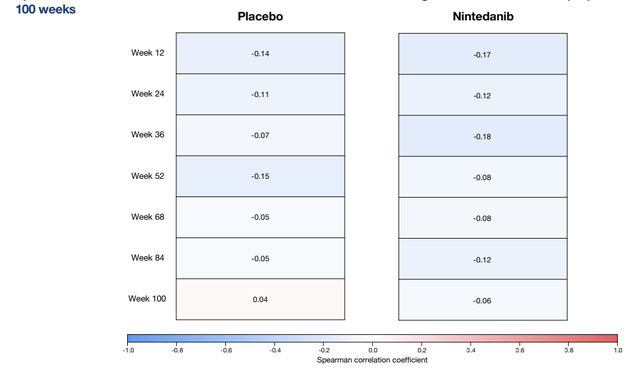
Spearman correlation coefficients between FVC (mL) at baseline and changes from baseline in mRSS at time points over 100 weeks



Darker shades of red or blue denote stronger positive (red) or negative (blue) correlations.

- No meaningful correlations were observed between mRSS at baseline and changes from baseline in FVC (mL) at time points over 100 weeks.

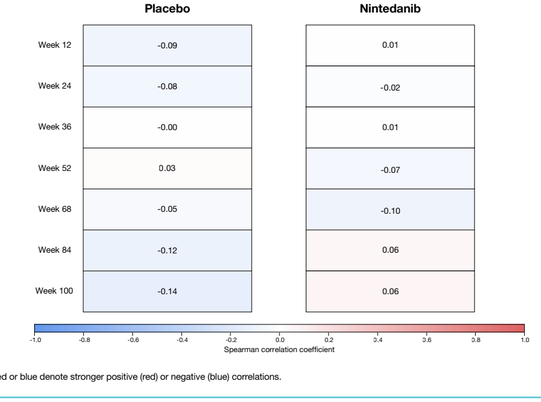
Spearman correlation coefficients between mRSS at baseline and changes from baseline in FVC (mL) at time points over 100 weeks



Darker shades of red or blue denote stronger positive (red) or negative (blue) correlations.

- No meaningful correlations were observed between changes from baseline in mRSS and FVC (mL) at time points over 100 weeks.

Spearman correlation coefficients between changes from baseline in mRSS and FVC (mL) at time points over 100 weeks



Darker shades of red or blue denote stronger positive (red) or negative (blue) correlations.

- The analysis that considered mRSS at baseline as a continuous variable showed no significant interaction between baseline mRSS and the rate of decline in FVC (mL/year) over 52 weeks (p=0.12).

Conclusions

- **In the SENSCIS trial, no meaningful correlations were observed between skin fibrosis at baseline, or progression of skin fibrosis over 100 weeks, and progression of SSc-ILD over the same period.**
- **These findings suggest that in the overall patient population in the SENSCIS trial, progression of skin fibrosis was not associated with concurrent decline in FVC.**
- **The relationship between progression of skin fibrosis and later decline in FVC observed over several years of follow-up in the EUSTAR database[2] could not be investigated using data from the SENSCIS trial due to the limited follow-up period.**

References

1. Distler O et al. N Engl J Med 2019;380:2518–28.
2. Wu W et al. Ann Rheum Dis 2019;78:648-56.

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