Associations between extent of fibrotic interstitial lung disease (ILD) and forced vital capacity (FVC) at baseline and change in FVC in subjects with systemic sclerosis-associated ILD (SSc-ILD) in the SENSCIS trial

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INTRODUCTION

- In the SENSCIS trial in subjects with SSc-ILD, nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 44% versus placebo.[1]
- Various approaches have been used to assess the extent of fibrotic ILD on HRCT and to evaluate associations between the extent of fibrotic ILD at baseline and outcomes in patients with SSc-ILD. In some studies, a greater extent of fibrotic SSc-ILD on HRCT and/or a lower FVC at baseline have been associated with an increased risk of mortality.[2-4]

AIM

- To assess associations between the extent of fibrotic ILD on HRCT and FVC at baseline and change in FVC over 52 weeks in subjects with SSc-ILD in the SENSCIS trial.

METHODS

Trial design

- Subjects in the SENSCIS trial had SSc with onset of first non-Raynaud symptom ≤7 years before screening, FVC ≥40% predicted, DLco 30–89% predicted, and fibrotic ILD ≥10% extent on an HRCT scan taken in the last ≤12 months. The extent of fibrotic ILD was assessed visually in the whole lung to the nearest 5% and did not include pure (non-fibrotic) ground glass opacities.
- Subjects taking prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomization were allowed to participate.
- Subjects were randomized to receive nintedanib or placebo until the last subject had reached week 52 but for ≤100 weeks.

Analyses

- We used a flexible regression modeling approach that considered potentially non-linear effects and, for change in FVC, interactions.
- We assessed the:
  - Association between extent of fibrotic ILD and FVC % predicted at baseline.
  - Association between extent of fibrotic ILD at baseline and change in FVC % predicted at week 52
  - Association between the interaction of extent of fibrotic ILD and FVC % predicted at baseline and change in FVC % predicted at week 52. Missing values for change in FVC over 52 weeks were imputed using a worst observation carried forward approach
- Linear associations were evaluated using Pearson correlation coefficients (r).

CONCLUSIONS

- Using contemporary methodology involving few assumptions, we found weak evidence of a modest inverse association between the extent of fibrotic ILD at baseline and decline in FVC over 52 weeks among subjects with SSc-ILD who received placebo.
- There were small but not statistically significant differences in the effect of nintedanib on slowing the rate of decline in FVC among subjects with differing extents of fibrotic ILD or FVC % predicted at baseline.
- These findings suggest that patients with SSc-ILD benefit from treatment with nintedanib largely irrespective of the extent of fibrotic ILD or FVC at baseline.

RESULTS

Baseline characteristics

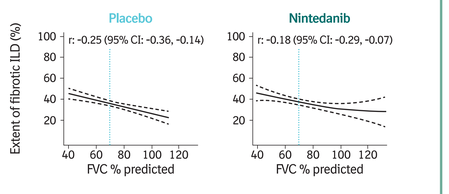
	Nintedanib (n=288)	Placebo (n=288)
Mean age (years)	54.6	53.4
Female, %	76.7	73.6
Median time since onset of first non-Raynaud symptom, years	3.4	3.5
Anti-topoisomerase I antibody positive, %	60.1	61.5
Diffuse cutaneous SSc, %	53.1	50.7
Mean extent of fibrotic ILD on HRCT (%)*	36.8	35.2
Mean FVC % predicted	72.4	72.7
Mean DLco % predicted†	52.9	53.2
Taking mycophenolate, %	48.3	48.6

*Assessed in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included. †Corrected for hemoglobin; 7 subjects had missing DLco values.

Association between extent of fibrotic ILD and FVC % predicted at baseline

- In both the placebo and nintedanib groups, a greater extent of fibrotic ILD at baseline was associated with a lower FVC % predicted at baseline. An extent of fibrotic ILD of 40% was associated with an FVC of 70% predicted.

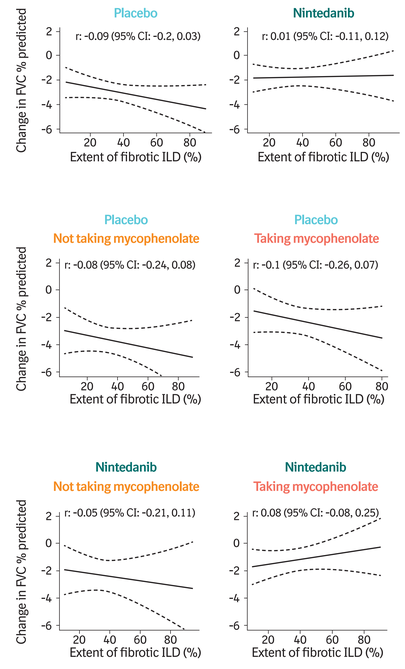
Association between extent of fibrotic ILD and FVC % predicted at baseline



Associations between extent of fibrotic ILD at baseline and decline in FVC % predicted at week 52

- In the placebo group, there was weak evidence of a modest inverse association between the extent of fibrotic ILD at baseline and decline in FVC % predicted overall and in subgroups by use of mycophenolate at baseline.
- In the nintedanib group, there was no evidence of an association between the extent of fibrotic ILD at baseline and decline in FVC % predicted overall or in subgroups by use of mycophenolate at baseline.

Association between extent of fibrotic ILD at baseline and decline in FVC % predicted at week 52

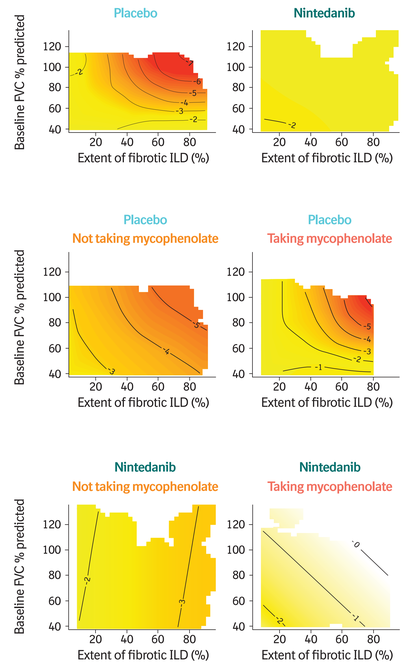


Dashed lines indicate 95% CIs.

Interaction of extent of fibrotic ILD and FVC % predicted at baseline and FVC decline over 52 weeks

- In the placebo group, higher values of both extent of fibrotic ILD and FVC % predicted at baseline tended to be associated with greater decline in FVC % predicted. This association was more pronounced in subjects taking mycophenolate at baseline.
- In the nintedanib group, there was no evidence of an association between the interplay of the extent of fibrotic ILD and FVC % predicted at baseline and decline in FVC % predicted overall or in subgroups by use of mycophenolate.

Contour plots of change in FVC % predicted at week 52 by extent of fibrotic ILD and FVC % predicted at baseline



Darker shading indicates greater decline in FVC % predicted at week 52.

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