Decline in forced vital capacity (FVC) in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) with and without cough: data from the SENSCIS trial

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INTRODUCTION

- Cough is common in patients with SSc-ILD[1] but its severity and timing of onset are variable.
- Little evidence is available on the association between cough and progression of SSc-ILD.
- The SENSCIS trial enrolled patients with SSc-ILD irrespective of symptoms. Nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo, with adverse events characterized mainly by gastrointestinal events.[2]

AIM

- To assess the characteristics at baseline, rate of decline in FVC, and the effect of nintedanib on the rate of decline in FVC, in patients with and without cough at baseline in the SENSCIS trial.

METHODS

Trial design

- Patients in the SENSCIS trial had SSc with first non-Raynaud symptom within ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT (based on assessment of the whole lung), FVC ≥40% predicted, and DLco 30–89% predicted.
- Patients taking prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomization were allowed to participate.
- Patients were randomized to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks.

Analyses

- In *post-hoc* analyses, we analyzed outcomes in subgroups with and without cough at baseline based on responses to the St. George's Respiratory Questionnaire (SGRQ).[3]
  - Patients who reported having cough "most days a week", "several days a week" or "a few days a month" (rather than "only with chest infection" or "not at all") over the last month were considered to have cough.
- We analyzed the following outcomes:
  - Rate of decline in FVC (mL/year) over 52 weeks
  - Proportions of patients with absolute and relative declines in FVC >5% predicted and FVC >10% predicted at week 52. Missing values were imputed using a worst value carried forward approach.
  - Time to absolute decline in FVC ≥10% predicted or death.
- Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib between the subgroups.

CONCLUSIONS

- In patients with SSc-ILD in the SENSCIS trial, patients with cough at baseline had a numerically greater extent of fibrotic ILD and numerically lower FVC % predicted than patients without cough. However, both patients with and without cough had a significant extent of fibrotic ILD on HRCT and impairment in FVC.
- The rate of decline in FVC in the placebo group was similar irrespective of the presence of cough at baseline.
- The effect of nintedanib on reducing the rate of FVC decline was numerically more pronounced in patients without than with cough at baseline, but no statistically significant heterogeneity was observed between these subgroups. The adverse event profile of nintedanib was consistent between the subgroups.
- These data suggest that the presence of cough alone should not be used to determine when to initiate nintedanib in patients with SSc-ILD.

RESULTS

Patients

Baseline characteristics

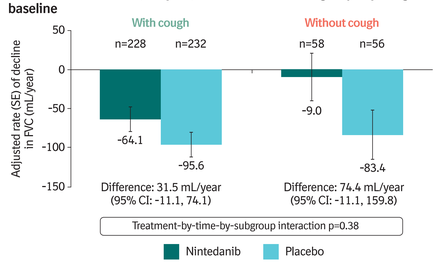
Patients with cough (n=461)		Patients without cough (n=114)
54.1	Mean age (years)	53.2
73.3	Female, %	83.3
52.5	Diffuse cutaneous SSc, %	49.1
3.5	Mean time since onset of non-Raynaud symptom (years)	3.5
71.5	Mean FVC % predicted	76.7
52.5	Mean DLco % predicted	55.6
37.2	Mean extent of fibrotic ILD on HRCT* (%)	30.7
33.6	GERD†, %	20.2
80.3	Drugs for gastric acid-related disorders, %	77.2
50.1	Corticosteroids, %	49.1
8.7	ACE inhibitors, %	6.1
48.4	Mycophenolate, %	49.1

*Assessed in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included. †Reported as comorbidity based on preferred term "gastroesophageal reflux disease" in the Medical Dictionary for Regulatory Activities (MedDRA). ACE, angiotensin-converting enzyme.

Rate of decline in FVC (mL/year) over 52 weeks

- In the placebo group, the rate of decline in FVC (mL/year) was similar in patients with and without cough at baseline.
- Both in patients with and without cough at baseline, the rate of decline in FVC was lower in patients treated with nintedanib than placebo. The treatment effect of nintedanib was numerically more pronounced in patients without than with cough, but no statistically significant heterogeneity was observed between these subgroups.

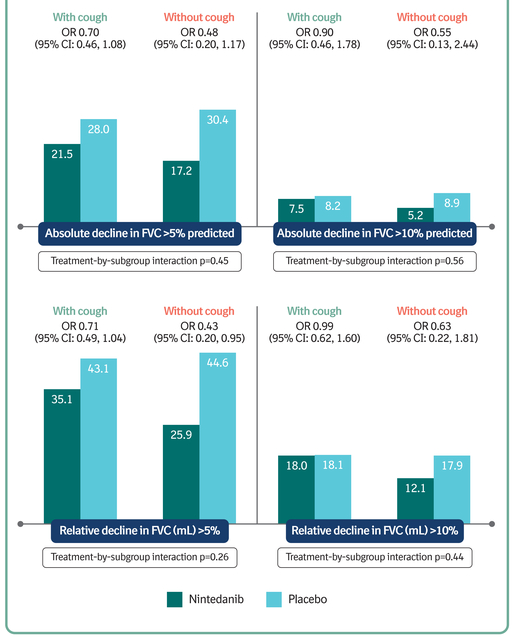
Rate of decline in FVC (mL/year) over 52 weeks in subgroups by cough at baseline



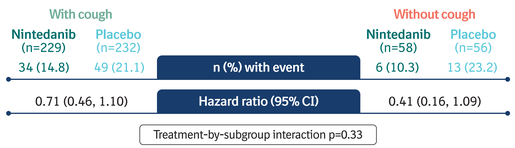
Categorical declines in FVC

- No statistically significant heterogeneity was detected between subgroups by cough in the effect of nintedanib versus placebo on categorical declines in FVC, or time to absolute decline in FVC ≥10% predicted or death.

Proportions of patients with absolute and relative declines in FVC at week 52 in subgroups by cough at baseline

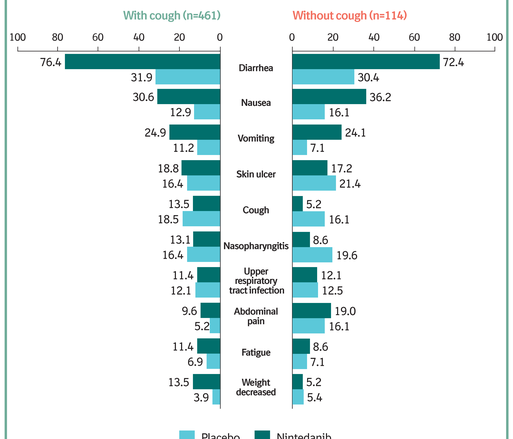


Time to absolute decline in FVC ≥10% predicted or death at week 52 in subgroups by cough at baseline



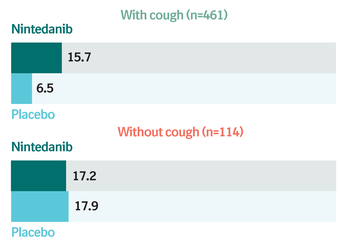
Adverse events

Adverse events (reported irrespective of causality) in subgroups by cough at baseline



Adverse events were coded using preferred terms in the MedDRA. Data are % of patients with ≥1 such adverse event, reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Adverse events reported in >10% of patients in either treatment group in the overall trial population are shown.

Proportions of patients with adverse events leading to treatment discontinuation in subgroups by cough at baseline



Data are % of patients with ≥1 such adverse event, reported over 52 weeks.

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