Effect of nintedanib on progression of systemic sclerosis-associated interstitial lung disease (SSc-ILD): further analyses of the SENSCIS® trial

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Introduction

- Decline in forced vital capacity (FVC) in patients with SSc-ILD is an indicator of ILD progression and is associated with mortality.[1,2]
- In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 44% compared with placebo.[3]

Aim

- To assess the effect of nintedanib on categorical changes in FVC % predicted and other measures of ILD progression in the SENSCIS trial.

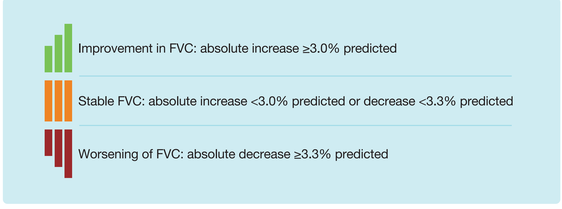
Methods

Patients

- Patients with 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 were enrolled in the SENSCIS trial.
- 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. Patients could remain on blinded treatment until the last patient had reached week 52 but for ≤100 weeks.

Analyses

- In *post-hoc* analyses, we assessed:
  - Cumulative distribution of changes in FVC % predicted at week 52
  - Proportion of patients with absolute categorical changes in FVC % predicted at week 52
  - Proportions of patients who met proposed thresholds for minimal clinically important differences for improvement in FVC, stable FVC, and worsening of FVC at week 52, based on data from Scleroderma Lung Studies I and II, anchored to the health transition question from the Medical Outcomes Short Form-36:[4]

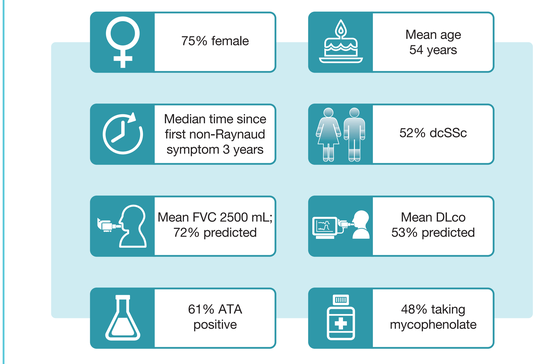


  - Time to i) an absolute decline in FVC ≥5% predicted or death; ii) an absolute decline in FVC ≥10% predicted or death; and iii) an absolute decline in FVC ≥10% predicted or absolute decline in FVC ≥5% to <10% predicted with an absolute decline in DLco ≥15% predicted, or death, over 52 weeks ± 7 days.
- Missing values were imputed using a worst value carried forward approach.
- Analyses were descriptive and exploratory.

Results

- At baseline, patients in the SENSCIS trial (n=576) had moderately impaired FVC; almost half were taking mycophenolate (Figure 1).

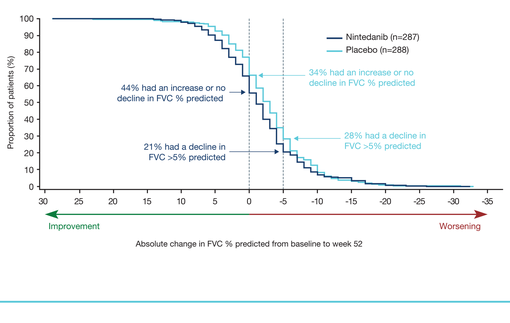
Figure 1. *Baseline characteristics of patients in the SENSCIS trial*



Categorical changes in FVC % predicted

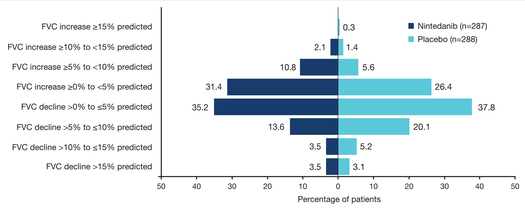
- The proportion of patients with a given decline in FVC % predicted was lower in patients treated with nintedanib than placebo across a broad spectrum (Figure 2).

Figure 2. *Cumulative distribution of changes in FVC % predicted at week 52*



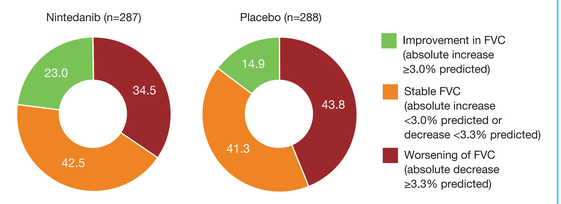
- The proportions of patients with FVC declines of >5% to ≤10% predicted and >10% to ≤15% predicted at week 52 were lower in the nintedanib group than in the placebo group (Figure 3).

Figure 3. *Proportions of patients with absolute increases or declines in FVC % predicted at week 52*



- The proportion of patients with worsening of FVC was lower, and the proportion of patients with improvement in FVC was higher, in patients treated with nintedanib than placebo (Figure 4).

Figure 4. *Proportion of patients who met proposed thresholds for improvement in FVC, stable FVC and worsening of FVC[a] at week 52*



[a]Odds ratio (OR) for between-group difference 1.69 (95% CI: 1.11, 2.59) (p=0.014) for improvement in FVC; 1.05 (95% CI: 0.75, 1.46) (p=0.774) for stable FVC; and 0.68 (95% CI: 0.48, 0.95) (p=0.024) for worsening of FVC.

Time to lung function decline or death

- The proportion of patients who had an absolute decline in FVC ≥10% predicted or died was lower in the nintedanib group than the placebo group (Figures 5 and 6).

Figure 5. *Proportions of patients with lung function decline or death over 52 weeks*

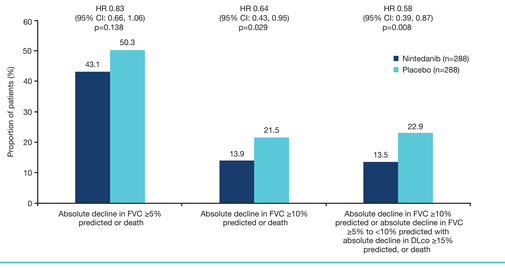
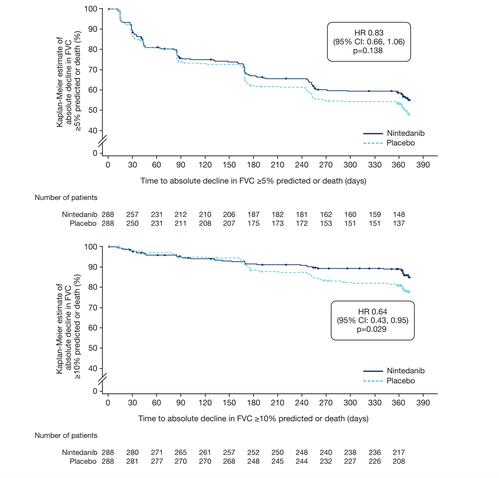


Figure 6. *Time to (a) absolute decline in FVC ≥5% predicted or death and (b) absolute decline in FVC ≥10% predicted or death over 52 weeks*



Conclusions

- **In the SENSCIS trial, the proportions of patients with SSc-ILD who had clinically relevant declines in FVC over 52 weeks were consistently lower in patients treated with nintedanib compared to placebo.**
- **These results provide further evidence that nintedanib has a clinically meaningful benefit on slowing the rate of ILD progression in patients with SSc-ILD.**

References

1. Hoffmann-Vold AM et al. Am J Respir Crit Care Med 2019;200:1258–66. 2. Volkmann ER et al. Ann Rheum Dis 2019;78:122–30. 3. Distler O et al. N Engl J Med 2019;380:2518–28. 4. Kafaja S et al. Am J Respir Crit Care Med 2018;197:644–52.

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