Poster

Effect of nintedanib in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) by composite physiologic index (CPI) at baseline

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Effect of nintedanib in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) by composite physiologic index (CPI) at baseline

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INTRODUCTION

- The composite physiologic index (CPI) is a measure of the severity of pulmonary fibrosis, calculated based on per cent predicted values for DLco, FVC and FEV_1.[1] A higher score on the CPI has been associated with worse prognosis in patients with various ILDs.[1–5]
- 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.[6]

AIM

- To assess the effect of nintedanib in subgroups based on CPI at baseline in the SENSCIS trial.

METHODS

Trial design[6]

- Patients had SSc with first non-Raynaud symptom in the prior ≤7 years, extent of fibrotic ILD on HRCT ≥10%, FVC ≥40% predicted, DLco 30–89% predicted.
- Patients taking prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months were allowed to participate.
- Patients were randomized to receive nintedanib or placebo.

Analyses

CPI was calculated as:[1]

$$91.0 - (0.65 \times \text{DLco \% predicted}) - (0.53 \times \text{FVC \% predicted}) + (0.34 \times FEV_1 \text{ \% predicted})$$

- In *post-hoc* analyses, we analyzed the following outcomes over 52 weeks in subgroups by baseline CPI ≤45 vs >45:
  - rate of decline in FVC (mL/year)
  - time to absolute decline in FVC ≥10% predicted or death
  - proportions of patients with absolute declines in FVC % predicted >5% and >10% and relative declines in FVC (mL) >5% and >10% (with missing values at week 52 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 effect of nintedanib versus placebo between the subgroups.

CONCLUSIONS

- In the SENSCIS trial in patients with SSc-ILD, approximately half of the patients had a CPI >45 at baseline.
- The rate of FVC decline over 52 weeks was numerically greater in patients with CPI >45 than ≤45 in both the nintedanib and placebo groups.
- The effect of nintedanib vs placebo on reducing the rate of FVC decline was numerically more pronounced in patients with CPI >45 than ≤45, but no statistically significant heterogeneity was detected between these subgroups.

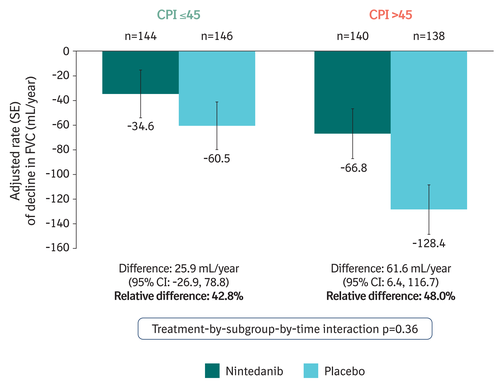
RESULTS

Baseline characteristics

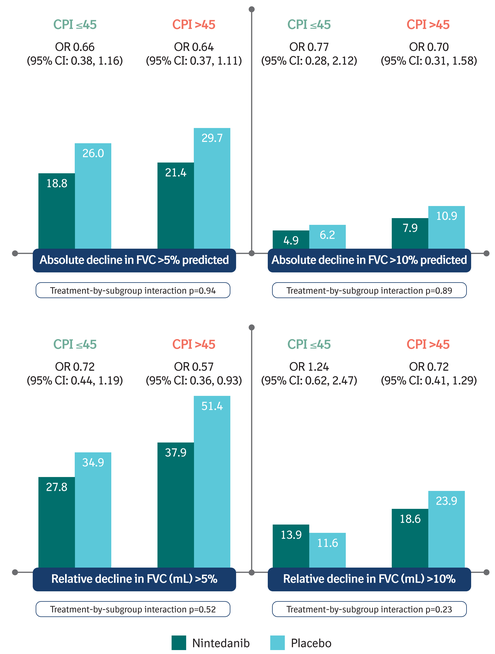
CPI ≤45 (n=290)		CPI >45 (n=279)
54.8	Mean age, years	53.2
80.3	Female, %	69.9
3.4	Mean time since onset of non-Raynaud symptom (years)	3.5
49.0	Diffuse cutaneous SSc, %	54.5
59.0	ATA positive, %	62.4
29.1	Mean extent of fibrotic ILD on HRCT (%)*	43.0
81.7	Mean FVC % predicted	63.2
64.6	Mean DLco % predicted	41.1
42.8	Taking mycophenolate mofetil	51.3

*Assessed in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included.
ATA, anti-topoisomerase I antibody.
CPI could not be calculated for 7 patients.

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



Proportions of patients with categorical declines in FVC at week 52



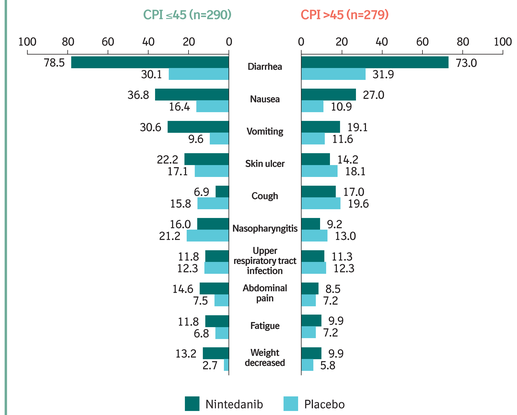
Missing values at week 52 were imputed using a worst value carried forward approach.

Time to absolute decline in FVC ≥10% predicted or death over 52 weeks

CPI ≤45			CPI >45	
Nintedanib (n=144)	Placebo (n=146)		Nintedanib (n=141)	Placebo (n=138)
18 (12.5)	30 (20.5)	n (%) with event	20 (14.2)	30 (21.7)
0.61 (0.34, 1.09)		Hazard ratio (95% CI)	0.65 (0.37, 1.15)	

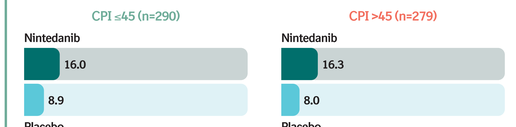
Treatment-by-subgroup interaction p=0.88

Adverse events

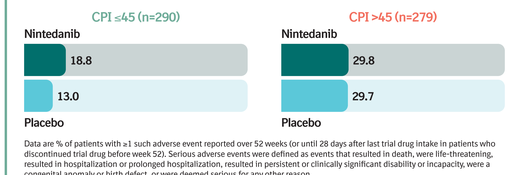


Adverse events were coded using preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of patients with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Adverse events 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



Proportions of patients with serious adverse events



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). Serious adverse events were defined as events that resulted in death, were life-threatening, resulted in hospitalization or prolonged hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed serious for any other reason.

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