Lung function decline in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) by time since first non-Raynaud symptom: subgroup analysis of the SENSCIS® trial

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Introduction

- While some studies have shown that decline in FVC is most rapid early in the course of SSc, SSc-ILD may also progress in patients with a longer duration of disease.[1,2]
- A decline in forced vital capacity (FVC) in patients with SSc-ILD is a predictor of mortality.[3]
- In the SENSCIS trial, nintedanib reduced the rate of decline in FVC (mL/year) in patients with SSc-ILD over 52 weeks by 44% compared with placebo, with an adverse event profile characterized mainly by gastrointestinal events.[4]

Aim

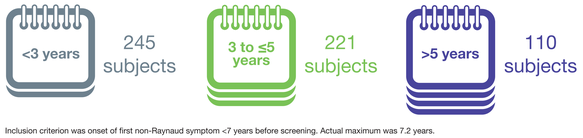
- To investigate outcomes in the SENSCIS trial in subgroups by time since onset of first non-Raynaud symptom.

Methods

- Subjects in the SENSCIS trial had SSc with first non-Raynaud symptom <7 years before screening, fibrotic ILD of ≥10% extent on an HRCT scan taken in the last ≤12 months, FVC ≥40% predicted and DLco 30–89% predicted.
- 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 1:1 to receive nintedanib or placebo until the last subject had reached week 52 but for ≤100 weeks.
- We analyzed the rate of decline in FVC (mL/year), categorical declines in FVC, and time to composite outcomes based on lung function decline and death in subgroups based on time since onset of first non-Raynaud symptom at randomization (<3, 3 to ≤5, >5 years). Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo across the subgroups. No adjustment for multiplicity was made.
- Adverse events are presented descriptively.

Results

Years since onset of first non-Raynaud symptom



Inclusion criterion was onset of first non-Raynaud symptom <7 years before screening. Actual maximum was 7.2 years.

Baseline characteristics in subgroups by time since onset of first non-Raynaud symptom

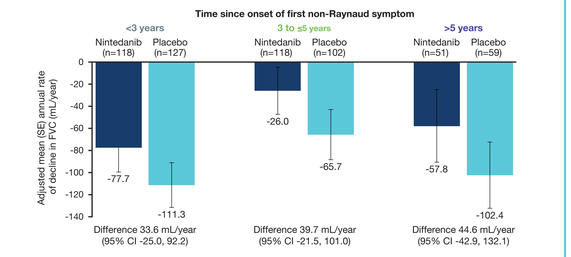
Years since onset	Female (%)	Age (yr)	BMI (kg/m²)	Diffuse cutaneous SSc (%)
<3	71.0	54.6	26.0	40.8
3 to ≤5	77.4	54.0	25.6	57.9
>5	80.0	52.4	26.2	64.5
<3	59.2	73.1	9.8	45.7
3 to ≤5	58.4	72.8	11.6	53.4
>5	69.1	70.6	13.3	44.5
	ATA-positive (%)	FVC % predicted	modified Rodnan skin score (mRSS)	Taking mycophenolate (%)

Mean or % of patients

Annual rate of decline in FVC (mL/year)

- The effect of nintedanib vs placebo on reducing the annual rate of decline in FVC was consistent across the subgroups by time since onset of first non-Raynaud symptom (Figure 1).

Figure 1. *Rate of decline in FVC (mL/year) over 52 weeks in subgroups by time since onset of first non-Raynaud symptom*

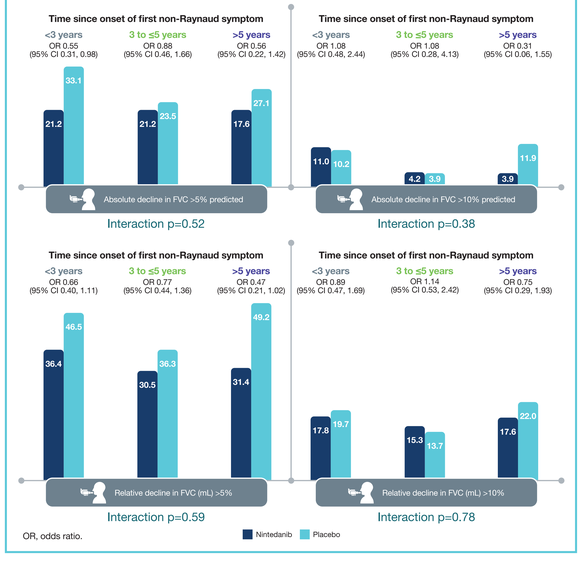


Treatment-by-time-by-subgroup interaction p=0.98

Categorical declines in FVC over 52 weeks

- No heterogeneity was detected in the effect of nintedanib versus placebo on categorical declines in FVC or time to composite outcomes based on lung function decline and death across the subgroups (Figure 2; Table).

Figure 2. *Absolute and relative declines in FVC in subgroups by time since onset of first non-Raynaud symptom*



OR, odds ratio.

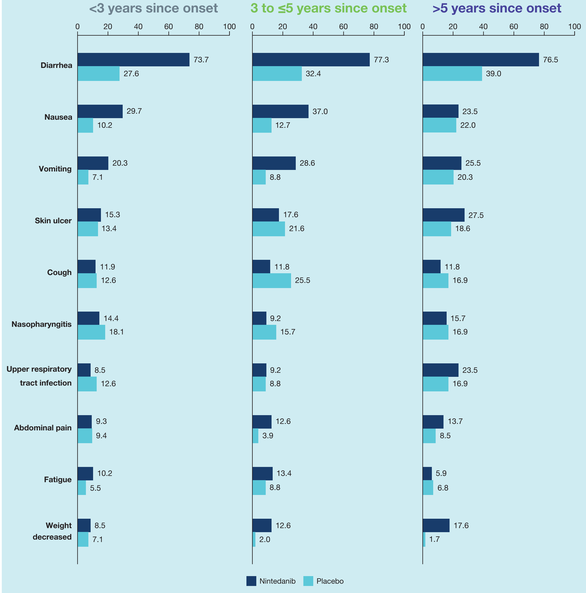
Table. *Time to composite outcomes in subgroups by time since onset of first non-Raynaud symptom*

	<3 years since onset		3 to ≤5 years since onset		>5 years since onset	
	Nintedanib (n=118)	Placebo (n=127)	Nintedanib (n=119)	Placebo (n=102)	Nintedanib (n=51)	Placebo (n=59)
Absolute decline in FVC ≥10% predicted or death over 52 weeks, n (%)	22 (18.6)	30 (23.6)	13 (10.9)	18 (17.6)	5 (9.8)	14 (23.7)
Hazard ratio (95% CI)	0.78 (0.45, 1.36)		0.59 (0.29, 1.20)		0.40 (0.14, 1.12)	
Treatment-by-subgroup interaction			p=0.52			
Absolute decline in FVC ≥10% predicted or absolute decline in FVC ≥5% to <10% predicted plus absolute decline in DLco ≥15% predicted, or death, n (%)	24 (20.3)	35 (27.6)	14 (11.8)	19 (18.6)	7 (13.7)	15 (25.4)
Hazard ratio (95% CI)	0.72 (0.43, 1.21)		0.60 (0.30, 1.19)		0.52 (0.21, 1.29)	
Treatment-by-subgroup interaction			p=0.83			
Relative decline in FVC % predicted ≥10%, or relative decline in FVC % predicted ≥5% to <10% plus relative decline in DLco % predicted ≥15%, or death, n (%)	39 (33.1)	59 (46.5)	36 (30.3)	40 (39.2)	19 (37.3)	27 (45.8)
Hazard ratio (95% CI)	0.69 (0.46, 1.03)		0.71 (0.45, 1.12)		0.88 (0.49, 1.58)	
Treatment-by-subgroup interaction			p=0.81			

Adverse events

- The adverse event profile of nintedanib was consistent across the subgroups (Figure 3).

Figure 3. *Most frequent adverse events in subgroups by time since onset of first non-Raynaud symptom*



AEs reported (irrespective of causality) in >10% of subjects in either treatment group in the overall population, coded using preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of subjects with ≥1 such AE, reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52).

Conclusions

- **In the SENSCIS trial, progression of SSc-ILD over 52 weeks was observed in patients with a time since onset of first non-Raynaud symptom of more than 3 years, as well as in patients with a shorter disease duration. The effect of nintedanib on reducing the rate of decline in FVC in patients with SSc-ILD was consistent across subgroups with differing times since onset of first non-Raynaud symptom.**

References

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