Effect of Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) and Risk Factors for Rapid Decline in Forced Vital Capacity: Further Analyses of the SENSCIS Trial

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INTRODUCTION

- The course of SSc-ILD is variable,[1] but risk factors for rapid progression include early SSc,[2] elevated inflammatory markers,[3,4] significant skin involvement[5] and diffuse cutaneous SSc (dcSSc).[5,6] In patients with such risk factors, nintedanib may not be considered an early treatment option.
- Some clinical trials have recruited patients with SSc who are at risk of rapid progression (e.g faSScinate[7], focuSSed[8], RESOLVE-1[9]).
- The SENSCIS trial of nintedanib versus placebo was conducted in a broad population of subjects with SSc-ILD. In the overall trial population, targeting fibrosis with nintedanib resulted in a 44% reduction in the rate of decline in FVC (mL/year) over 52 weeks.[10]

AIM

- To analyze the rate of FVC decline, and the effect of nintedanib on the rate of FVC decline, in the SENSCIS trial in subjects with risk factors for rapid FVC decline used in recent trials in patients with SSc.

METHODS

Trial design[10]

- Subjects had SSc with first non-Raynaud symptom in the prior ≤7 years, extent of fibrotic ILD on high-resolution computed tomography (HRCT) ≥10%, FVC ≥40% 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.
- Subjects were randomized to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks.

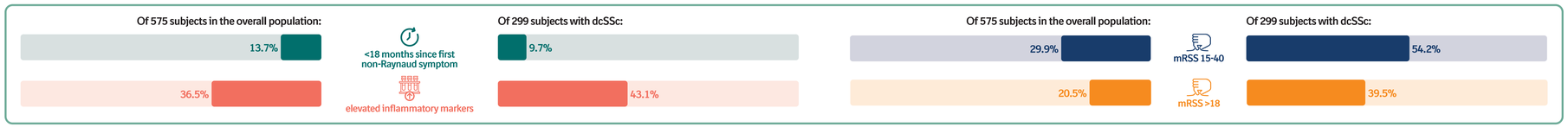
Analyses

- We analyzed *post-hoc* the rate of decline in FVC (mL/year) over 52 weeks in all subjects and in those with early SSc (<18 months since first non-Raynaud symptom), elevated inflammatory markers (C-reactive protein ≥6 mg/L and/or platelets ≥330 x 10^9/L), or significant skin fibrosis using two approaches (modified Rodnan skin score [mRSS] 15-40 or mRSS >18) at baseline.
- We also analyzed the rate of decline in FVC over 52 weeks in subjects with one of these risk factors plus dcSSc.

CONCLUSIONS

- Subjects in the SENSCIS trial who had early SSc, elevated inflammatory markers, or significant skin fibrosis had a more rapid decline in FVC over 52 weeks compared with the overall trial population.
- Across the subgroups, the rate of FVC decline was lower in patients treated with nintedanib than placebo.
- These results support the use of nintedanib as an early treatment option in patients with SSc-ILD.

RESULTS



Baseline characteristics of subjects with risk factors for rapid decline in FVC

	<18 months since first non-Raynaud symptom (n=79)	Elevated inflammatory markers (n=210)	mRSS 15-40 (n=172)	mRSS >18 (n=118)
Mean age, years	54.4	53.3	51.2	50.4
Female, %	68.4	74.3	77.3	77.1
Mean time since first non-Raynaud symptom, years	1.0	3.4	3.8	3.9
ATA positive, %	51.9	63.3	67.4	67.8
Mean mRSS	10.5	12.8	21.4	25.2
Mean extent of fibrotic ILD on HRCT, %*	33.5	36.7	38.3	38.5
Mean FVC % predicted	73.4	70.2	69.1	68.2
Mean DLco % predicted†	56.0	49.5	52.6	51.4
Taking mycophenolate, %	27.8	54.3	54.7	57.6

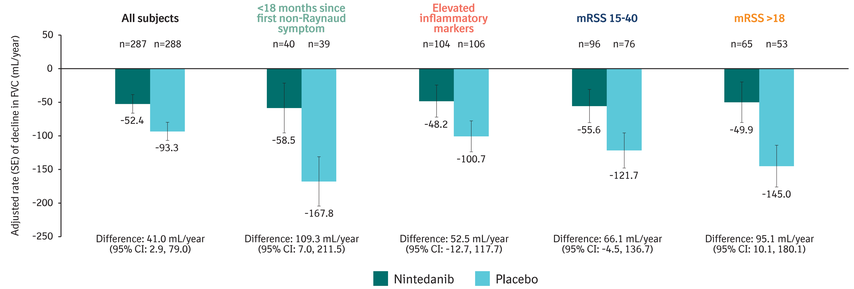
*Assessed in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included. †Corrected for hemoglobin.

Baseline characteristics of subjects with dcSSc and risk factors for rapid decline in FVC

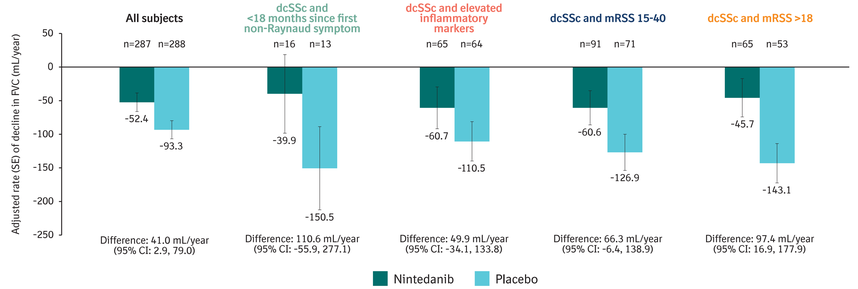
	dcSSc and <18 months since first non-Raynaud symptom (n=29)	dcSSc and elevated inflammatory markers (n=129)	dcSSc and mRSS 15-40 (n=162)	dcSSc and mRSS >18 (n=118)
Mean age, years	50.9	51.3	51.3	50.4
Female, %	58.6	74.4	77.8	77.1
Mean time since first non-Raynaud symptom, years	1.1	3.6	3.8	3.9
ATA positive, %	75.9	69.8	69.8	67.8
Mean mRSS	19.6	17.6	21.8	25.2
Mean extent of fibrotic ILD on HRCT, %*	37.6	37.6	37.3	38.5
Mean FVC % predicted	71.8	69.9	68.7	68.2
Mean DLco % predicted†	60.1	50.6	52.6	51.4
Taking mycophenolate, %	31.0	53.5	54.9	57.6

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

Rate of decline in FVC (mL/year) over 52 weeks in subjects with risk factors for rapid decline in FVC



Rate of decline in FVC (mL/year) over 52 weeks in subjects with dcSSc and risk factors for rapid decline in FVC



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