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]
- Some clinical trials have recruited patients with SSc who were at risk of rapid progression (e.g faSScinate[7], focuSSced[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 pulmonary fibrosis with nintedanib resulted in a 44% reduction in the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks.[10]

AIM

- To analyse 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 and DLco 30–89% predicted.
- Subjects taking prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomisation were allowed to participate.
- Subjects were randomised to receive nintedanib or placebo until the last subject had reached week 52 but for ≤100 weeks.

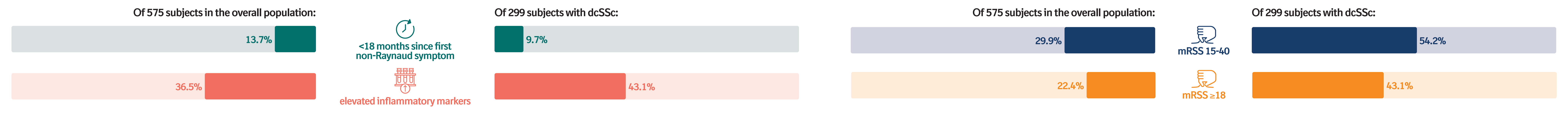
Analyses

- We analysed *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 analysed the rate of decline in FVC over 52 weeks in subjects with one of these risk factors plus dcSSc.

CONCLUSIONS

- Subjects with SSc-ILD in the SENSCIS trial who had early SSc, elevated inflammatory markers, or extensive skin fibrosis had a more rapid decline in FVC over 52 weeks than the overall trial population.
- By targeting pulmonary fibrosis, nintedanib reduced the rate of decline in FVC across the subgroups based on risk factors for rapid FVC decline.
- These results support the prompt initiation of nintedanib in patients with SSc-ILD to preserve lung function and improve patient outcomes.

RESULTS


Of 575 subjects in the overall population:
13.7%
36.5%
<18 months since first non-Raynaud symptom
elevated inflammatory markers
Of 299 subjects with dcSSc:
9.7%
43.1%
Of 575 subjects in the overall population:
29.9%
22.4%
mRSS 15-40
mRSS ≥18
Of 299 subjects with dcSSc:
54.2%
43.1%

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=129)
Mean age, years	54.4	53.3	51.2	50.5
Female, %	68.4	74.3	77.3	78.3
Mean time since first non-Raynaud symptom, years	1.0	3.4	3.8	3.9
ATA positive, %	51.9	63.3	67.4	67.4
Mean mRSS	10.5	12.8	21.4	24.6
Mean extent of fibrotic ILD on HRCT, %*	33.5	36.7	38.3	38.6
Mean FVC % predicted	73.4	70.2	69.1	68.3
Mean DLco % predicted†	56.0	49.5	52.6	51.6
Taking mycophenolate, %	27.8	54.3	54.7	58.1

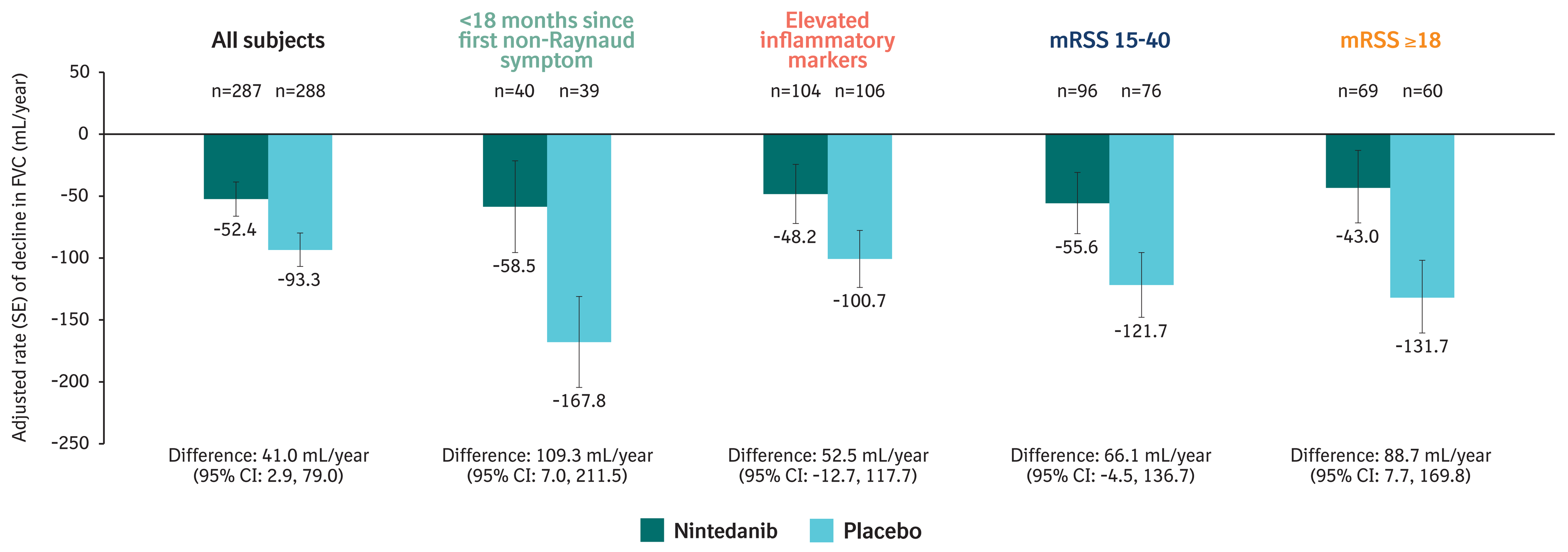
*Assessed visually in whole lung to nearest 5% by central review. Pure (non-fibrotic) ground glass opacity was not included. †Corrected for haemoglobin.

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

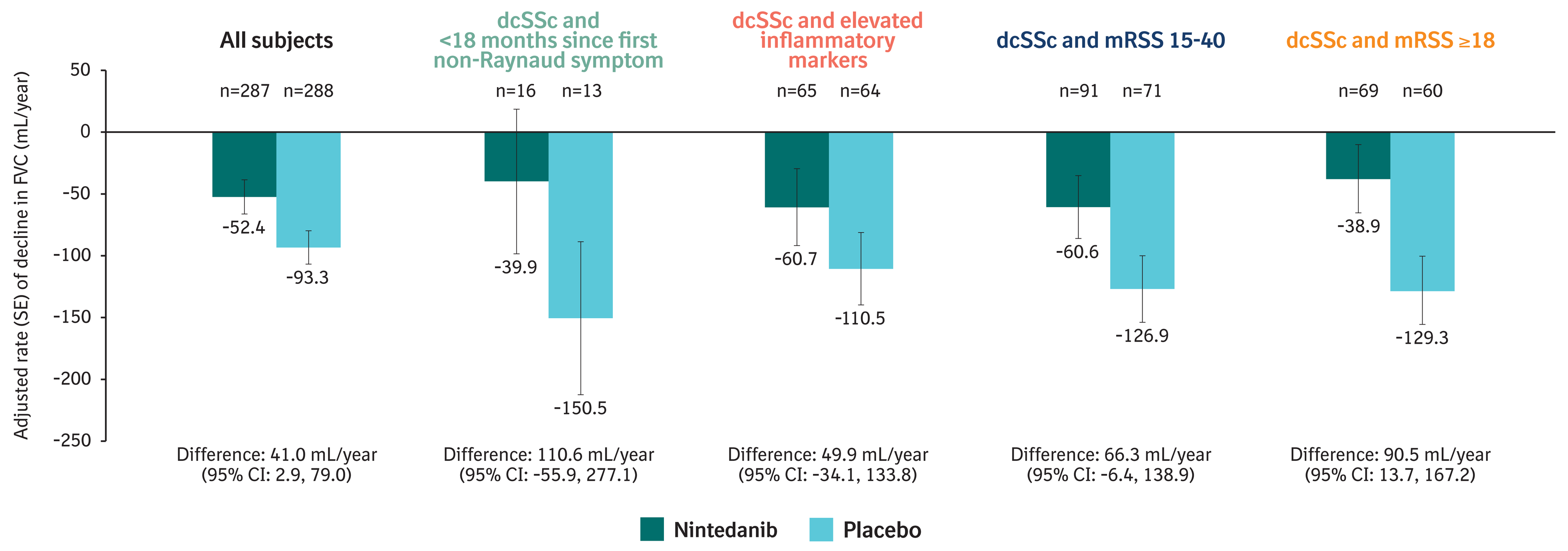
	dcSSc and <18 months since first non-Raynaud symptom (n=29)	dcSSc and elevated inflammatory markers (n=129)	dcSSc and mRSS 15-40 (n=162)	dcSSc and mRSS ≥18 (n=129)
Mean age, years	50.9	51.3	51.3	50.5
Female, %	58.6	74.4	77.8	78.3
Mean time since first non-Raynaud symptom, years	1.1	3.6	3.8	3.9
ATA positive, %	75.9	69.8	69.8	67.4
Mean mRSS	19.6	17.6	21.8	24.6
Mean extent of fibrotic ILD on HRCT, %*	37.6	37.6	37.3	38.6
Mean FVC % predicted	71.8	69.9	68.7	68.3
Mean DLco % predicted†	60.1	50.6	52.6	51.6
Taking mycophenolate, %	31.0	53.5	54.9	58.1

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

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


All subjects
<18 months since first non-Raynaud symptom
Elevated inflammatory markers
mRSS 15-40
mRSS ≥18
n=287 n=288
n=40 n=39
n=104 n=106
n=96 n=76
n=69 n=60
Adjusted rate (SE) of decline in FVC (mL/year)
50
0
-50
-100
-150
-200
-250
-52.4
-93.3
-58.5
-167.8
-48.2
-100.7
-55.6
-121.7
-43.0
-131.7
Difference: 41.0 mL/year (95% CI: 2.9, 79.0)
Difference: 109.3 mL/year (95% CI: 7.0, 211.5)
Difference: 52.5 mL/year (95% CI: -12.7, 117.7)
Difference: 66.1 mL/year (95% CI: -4.5, 136.7)
Difference: 88.7 mL/year (95% CI: 7.7, 169.8)
Nintedanib
Placebo

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


All subjects
dcSSc and <18 months since first non-Raynaud symptom
dcSSc and elevated inflammatory markers
dcSSc and mRSS 15-40
dcSSc and mRSS ≥18
n=287 n=288
n=16 n=13
n=65 n=64
n=91 n=71
n=69 n=60
Adjusted rate (SE) of decline in FVC (mL/year)
50
0
-50
-100
-150
-200
-250
-52.4
-93.3
-39.9
-150.5
-60.7
-110.5
-60.6
-126.9
-38.9
-129.3
Difference: 41.0 mL/year (95% CI: 2.9, 79.0)
Difference: 110.6 mL/year (95% CI: -55.9, 277.1)
Difference: 49.9 mL/year (95% CI: -34.1, 133.8)
Difference: 66.3 mL/year (95% CI: -6.4, 138.9)
Difference: 90.5 mL/year (95% CI: 13.7, 167.2)
Nintedanib
Placebo

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REFERENCES

1. Hoffmann-Vold AM et al. Ann Rheum Dis 2021;80:219–227.
2. Jaeger VK et al. PLoS One 2016;11:e0163894.
3. Liu X et al. Arthritis Care Res (Hoboken) 2013;65:1375–1380.
4. Ross L et al. Clin Exp Rheumatol 2018;36(Suppl 113):126–134.
5. Nihtyanova SI et al. Arthritis Rheumatol 2014;66:1625–1635.
6. Gilson M et al. Eur Respir J 2010;35:112–117.
7. Khanna D et al. Lancet 2016;387:2630–2640.
8. Khanna D et al. Lancet Respir Med 2020;8:963–974.
9. Spiera S et al. Clin Exp Rheumatol 2021;39 Suppl 131:124–133.
10. Distler O et al. N Engl J Med 2019;380:2518–2528.

ACKNOWLEDGEMENTS AND DISCLOSURES

The SENSCIS trial was supported by Boehringer Ingelheim International GmbH (BI). The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment for the development of this poster. Elizabeth Ng of FleishmanHillard, London, UK, provided editorial and formatting assistance, which was contracted and funded by BI. BI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. Dinesh Khanna reports grants from Bristol Myers Squibb, Horizon Therapeutics, Pfizer; consulting fees from AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, CSL Behring, Genentech, Horizon Therapeutics, Janssen, Prometheus, Talaris, Theraly; fees for presentations from AbbVie, Boehringer Ingelheim, CSL Behring, Genentech, Horizon Therapeutics, Janssen; has a leadership or fiduciary role with Eicos; has received royalties or licenses for the University of California Los Angeles Scleroderma Clinical Trials Consortium (SCTC) Gastrointestinal Tract instrument 2.0; and owns stock in Eicos. Christopher P Denton reports consulting and/or speaker fees from Acceleron, Actelion, Arxx Therapeutics, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Corbus, CSL Behring, Galapagos, GlaxoSmithKline, Horizon, Inventiva, Leadiant Biosciences, Mallinckrodt, Roche, Sanofi and UCB.

Poster presented at the Annual European Congress of Rheumatology, 1–4 June 2022.