Changes in Imaging Markers in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Treated with Nintedanib: Sub-Study of the SENSCIS® Trial

Stephen Humphries,[1] Eric Hachulla,[2] Mark Hamblin,[3] Takashi Ogura,[4] Dag Wormanns,[5] Carina Ittrich,[6] Frank Risse,[6] Margarida Alves,[7] Martina Gahlemann[8], David A Lynch[1] on behalf of the SENSCIS HRCT sub-study investigators

[1]National Jewish Health, Denver, Colorado, USA; [2]Department of Internal Medicine and Clinical Immunology, Université de Lille, Lille, France; [3]University of Kansas Hospital, Kansas City, Kansas, USA; [4]Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Centre, Yokohama, Japan; [5]Evangelische Lungenklinik, Berlin, Germany; [6]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany; [7]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [8]Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland

Introduction

- Nintedanib is approved by the FDA for reducing the rate of decline in forced vital capacity (FVC) in patients with SSc-ILD.
- 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.[1]
- The effects of nintedanib on markers of lung damage on high-resolution computed tomography (HRCT) were assessed in a sub-study.

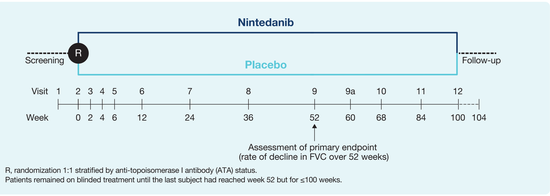
Aim

- To assess the effects of nintedanib on changes in qualitative and quantitative markers of lung damage on HRCT in patients with SSc-ILD.

Methods

Design of the SENSCIS trial[1]

- Patients had SSc with onset of first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT (based on assessment of the whole lung), FVC ≥40% predicted and diffusing capacity of the lungs for carbon monoxide (DLco) 30–89% predicted.



R, randomization 1:1 stratified by anti-topoisomerase I antibody (ATA) status.
Patients remained on blinded treatment until the last subject had reached week 52 but for ≤100 weeks.

Qualitative assessments of HRCT scans in HRCT sub-study

- At baseline and at week 52 or 60, two expert radiologists visually assessed the extent (%) of regions with evidence of abnormalities (honeycombing and/or reticulation and/or ground-glass opacity [GGO]) in both lungs. The radiologists were blinded to the time-points at which the scans had been taken.
- Analyses were conducted in patients who received trial medication up to at least week 24 and had an evaluable HRCT scan at week 52/60.
- Changes from baseline were categorized from "much better" to "much worse" (or as unknown):

Much better*	Moderate decrease in honeycombing and/or reticulation and/or fibrotic GGO Decrease was >10%
Better*	Definite but mild decrease in honeycombing and/or reticulation and/or fibrotic GGO Decrease was ≤10% Decrease in extent of fibrosis, including change from fibrotic GGO to pure GGO, was considered improvement
Same	No change in honeycombing and/or reticulation and/or fibrotic GGO
Worse*	Definite but mild increase in honeycombing and/or reticulation and/or fibrotic GGO Increase was ≤10% Increase in extent of fibrosis, including change from pure GGO to fibrotic GGO, was considered worsening
Much worse*	At least a moderate increase in honeycombing and/or reticulation and/or fibrotic GGO; increase was >10%

*Disagreement between the radiologists in the categories "much better" or "better" and "worse" or "much worse" were considered "intermediate better" or "intermediate worse". Any increase or decrease in coarsening or extent of honeycombing was considered worsening or improvement (even in the setting of an equal or larger decrease or increase in reticulation or fibrotic GGO). A change in the extent of pure GGO by itself without a change in the degree of fibrosis was not considered as worsening or improvement.

- An ordinal logistic regression analysis (proportional odds model) adjusted for ATA status was used to compare changes between the treatment groups.

Quantitative assessments of HRCT scans

- Changes from baseline in the following parameters were assessed using data-driven texture analysis:[2]
  - Quantitative fibrosis score: extent (%) of reticular patterns with architectural distortion, with an increase indicating worsening fibrosis
  - Lung attenuation skewness: based on density histograms, with a decrease indicating worsening fibrosis
  - Lung attenuation kurtosis: based on density histograms, with a decrease indicating worsening fibrosis.
- ANCOVA, with fixed categorical effects of treatment, sex, fixed continuous effect of baseline quantitative fibrosis score, age, height, and weight, was used to compare changes in quantitative fibrosis score between the treatment groups.

Results

Subjects

- Of 576 subjects in the SENSCIS trial, 150 participated in the HRCT sub-study.

Baseline characteristics of subjects in overall SENSCIS trial and HRCT sub-study

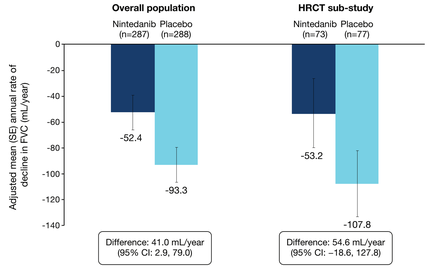
	Overall population (n=576)	HRCT sub-study (n=150)
Age, years, mean	54.0	54.3
Female	75.2%	69.3%
ATA positive	60.8%	56.7%
dcSSc	51.9%	44.7%
Extent of fibrotic ILD*	36%	35%
FVC, % predicted	72.5%	73.9%
Taking mycophenolate	48.4%	50.7%

*Extent of fibrotic ILD was assessed visually in the whole lung to the nearest 5%. The assessment did not include pure (non-fibrotic) ground glass opacities.
dcSSc, diffuse cutaneous SSc.

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

- The rate of decline in FVC over 52 weeks was similar in the overall trial population and in the subjects who participated in the HRCT sub-study (Figure 1).

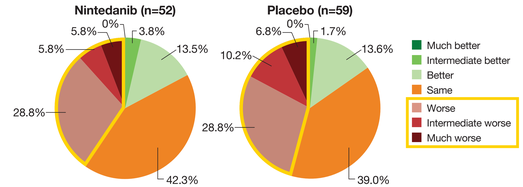
Figure 1. *Rate of decline in FVC (mL/year) over 52 weeks in the overall SENSCIS trial population and in the HRCT sub-study*



Changes in qualitative imaging parameters

- For assessment of qualitative imaging parameters, evaluable data were available from 111 subjects.
- Compared with the placebo group, a lower proportion of subjects in the nintedanib group had a worsening in qualitative parameters (i.e., "worse", "intermediate worse", or "much worse") from baseline to week 52/60 (Figure 2).
- Ordinal logistic regression analysis demonstrated a numerically greater risk of worsening in qualitative parameters in subjects who received placebo rather than nintedanib (OR 1.24 [95% CI: 0.63, 2.47]; p=0.53).

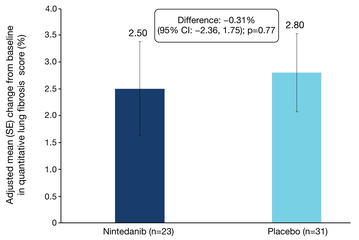
Figure 2. *Changes in the extent of regions with evidence of abnormalities (honeycombing and/or reticulation and/or ground-glass opacity) at week 52/60*



Changes in quantitative imaging parameters

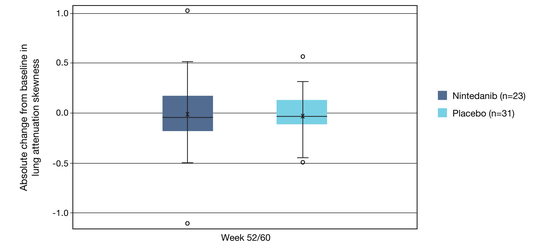
- For assessment of quantitative imaging parameters, evaluable data were available from 54 subjects.
- A numerically greater increase in quantitative lung fibrosis score was observed in the placebo group compared with the nintedanib group (Figure 3).

Figure 3. *Change in quantitative fibrosis score at week 52/60*



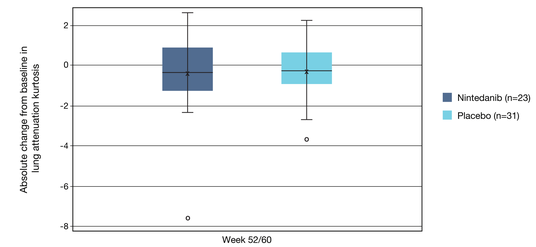
- No notable changes were observed in lung attenuation skewness or kurtosis in either treatment group (Figures 4 and 5).

Figure 4. *Change in lung attenuation skewness at week 52/60*



The markers within the boxes denote the means, the mid-line of the boxes the medians, and the boundaries of the boxes the 25th and 75th percentiles. The upper whiskers denote the values 1.5 × the interquartile range above the 75th percentile, the lower whiskers the values 1.5 × the interquartile range below the 25th percentile and the circles denote values that fell outside the range of the whiskers.

Figure 5. *Change in lung attenuation kurtosis at week 52/60*



The markers within the boxes denote the means, the mid-line of the boxes the medians, and the boundaries of the boxes the 25th and 75th percentiles. The upper whiskers denote the values 1.5 × the interquartile range above the 75th percentile, the lower whiskers the values 1.5 × the interquartile range below the 25th percentile and the circles denote values that fell outside the range of the whiskers.

Conclusions

- **In a sub-study of the SENSCIS trial, there were small qualitative and quantitative changes on HRCT over 52–60 weeks.**
- **Numerical non-significant trends towards less worsening on HRCT, in line with a slowing of ILD progression, were observed in patients treated with nintedanib versus placebo.**
- **These analyses were limited by the small number of patients who had an evaluable HRCT scan at the follow-up visit.**

References

1. Distler O et al. N Engl J Med 2019;380:2518–2528.
2. Humphries SM et al. Radiology 2017;285:270-278.

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. Editorial support and formatting assistance was provided by Julie Fleming and Wendy Morris of FleishmanHillard Fishburn, London, UK, 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.

SH reports research support from Veracyte and has served as a consultant for BI and Imidex. EH has served as a consultant for BI, Actelion, Roche, Chugai. MH reports grants from BI, Genentech, Biogen, FibroGen, Galapagos, Galecto, Promedior, Mallinckrodt and speaker fees from BI and Genentech. TO has served as a consultant and/or speaker for BI, Eisai, Shionogi. DW has served as a consultant and/ or speaker for BI, Roche, GE Healthcare. CI, FR, MA and MG are employees of BI. DAL has served as a consultant for BI, Parexel, Veracyte, Daiichi Sankyo.

Scan QR code or visit URL for a device-friendly version of this poster.

https://www.usscicomms.com/respiratory/ACR2020/Humphries

Poster developed for the American College of Rheumatology Convergence Conference, 5–9 November 2020.