Impact of forced vital capacity decline on hospitalization events in systemic sclerosis-associated interstitial lung disease: a joint model analysis using data from the SENSCIS® trial

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BACKGROUND

- Hospitalizations of patients with SSc-ILD are serious events and have health economic implications.[1,2]
- A decline in FVC is an indicator of ILD progression in SSc-ILD and is associated with mortality.[3,4]
- The impact of FVC decline on hospitalizations in patients with SSc-ILD is largely unknown.

AIM

- To evaluate the association between longitudinal FVC decline and time-to-hospitalization endpoints in patients with SSc-ILD over 52 weeks.

METHODS

- Phase III SENSCIS® trial of nintedanib vs placebo in patients with SSc-ILD (N=576).[5]
- Patients with FVC and hospitalization data were included in this analysis (n=574).

A joint model for longitudinal[a] and time-to-event[b] data to investigate the association between rate of FVC% predicted decline and hospitalization-related endpoints over 52 weeks.

Hospitalization-related endpoints

- **All-cause hospitalizations or death**
- **SSc-related hospitalizations or death**
- **Admission to ER or hospital followed by ICU or death**

[a]Longitudinal sub-model: normal mixed effects model of FVC% predicted, trajectories modeled by a linear trend with an unstructured variance-covariance matrix, a separate mean slope for patients on treatment, and ATA status and FVC% predicted at baseline as predictor variables.
[b]Time-to-event sub-model: piecewise exponential model stratified by ATA status with FVC% predicted as the endogenous time-dependent covariate and five knots to model the baseline hazard.

Lung function decline is associated with an increased risk of hospitalization or death in patients with SSc-ILD

CONCLUSIONS

- FVC decline has a clinically relevant association with the risk of all-cause and SSc-related hospitalizations or death in patients with SSc-ILD.
- These findings support the use of serial FVC measurements in clinical studies.
- Slowing lung function decline in patients with SSc-ILD may prevent hospitalizations.

RESULTS

FVC% predicted during the SENSCIS® trial[5]

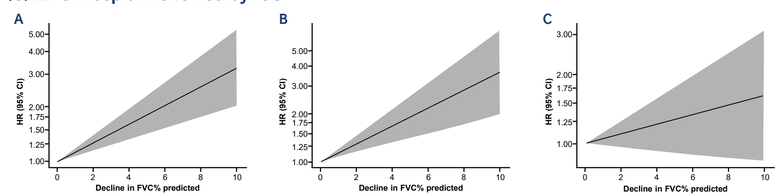
	Mean baseline, % (SD)	Annual rate of decline over 52 weeks, mL/year (SD)
Nintedanib (n=288)	72.4 (16.8)	−52.4 (13.8)
Placebo (n=288)	72.7 (16.6)	−93.3 (13.5)

Association between slope of FVC% predicted and risk of time to first hospitalization endpoints during the treatment period over 52 weeks

	Time to first all-cause hospitalization or death (N=568)	Time to first SSc-related hospitalization or death (N=570)	Time to first admission to ER or hospital followed by ICU or death (N=572)
Longitudinal sub-model			
Estimated slope difference nintedanib vs placebo (95% CI)	1.16 (0.00, 2.32)	1.44 (0.33, 2.55)	1.33 (0.18, 2.48)
P-value	0.0497	0.0109	0.0238
Time-to-event sub-model			
Number of patients with event, n (%)	78 (13.7)	42 (7.4)	75 (13.1)
Change in FVC% predicted vs no change, HR (95% CI)			
1-unit decrease	1.13 (1.07, 1.18)	1.14 (1.07, 1.21)	1.05 (0.98, 1.12)
3-unit decrease	**1.43 (1.24, 1.65)**	**1.48 (1.23, 1.77)**	**1.15 (0.95, 1.41)**
5-unit decrease	1.81 (1.42, 2.30)	1.91 (1.41, 2.60)	1.27 (0.91, 1.76)
P-value	**<0.0001**	**<0.0001**	**0.1549**

A 3-unit decline in FVC% predicted corresponded to a 43% and 48% increased risk of all-cause and SSc-related hospitalization or death, respectively

Association between slope of FVC% predicted and risk of first hospitalization endpoint or death during the treatment period over 52 weeks: (A) all-cause; (B) SSc-related; and (C) ER or hospital followed by ICU



With each unit decline in FVC % predicted, the HRs (95% CI) for the association between slope of FVC% predicted and the risk of first all-cause or SSc-related hospitalization event or death significantly increase.

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Abbreviations

ATA, anti-topoisomerase antibody; CI, confidence interval; ER, emergency room; FVC, forced vital capacity; HR, hazard ratio; ICU, intensive care unit; ILD, interstitial lung disease; SD, standard deviation; SSc-ILD, systemic sclerosis-associated ILD.

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