Continued Treatment with Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Interim Analysis of SENSCIS®-ON

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Introduction

- In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo, with adverse events that were manageable for most patients.[1]

Aim

- SENSCIS-ON (NCT03313180) is an open-label extension study that is collecting data on FVC decline and adverse events in patients treated with nintedanib over the longer term.

Methods

- Patients eligible to participate in SENSCIS-ON came from two parent trials:

1 **Placebo-controlled SENSCIS trial of nintedanib in patients with SSc-ILD[1]**

- Patients remained on blinded treatment until the last patient had reached week 52 but for ≤100 weeks
- Patients who completed the SENSCIS trial on treatment and attended a follow-up visit 28 days later were eligible to enter SENSCIS-ON

2 **Open-label, drug–drug interaction study of nintedanib and Microgynon (ethinylestradiol + levonorgestrel) in female patients with SSc-ILD**

- Patients received nintedanib over a period of ≥14 days to approximately 28 days
- Patients who completed the study on treatment were eligible to enter SENSCIS-ON

- We analyzed the change from baseline in FVC (mL) and adverse events over 52 weeks in SENSCIS-ON in:
  - Patients who had received nintedanib in the SENSCIS trial and continued nintedanib in SENSCIS-ON (known as the "continued nintedanib" group)
  - Patients who had received placebo in the SENSCIS trial and initiated nintedanib in SENSCIS-ON, or who had received nintedanib for a short period in the drug-drug interaction study (known as the "initiated nintedanib" group).
- Analyses were pre-specified and descriptive.

Results

Disposition of patients

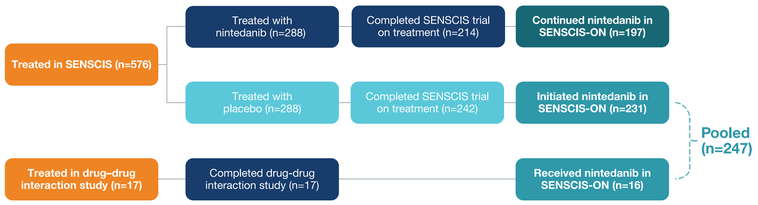
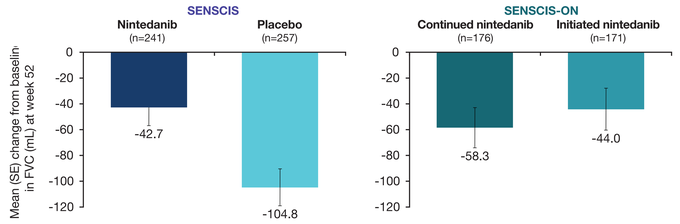
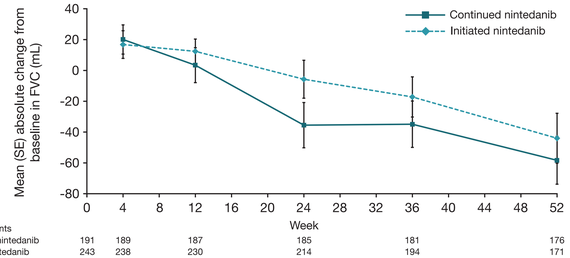


Figure 1. *Change from baseline in FVC (mL) at week 52 in SENSCIS and SENSCIS-ON*



Mean (SD) FVC at the start of SENSCIS was 2459 (736) and 2541 (816) mL in the nintedanib and placebo groups, respectively.
Mean (SD) FVC at the start of SENSCIS-ON was 2379 (754) and 2443 (814) mL in the continued nintedanib and initiated nintedanib groups, respectively.

Figure 2. *Absolute change from baseline in FVC (mL) over time in SENSCIS-ON*



No. of patients						
Continued nintedanib	191	189	187	185	181	176
Initiated nintedanib	243	238	230	214	194	171

Baseline was the last measurement before the date of first trial drug intake in SENSCIS-ON.

Table 1. *Adverse events (irrespective of causality) over 52 weeks in SENSCIS and SENSCIS-ON*

	SENSCIS		SENSCIS-ON	
	Nintedanib (n=288)	Placebo (n=288)	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Any adverse event(s)	283 (98.3)	276 (95.8)	191 (97.0)	243 (98.4)
Adverse event(s) leading to permanent treatment discontinuation	46 (16.0)	25 (8.7)	9 (4.6)	53 (21.5)
Serious adverse event(s)*	69 (24.0)	62 (21.5)	42 (21.3)	60 (24.3)
Fatal adverse events	5 (1.7)	4 (1.4)	5 (2.5)	1 (0.4)

Data are n (%) of patients with ≥1 such event reported over 52 weeks (or until 28 days after last drug intake if earlier in SENSCIS or until 7 days after last trial drug intake if earlier in SENSCIS-ON).
*Adverse events that resulted in death, were life threatening, resulted in hospitalization or prolongation of hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

Table 2. *Most frequent adverse events over 52 weeks in SENSCIS and SENSCIS-ON*

	SENSCIS		SENSCIS-ON	
	Nintedanib (n=288)	Placebo (n=288)	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Diarrhea	218 (75.7)	91 (31.6)	134 (68.0)	170 (68.8)
Nausea	91 (31.6)	39 (13.5)	32 (16.2)	60 (24.3)
Vomiting	71 (24.7)	30 (10.4)	27 (13.7)	53 (21.5)
Skin ulcer	53 (18.4)	50 (17.4)	36 (18.3)	43 (17.4)
Nasopharyngitis	36 (12.5)	49 (17.0)	28 (14.2)	33 (13.4)
Upper respiratory tract infection	33 (11.5)	35 (12.2)	27 (13.7)	26 (10.5)
Cough	34 (11.8)	52 (18.1)	24 (12.2)	21 (8.5)
Weight decreased	34 (11.8)	12 (4.2)	14 (7.1)	26 (10.5)
Abdominal pain	33 (11.5)	21 (7.3)	6 (3.0)	33 (13.4)

Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are n (%) of patients with ≥1 such event reported over 52 weeks (or until 28 days after last drug intake if earlier in SENSCIS or until 7 days after last trial drug intake if ear lier in SENSCIS-ON). Events reported in >10% of patients in either group in SENSCIS-ON are shown.

Table 3. *Most frequent liver laboratory adverse events over 52 weeks in SENSCIS and SENSCIS-ON*

	SENSCIS		SENSCIS-ON	
	Nintedanib (n=288)	Placebo (n=288)	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Alanine aminotransferase increased	21 (7.3)	3 (1.0)	9 (4.6)	19 (7.7)
Gamma-glutamyltransferase increased	17 (5.9)	4 (1.4)	8 (4.1)	16 (6.5)
Aspartate aminotransferase increased	15 (5.2)	1 (0.3)	8 (4.1)	17 (6.9)
Hepatic enzyme increased	8 (2.8)	4 (1.4)	2 (1.0)	11 (4.5)
Blood alkaline phosphatase increased	5 (1.7)	1 (0.3)	1 (0.5)	4 (1.6)
Transaminases increased	3 (1.0)	1 (0.3)	4 (2.0)	2 (0.8)
Hepatic function abnormal	1 (0.3)	0 (0.0)	3 (1.5)	7 (2.8)

Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are n (%) of patients with ≥1 such event reported over 52 weeks (or until 28 days after last drug intake if earlier in SENSCIS or until 7 days after last trial drug intake if earlier in SENSCIS-ON).

Conclusions

- **The change in FVC in patients who received nintedanib over 52 weeks of SENSCIS-ON was similar to the change in FVC in patients who received nintedanib over 52 weeks of the SENSCIS trial.**
- **The adverse event profile of nintedanib over longer-term use was consistent with that reported over 52 weeks in the SENSCIS trial.**
- **These findings support a clinically meaningful benefit of nintedanib in slowing the progression of SSc-ILD.**

Reference

1. Distler O et al. N Engl J Med 2019;380:2518–2528.

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