Safety and Tolerability of Nintedanib in Patients with Autoimmune Disease-Related Interstitial Lung Diseases: Pooled Data from the SENSCIS and INBUILD Trials

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INTRODUCTION

- The efficacy and safety of nintedanib in patients with autoimmune disease-related ILDs have been investigated in two placebo-controlled trials: the SENSCIS trial in patients with systemic sclerosis-associated ILD (SSc-ILD)[1] and the INBUILD trial in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF).[2-3]

AIM

- To characterize the safety and tolerability of nintedanib in patients with autoimmune disease-related ILDs using pooled data from the SENSCIS and INBUILD trials.

METHODS

- Data were pooled from all patients in the SENSCIS trial and patients with autoimmune disease-related ILDs in the INBUILD trial.

Key inclusion criteria

SENSCIS trial[1]	INBUILD trial[2]
• Age ≥18 years • Diagnosis of SSc based on ACR/EULAR 2013 classification criteria[4] with first non-Raynaud symptom ≤7 years before screening • Predominant features on HRCT consistent with SSc-ILD • Fibrotic ILD of ≥10% extent on HRCT • FVC ≥40% predicted • DLco 30–89% predicted	• Age ≥18 years • Clinical diagnosis of diffuse fibrosing ILD other than IPF • Reticulation with traction bronchiectasis (with or without honeycombing) on HRCT • Progressive ILD defined by worsening in lung function, symptoms, or imaging, despite management deemed appropriate in clinical practice • Fibrotic ILD of ≥10% extent on HRCT • FVC ≥45% predicted • DLco 30-80% predicted

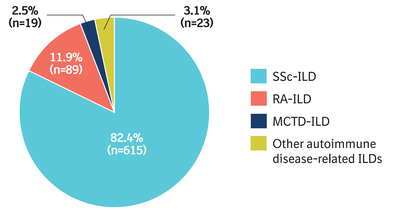
- In both trials, patients were randomized to receive nintedanib 150 mg bid or placebo. Recommendations were provided to investigators for the management adverse events.[2,5]
- Adverse events reported by the investigators irrespective of causality were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0. Adverse events reported over 52 weeks were analyzed.
- Based on the mechanism of action of nintedanib, major adverse cardiovascular events (MACE), myocardial infarction, bleeding, gastrointestinal perforation and hepatic adverse events were considered of particular interest.

CONCLUSIONS

- In patients with autoimmune-disease related ILDs, the adverse events associated with nintedanib were characterized predominantly by gastrointestinal events and were managed without treatment discontinuation in most patients.
- The adverse event profile of nintedanib in patients with autoimmune disease-related ILDs was consistent with that observed in patients with other ILDs.

RESULTS

- The pooled data set comprised 746 patients with autoimmune disease-related ILDs:



RA, rheumatoid arthritis; MCTD, mixed connective tissue disease.

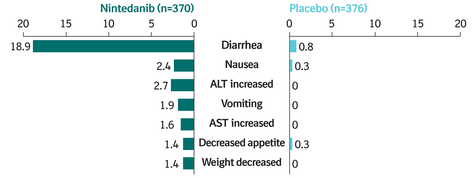
Baseline characteristics

	Nintedanib (n=370)	Placebo (n=376)
Mean (SD) age, years	56.5 (12.0)	56.1 (13.2)
Female, %	72.4	67.8
Mean (SD) body mass index, kg/m²	26.1 (4.9)	26.3 (5.2)
Mean (SD) years since diagnosis of ILD	3.1 (2.6)	2.9 (2.5)
Mean (SD) FVC % predicted	71.8 (16.5)	72.5 (16.1)
Mean (SD) DLco % predicted	51.1 (15.1)	52.7 (15.3)

- Mean (SD) exposure to trial medication was 10.4 (3.6) months in the nintedanib group and 11.3 (2.6) months in the placebo group.

Adverse events leading to dose reduction

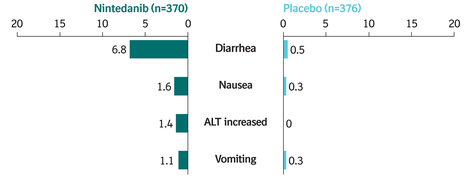
Most frequent adverse events leading to dose reduction



Adverse events were coded according to preferred terms in the MedDRA. Data are % of patients with ≥1 such adverse event over 52 weeks.
Adverse events leading to dose reduction in ≥1% of patients in either group are shown. Only permanent dose reductions were considered for the SENSCIS trial; all dose reductions were considered for the INBUILD trial.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

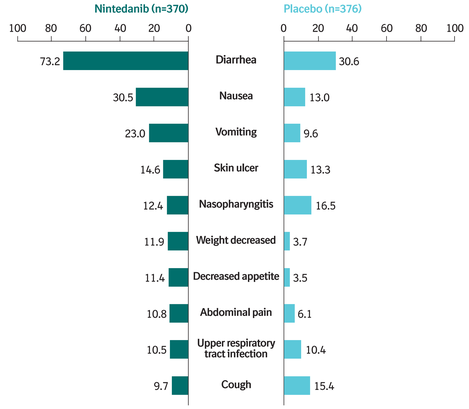
Adverse events leading to permanent treatment discontinuation

Most frequent adverse events leading to permanent treatment discontinuation



Adverse events were coded according to preferred terms in the MedDRA. Data are % of patients with ≥1 such adverse event over 52 weeks.
Adverse events leading to treatment discontinuation in ≥1% of patients in either group are shown.

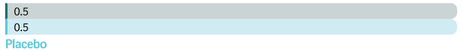
Most frequent adverse events



Adverse events were coded according to preferred terms in the MedDRA. Data are % of patients with ≥1 such adverse event over 52 weeks.
Adverse events reported in >10% of patients in either group based on single MedDRA preferred terms are shown.

Adverse events of particular interest

Serious diarrhea adverse events



Based on the MedDRA preferred term. Serious adverse events were defined as 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 serious for any other reason. Data are % of patients with ≥1 such adverse event over 52 weeks.

Major adverse cardiovascular events (MACE)

Based on fatal adverse events in MedDRA system organ classes "cardiac disorders" and "vascular disorders"; any fatal and non-fatal events in subordinate standardized MedDRA query "myocardial infarction" (broad definition); any fatal and non-fatal stroke events (based on selected preferred terms); and MedDRA preferred terms "sudden death", "cardiac death" and "sudden cardiac death". Data are % of patients with ≥1 such adverse event over 52 weeks.

Myocardial infarction

Based on standardized MedDRA query "myocardial infarction" (narrow definition). Data are % of patients with ≥1 such adverse event over 52 weeks.

Bleeding adverse events

Based on standardized MedDRA query "hemorrhage terms (excluding laboratory terms)" (narrow definition). Data are % of patients with ≥1 such adverse event over 52 weeks.

Serious bleeding adverse events

Based on standardized MedDRA query "hemorrhage terms (excluding laboratory terms)" (narrow definition). Serious adverse events were defined as 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 serious for any other reason. Data are % of patients with ≥1 such adverse event over 52 weeks.

Gastrointestinal perforation

Based on narrow standardized MedDRA query "gastrointestinal perforation". Data are % of patients with ≥1 such adverse event over 52 weeks.

Hepatic adverse events

Based on standardized MedDRA query 'liver related investigations, signs and symptoms' (broad definition). Data are % of patients with ≥1 such adverse event over 52 weeks.

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