Safety and tolerability of nintedanib in patients with fibrosing ILDs: a comparison of the INBUILD® and INPULSIS® trials

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Introduction

- The effects of nintedanib were investigated in patients with idiopathic pulmonary fibrosis (IPF) in the two INPULSIS trials[1] and in patients with other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype in the INBUILD trial.[2]
- In all these trials, nintedanib reduced the annual rate of decline in forced vital capacity (FVC) versus placebo. The relative reduction in the rate of FVC decline over 52 weeks was 49% in the INPULSIS trials[1] and 57% in the INBUILD trial.[2]

Aim

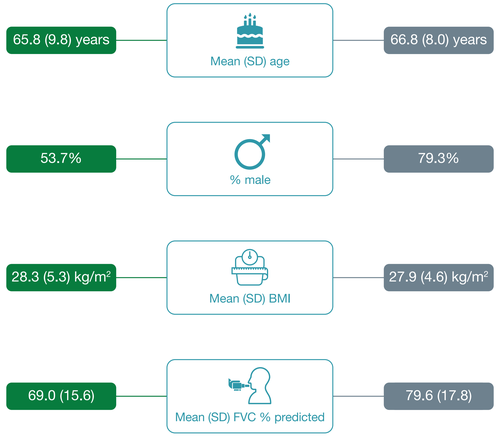
- To assess the safety and tolerability profile of nintedanib in the INPULSIS and INBUILD trials.

Methods

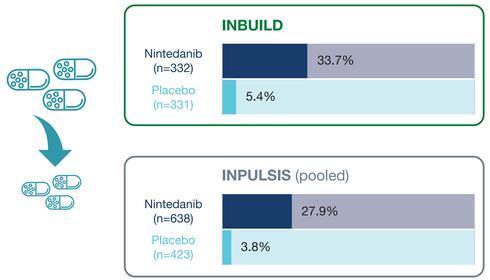
- In the INPULSIS and INBUILD trials, patients were randomized to receive nintedanib 150 mg bid or placebo.
- We present descriptive data on adverse events reported by the investigators, irrespective of causality, over 52 weeks of treatment (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52) and on the dose reductions and treatment interruptions used to manage adverse events.
- Analyses were based on patients who received ≥1 dose of trial drug.

Results

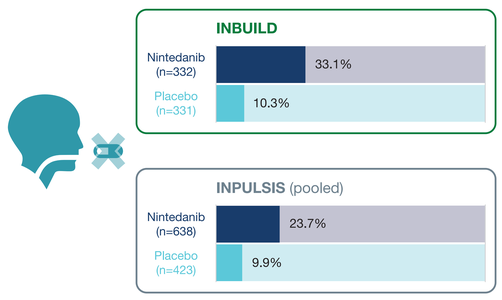
Baseline characteristics



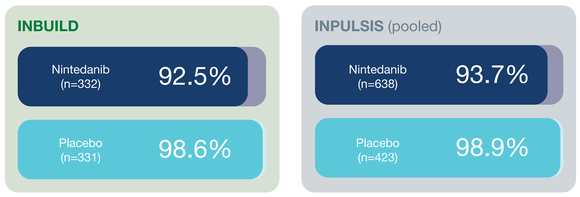
Proportions of patients who had ≥1 dose reduction over 52 weeks



Proportions of patients who had ≥1 treatment interruption over 52 weeks

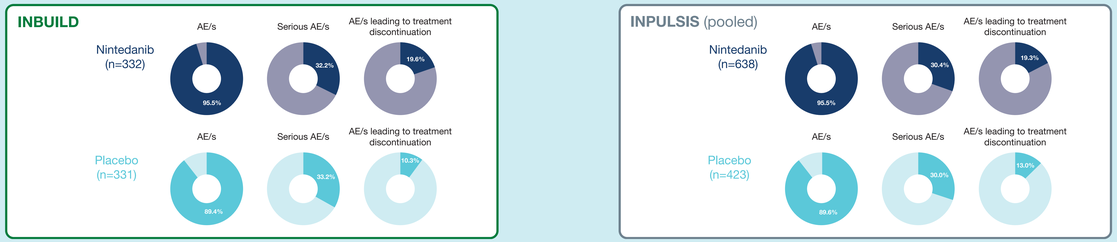


Mean dose intensity*



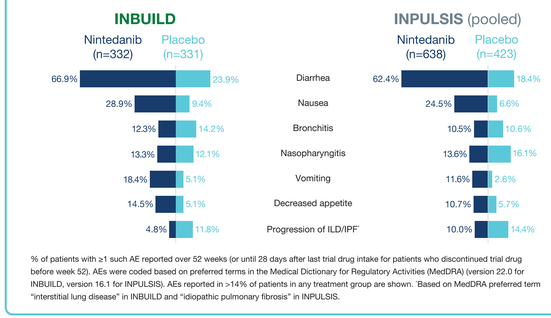
*Amount of drug administered divided by the amount of drug that would have been received if the 150 mg bid dose had been administered over the 52-week treatment period or until permanent treatment discontinuation.

Summary of adverse events



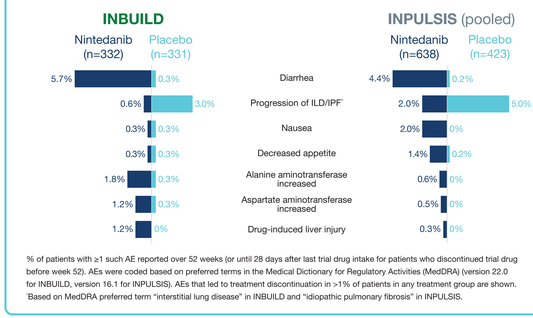
% of patients with ≥1 such AE reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52).

Most frequent adverse events



% of patients with ≥1 such AE reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). AEs were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA) (version 22.0 for INBUILD, version 16.1 for INPULSIS). AEs reported in >14% of patients in any treatment group are shown. ¨Based on MedDRA preferred term "interstitial lung disease" in INBUILD and "idiopathic pulmonary fibrosis" in INPULSIS.

Most frequent adverse events leading to permanent treatment discontinuation



% of patients with ≥1 such AE reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). AEs were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA) (version 22.0 for INBUILD, version 16.1 for INPULSIS). AEs that led to treatment discontinuation in >1% of patients in any treatment group are shown. ¨Based on MedDRA preferred term "interstitial lung disease" in INBUILD and "idiopathic pulmonary fibrosis" in INPULSIS.

In approximately **95%** of nintedanib-treated patients who reported **diarrhea**, all the events were rated as **mild or moderate in intensity.**

Conclusions

- **The safety and tolerability profile of nintedanib was similar in patients with IPF in the INPULSIS trials and in patients with other chronic fibrosing ILDs with a progressive phenotype in the INBUILD trial.**
- **The adverse event profile of nintedanib in patients with ILDs is characterized mainly by mild/moderate gastrointestinal events, which can be tolerated by most patients.**

References

1. Richeldi L et al. N Engl J Med 2014;370:2071-82.
2. Flaherty KR et al. N Engl J Med 2019;381:1718-27.

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