Nintedanib dose adjustments and adverse events in patients with progressive autoimmune disease-related interstitial lung diseases (ILDs) in the INBUILD® trial

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Introduction

- In the INBUILD trial in patients with chronic fibrosing ILDs and a progressive phenotype (other than idiopathic pulmonary fibrosis), nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) by 57% versus placebo.[1]
- Subgroup analyses suggested that the effect of nintedanib on reducing the rate of FVC decline was consistent across groups of patients with different ILD diagnoses.[2]
- The adverse event profile of nintedanib was characterised predominantly by gastrointestinal adverse events. Dose reductions (from 150 mg bid to 100 mg bid) and treatment interruptions were permitted to manage adverse events.[1]

Aim

- To assess adverse events and dose adjustments in patients with autoimmune disease-related ILDs in the INBUILD trial.

Methods

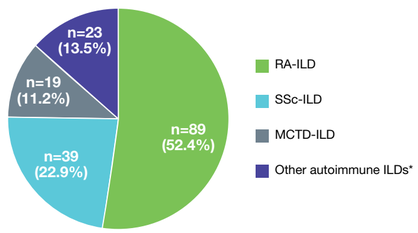
- Patients enrolled in the INBUILD trial had an ILD other than idiopathic pulmonary fibrosis, diagnosed by the investigator according to their usual clinical practice, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted and diffusing capacity of the lungs for carbon monoxide (DLco) ≥30%–<80% predicted.[1]
- Patients met ≥1 of the following criteria for ILD progression in the 24 months before screening, despite management deemed appropriate in clinical practice:

- Patients were randomised to receive nintedanib 150 mg bid or placebo, stratified by HRCT pattern (usual interstitial pneumonia [UIP]-like fibrotic pattern or other fibrotic patterns).[1]
- Restricted immunomodulatory therapies (azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, rituximab, cyclophosphamide, oral corticosteroids >20 mg/day) were excluded at randomization, but could be initiated after 6 months of study treatment in cases of deterioration of ILD or CTD. Investigators were asked not to consider patients with autoimmune disease that was managed using any of these restricted therapies for participation in the trial.
- Adverse events reported by the investigators, irrespective of causality, and dose adjustments were assessed in patients who received ≥1 dose of trial drug.

Results

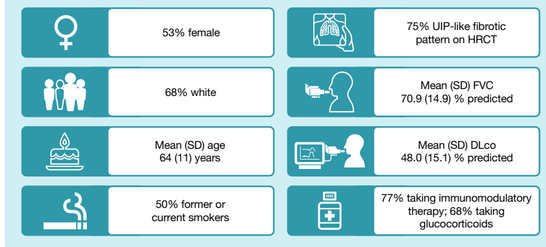
Patients

- 170 patients in the INBUILD trial had autoimmune disease-related ILDs:

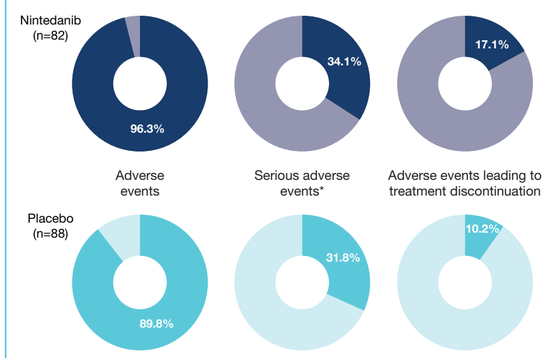


*Patients with an autoimmune disease noted in the "Other fibrosing ILDs" category of the case report form, including Sjögren's disease-related ILD, interstitial pneumonia with autoimmune features (IPAF), and undifferentiated autoimmune disease-related ILD.

Baseline characteristics

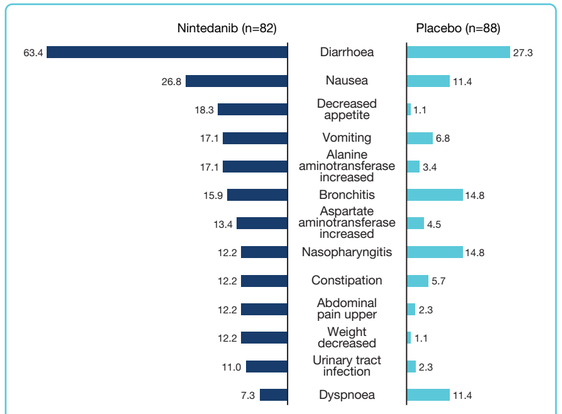


Adverse event summary



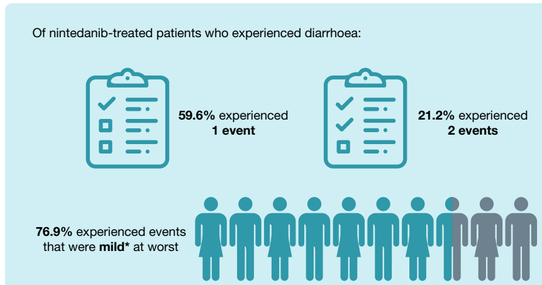
Data are % of patients with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). *Adverse event that resulted in death, was life-threatening, resulted in hospitalisation or prolongation of hospitalisation, resulted in persistent or clinically significant disability or incapacity, was a congenital anomaly or birth defect, or was deemed to be serious for any other reason.

Most frequent adverse events



Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of patients with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). Adverse events reported in >10% of patients in either treatment group are shown.

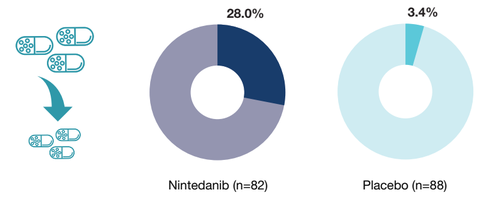
Diarrhoea adverse events



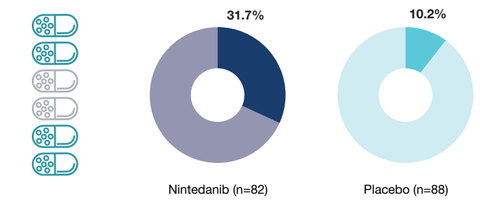
*Common Terminology Criteria for adverse events grade 1.

Dose adjustments

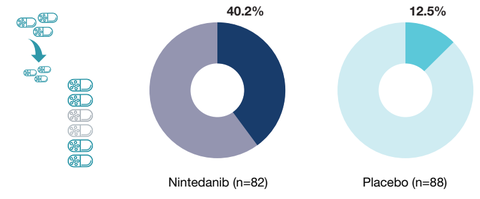
Proportions of patients with ≥1 dose reduction over 52 weeks



Proportions of patients with ≥1 treatment interruption over 52 weeks



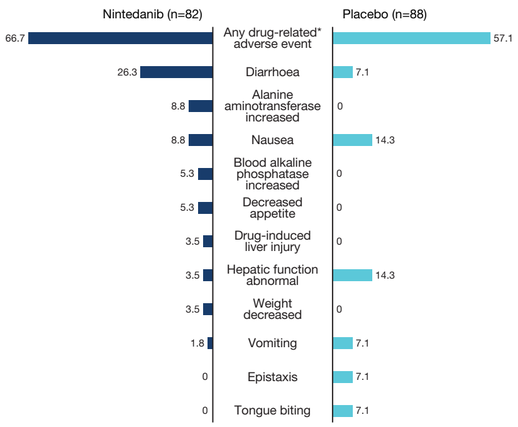
Proportion of patients with ≥1 dose adjustment (dose reduction and/or treatment interruption) over 52 weeks



Mean (SD) dose intensity*

*Amount of drug administered divided by amount that would have been received had 150 mg bid been administered over 52 weeks or until permanent treatment discontinuation, which occurred in 25.6% and 17.0% of patients in the nintedanib and placebo groups, respectively.

Drug-related* adverse events that led to dose adjustment



Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of the events leading to dose adjustment in the respective treatment group (n=57 events in the nintedanib group and n=14 events in the placebo group). Adverse events reported with a frequency of >3% in either treatment group are shown. *In the opinion of the investigator.

Conclusions

- **The adverse events associated with nintedanib therapy in patients with progressive autoimmune disease-related ILDs in the INBUILD trial were consistent with those in the overall trial population[1] and with the established safety profile of nintedanib in patients with IPF.[3]**
- **Most patients with autoimmune disease-related ILDs remained on therapy for 52 weeks, suggesting that the dose adjustments used to manage adverse events were effective at minimising treatment discontinuations.**

References

1. Flaherty KR et al. N Engl J Med 2019;381:1718–27.
2. Wells AU et al. Lancet Respir Med 2020;8:453–460.
3. Lancaster L et al. BMJ Open Respir Res 2019;6:e000397.

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