Effects of nintedanib in patients with progressive fibrosing interstitial lung disease associated with rheumatoid arthritis (RA-ILD) in the INBUILD trial

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INTRODUCTION

- In the INBUILD trial in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 57% compared with placebo.[1]
- Of the 663 patients in the INBUILD trial, 89 had RA-ILD.

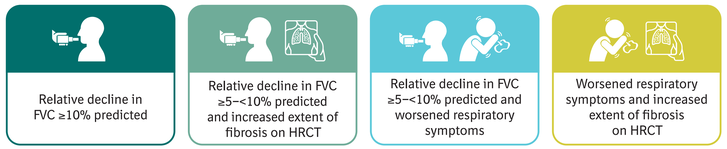
AIM

- To assess the efficacy and safety of nintedanib in patients with RA-ILD in the INBUILD trial.

METHODS

Trial design

- Patients in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on high-resolution computed tomography (HRCT), FVC ≥45% predicted, and diffusing capacity of the lungs for carbon monoxide (DLco) ≥30%–<80% predicted. Patients with IPF were excluded.
- Patients met ≥1 of the following criteria for ILD progression within the 24 months before screening, despite management deemed appropriate in clinical practice:



- Oral glucocorticoids at a dose of ≤20 mg/day prednisone or equivalent was permitted at randomisation and during the trial. Patients taking stable doses of medications to treat autoimmune disease were eligible to participate, except for azathioprine, cyclosporine, mycophenolate, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids >20 mg/day. Initiation of these therapies was allowed after 6 months of the trial in patients with deterioration of ILD or autoimmune disease.

Analyses

- In patients with RA-ILD, we analysed the rate of decline in FVC (mL/year) over 52 weeks overall, in subgroups by high-sensitivity C-reactive protein (hs-CRP) at baseline (<1 vs ≥1 mg/L; <3 vs ≥3 mg/L), and in subgroups by use of disease-modifying anti-rheumatic drugs (DMARDs) and/or glucocorticoids (yes/no) at baseline.
- Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib between subgroups.

CONCLUSIONS

- In the INBUILD trial, nintedanib slowed the rate of decline in FVC in patients with progressive fibrosing RA-ILD, with adverse events that were manageable for most patients. The efficacy and safety of nintedanib in subjects with RA-ILD were consistent with those observed in the overall trial population. Interpretation of subgroup analyses of the RA-ILD subgroup is limited by the small number of patients.

RESULTS

Baseline characteristics of patients with RA-ILD (n=89)

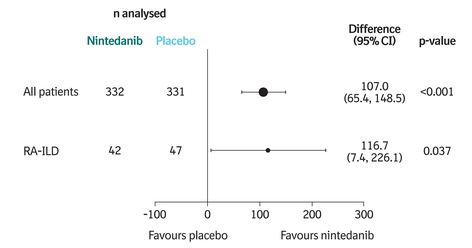
Nintedanib (n=42)		Placebo (n=47)
66.8	Mean age (years)	67.0
59.5	Male, %	61.7
10.1	Mean time since RA diagnosis (years)	9.8
3.4	Mean time since ILD diagnosis (years)	3.7
66.7	Former or current smoker, %	61.7
85.7	UIP-like fibrotic pattern on HRCT, %	87.2
70.8	Mean FVC % predicted	72.0
45.2	Mean DLco % predicted*	50.0
8.2	Median hs-CRP, mg/L†	3.8
26.2	Biologic DMARDs, %	17.0
52.4	Non-biologic DMARDs, %	55.3
76.2	Glucocorticoids, %‡	70.2

*Corrected for haemoglobin. †Data missing for 4 patients. ‡≤20 mg/day prednisone or equivalent.

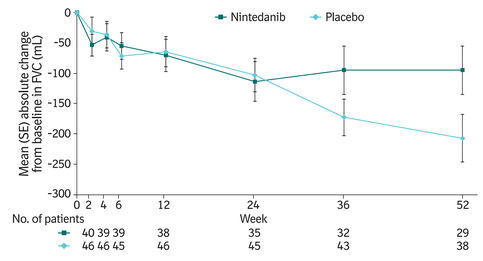
Rate of decline in FVC (mL/year)

- The adjusted mean (SE) rate of decline in FVC over 52 weeks in patients with RA-ILD was -82.6 (41.3) mL/year in the nintedanib group versus -199.3 (36.2) mL/year in the placebo group (difference 116.7 mL/year [95% CI 7.4, 226.1]; p=0.037).

Rate of decline in FVC (mL/year) over 52 weeks with nintedanib versus placebo



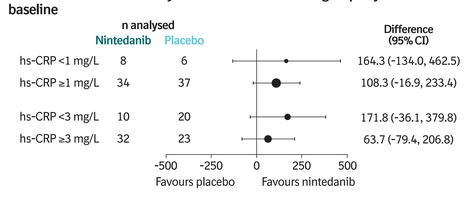
Absolute change from baseline in FVC (mL) over 52 weeks



Subgroups by hs-CRP at baseline

- The exploratory interaction p-values did not indicate heterogeneity in the treatment effect of nintedanib between subgroups by hs-CRP at baseline.

Rate of decline in FVC (mL/year) over 52 weeks in subgroups by hs-CRP at baseline

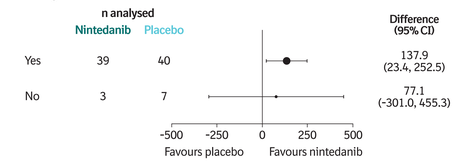


Treatment-by-subgroup-by-time interaction p=0.73 for hs-CRP <1 vs ≥1 mg/L and p=0.40 for hs-CRP <3 vs ≥3 mg/L.

Subgroups by DMARDs and/or glucocorticoids at baseline

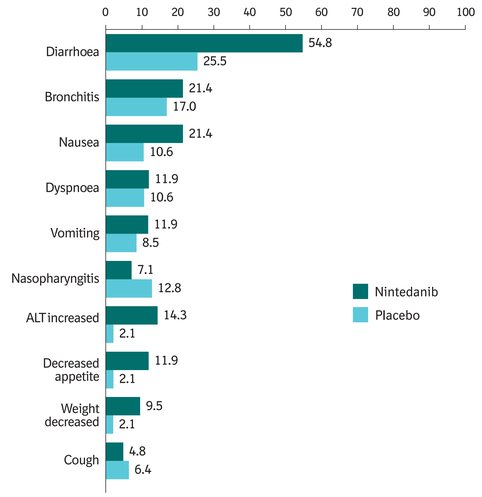
- The exploratory interaction p-value did not indicate heterogeneity in the treatment effect of nintedanib between patients taking and not taking DMARDs and/or glucocorticoids at baseline.

Rate of decline in FVC (mL/year) over 52 weeks in subgroups by use of DMARDs and/or glucocorticoids at baseline



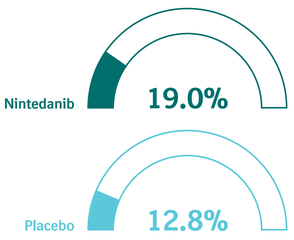
Treatment-by-subgroup-by-time interaction p=0.76.

Adverse events (reported irrespective of causality)



Adverse events were coded using preferred terms in the Medical Dictionary for Regulatory Activities. Data are % of patients with ≥1 such adverse event reported over 52 weeks for until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Adverse events reported in >12% of patients in either treatment group in the overall trial population are shown. ALT, alanine aminotransferase.

Adverse events leading to treatment discontinuation



Data are % of patients with ≥1 such adverse event reported over 52 weeks.

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REFERENCE
1. Flaherty KR et al. N Engl J Med 2019;381:1718–1727.

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