# Effects of nintedanib in patients with progressive fibrosing ILDs and differing baseline FVC: further analyses of the INBUILD® trial

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## Introduction

- In patients with chronic fibrosing interstitial lung diseases (ILDs) and a progressive phenotype, decline in forced vital capacity (FVC) is predictive of mortality.[1–4]
- In the INBUILD trial in subjects with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib slowed the rate of decline in FVC (mL/year) over 52 weeks by 57% versus placebo (difference 107.0 mL/year [95% CI: 65.4, 148.5]).[5]


relative reduction in rate of decline in FVC (mL/year) over 52 weeks

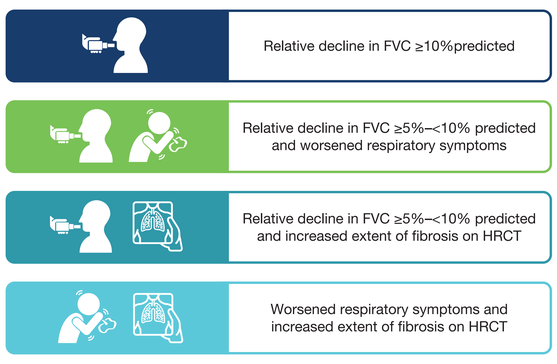
## Aim

- To assess the effect of nintedanib on the rate of decline in FVC in subjects with differing FVC at baseline in the INBUILD trial.

## Methods

### Trial design[5]

- Subjects in the INBUILD trial had an ILD other than IPF, diagnosed according to the investigator's usual clinical practice; reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on HRCT based on central review; FVC ≥45% predicted; diffusion capacity of the lung for carbon monoxide (DLco) ≥30%–<80% predicted.
- Subjects met ≥1 of the following criteria for ILD progression in the 24 months before screening, despite management deemed appropriate in clinical practice:




- Subjects were randomised to receive nintedanib or placebo, stratified by fibrotic pattern on HRCT (usual interstitial pneumonia [UIP]-like fibrotic pattern or other fibrotic patterns).

### Analyses

- We assessed the rate of decline in FVC (mL/year) over 52 weeks in subgroups by FVC % predicted at baseline (≤50%, >50%–≤70%, >70% predicted).
- Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo across the subgroups. No adjustment for multiplicity was made.
- Adverse events are presented descriptively.

## Results

### Subjects

- Of 663 subjects, 75 (11.3%) had FVC ≤50% predicted; 314 (47.4%) had FVC >50%–≤70% predicted and 274 (41.3%) had FVC >70% predicted at baseline.

**Baseline characteristics in subgroups by FVC % predicted**

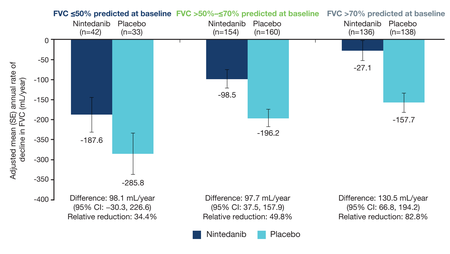
| Overall population | | | | Subjects with a UIP-like fibrotic pattern on HRCT | | |
|---|---|---|---|---|---|---|
| FVC ≤50 % predicted (n=75) | FVC >50–≤70 % predicted (n=314) | FVC >70 % predicted (n=274) | | FVC ≤50 % predicted (n=36) | FVC >50–≤70 % predicted (n=190) | FVC >70 % predicted (n=186) |
| 58.7 | 51.3 | 55.1 | Male (%) | 72.2 | 58.9 | 58.6 |
| 63.5 (9.9) | 65.4 (9.7) | 66.8 (9.7) | Age (years) | 66.4 (8.0) | 67.6 (8.6) | 68.7 (8.3) |
| 50.7 | 49.0 | 53.3 | Former or current smoker (%) | 69.4 | 55.8 | 56.5 |
| 48.0 | 60.5 | 67.9 | UIP-like fibrotic pattern on HRCT (%) | 100 | 100 | 100 |
| 1673 (374) | 2073 (511) | 2806 (739) | FVC (mL) | 1637 (373) | 2059 (482) | 2826 (737) |
| 47.4 (1.8) | 61.1 (5.6) | 84.0 (11.3) | FVC % predicted | 47.2 (2.0) | 61.3 (5.6) | 84.6 (11.6) |
| 37.5 (6.9) | 44.1 (13.9) | 50.8 (13.0) | DLco % predicted | 35.6 (5.7) | 44.6 (15.4) | 50.8 (12.6) |

Mean (SD) or % of subjects.

### Rate of decline in FVC (mL/year) over 52 weeks by FVC % predicted at baseline in the overall population

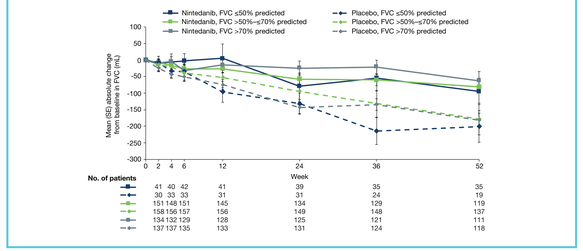
- In the placebo group, the mean rate of decline in FVC over 52 weeks was numerically greater in subjects with FVC ≤50% predicted at baseline than in the other subgroups (Figure 1; Figure 2).
- The effect of nintedanib versus placebo on reducing the rate of decline in FVC was numerically more pronounced in subjects with FVC >70% predicted at baseline, but the interaction p-value did not indicate a heterogeneous treatment effect of nintedanib across the subgroups (p=0.75) (Figure 1).

***Figure 1.*** *Rate of decline in FVC (mL/year) over 52 weeks in the overall population in subgroups by FVC % predicted at baseline*




Treatment-by-subgroup-by-time interaction p=0.75.

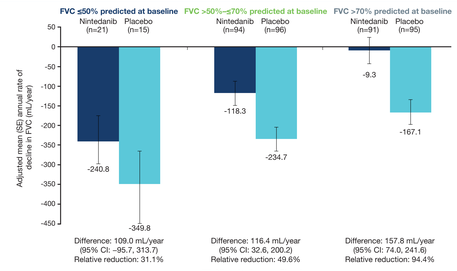
***Figure 2.*** *Observed change from baseline in FVC (mL) in the overall population in subgroups by FVC % predicted at baseline*




### Rate of decline in FVC (mL/year) over 52 weeks by FVC % predicted at baseline in subjects with a UIP-like fibrotic pattern on HRCT

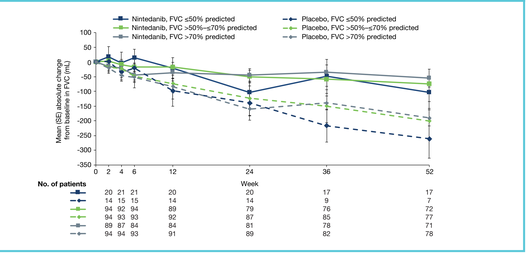
- In the placebo group, the mean rate of decline in FVC over 52 weeks was numerically greater in subjects with greater impairment in FVC (Figure 3; Figure 4).
- The effect of nintedanib versus placebo on reducing the rate of decline in FVC was numerically more pronounced in subjects with FVC >70% predicted at baseline, but the interaction p-value did not indicate a heterogeneous treatment effect of nintedanib across the subgroups (p=0.76) (Figure 3).

***Figure 3.*** *Rate of decline in FVC (mL/year) over 52 weeks in subjects with UIP-like fibrotic pattern on HRCT in subgroups by FVC % predicted at baseline*




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

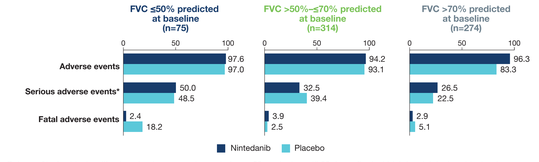
***Figure 4.*** *Observed change from baseline in FVC (mL) in subjects with UIP-like fibrotic pattern on HRCT in subgroups by FVC % predicted at baseline*




### Adverse events

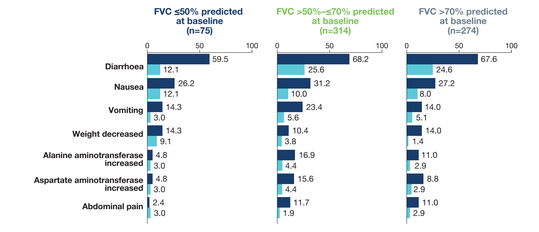
- The adverse event profile of nintedanib was generally consistent across the subgroups by FVC % predicted at baseline, but serious and fatal adverse events were reported in greater proportions of subjects who had FVC <50% predicted at baseline, reflecting their greater disease severity (Figures 5 and 6).

***Figure 5.*** *Adverse events (reported irrespective of causality) in subgroups by FVC % predicted at baseline*




Data are % of subjects with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake in subjects who discontinued trial drug before week 52). *Adverse events that resulted in death, were life-threatening, resulted in hospitalisation or prolongation of hospitalisation, 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.

***Figure 6.*** *Most frequent gastrointestinal, weight loss and hepatic adverse events (reported irrespective of causality) in subgroups by FVC % predicted at baseline*




Gastrointestinal, weight loss and liver enzyme adverse events were coded using preferred terms in the Medical Dictionary for Regulatory Activities. Data are % of subjects with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake in subjects who discontinued trial drug before week 52). Adverse events reported in >10% of subjects in either the nintedanib or placebo group in the overall population are shown.

## Conclusions

- **In the INBUILD trial, nintedanib slowed the rate of decline in FVC in subjects with progressive fibrosing ILDs other than IPF, irrespective of their degree of FVC impairment at baseline.**

## References

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