Effects of Nintedanib in Patients with Progressive Fibrosing Autoimmune Disease-Related Interstitial Lung Diseases (ILDs) in the INBUILD® Trial: Subgroups by HRCT Pattern

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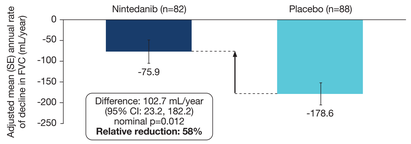
Introduction

- The INBUILD trial was a randomized placebo-controlled trial of nintedanib in patients with chronic fibrosing ILDs with a progressive phenotype other than idiopathic pulmonary fibrosis (IPF).[1]
  - Over 52 weeks, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) by 57% in the overall population and by 61% in the co-primary analysis population of patients with a usual interstitial pneumonia (UIP)-like fibrotic pattern on HRCT.[1]
  - Although the INBUILD trial was not designed to study individual ILDs, subgroup analyses suggested that there was no heterogeneity in the treatment effect of nintedanib across subgroups by ILD diagnosis.[2]
  - In the subgroup with autoimmune disease-related ILDs, nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 58% versus placebo:

Rate of decline in FVC (mL/year) over 52 weeks in patients with autoimmune disease-related ILDs



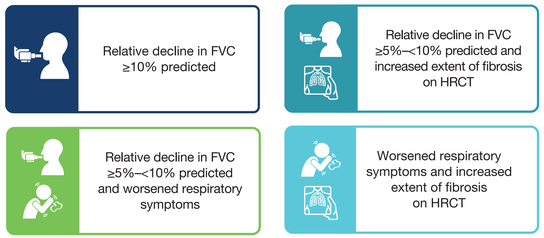
Aim

- To assess the effect of nintedanib on FVC decline in patients with autoimmune disease-related ILDs in the INBUILD trial in subgroups by fibrotic pattern on HRCT.

Methods

Trial design[1]

- Subjects had an ILD other than IPF, 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.
- Patients met ≥1 of the following criteria for ILD progression within the 24 months before screening, despite management as deemed appropriate in clinical practice:



- Patients were randomized to receive nintedanib 150 mg bid or placebo, stratified by HRCT pattern (UIP-like fibrotic pattern or other fibrotic patterns), based on central review by expert radiologists.

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https://www.usscicomms.com/respiratory/ACR2020/Dellaripa

Fibrotic patterns on HRCT

A	Definite honeycomb lung destruction with basal and peripheral predominance
B	Presence of reticular abnormality and traction bronchiectasis consistent with fibrosis with basal and peripheral predominance
C	Atypical features are absent, specifically nodules and consolidation. Ground glass opacity, if present, is less extensive than reticular opacity pattern

A+B+C A+C B+C	UIP-like fibrotic pattern on HRCT
A+B A B None	Other fibrotic patterns on HRCT

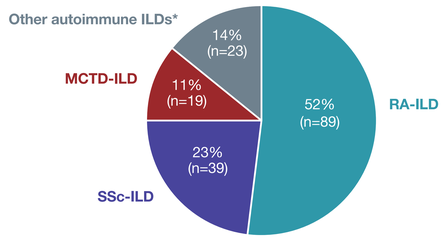
Analyses

- In patients with autoimmune disease-related ILDs, we assessed the rate of decline in FVC (mL/year) in subgroups by fibrotic pattern on HRCT at baseline (UIP-like fibrotic pattern vs other fibrotic patterns).
- An exploratory interaction p-value was calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo between the subgroups. No adjustment for multiplicity was made.

Results

Patients

Patients with autoimmune disease-related ILDs (n=170)



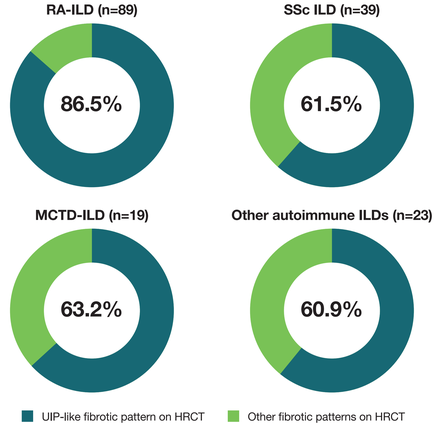
*Patients with an autoimmune disease noted in the "Other fibrosing ILDs" category of the case report form, including Sjögren's disease-related ILD, IPAF and undifferentiated autoimmune disease-related ILD. RA, rheumatoid arthritis; SSc systemic sclerosis; MCTD, mixed connective tissue disease; IPAF, interstitial pneumonia with autoimmune features.

Baseline characteristics of patients with autoimmune disease-related ILDs in subgroups by HRCT pattern

	Male (%)	Age (years)	BMI (kg/m²)
UIP-like fibrotic pattern	51.2	65.8	26.9
Other fibrotic patterns	34.9	59.6	28.8
	Former/current smoker	FVC % predicted	DLco % predicted
UIP-like fibrotic pattern	55.1	70.6	48.2
Other fibrotic patterns	34.9	71.6	47.3

Data are mean or % of patients.

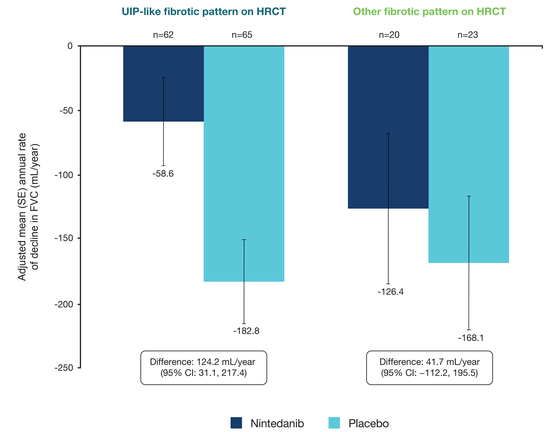
Proportion of patients with UIP-like fibrotic pattern on HRCT by ILD diagnosis



Rate of decline in FVC (mL/year) over 52 weeks

- In the placebo group, the rate of decline in FVC over 52 weeks was similar in patients with a UIP-like fibrotic pattern and with other fibrotic patterns on HRCT (Figure).
- The effect of nintedanib versus placebo on reducing the rate of decline in FVC was numerically greater in patients with a UIP-like fibrotic pattern on HRCT than in those with other fibrotic patterns on HRCT, but the exploratory interaction p-value did not indicate heterogeneity in the treatment effect between these subgroups (Figure).

Figure. Rate of decline in FVC (mL/year) over 52 weeks in patients with autoimmune disease-related ILDs in subgroups by HRCT pattern at baseline



Treatment-by-subgroup-by-time interaction p=0.37

Conclusion

- **In patients with progressive fibrosing autoimmune disease-related ILDs in the INBUILD trial, nintedanib slowed the rate of FVC decline both in patients with a UIP-like fibrotic pattern on HRCT and in patients with other fibrotic patterns on HRCT, with a numerically greater effect in patients with a UIP-like fibrotic pattern on HRCT.**

References

1. Flaherty KR et al. N Engl J Med 2019;381:1718–1727.
2. Wells AU et al. Lancet Respir Med 2020;8:453–460.

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