# Effect of nintedanib on quantitative CT in patients with progressive pulmonary fibrosis: results from the INBUILD trial.

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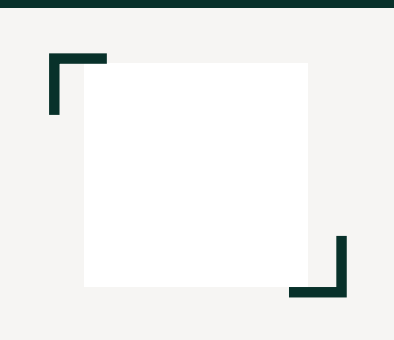
Objective

To evaluate the effects of nintedanib on quantitative CT measurements derived using the University of California Los Angeles (UCLA) and e-Lung (Brainomix) algorithms in a sub-study of the INBUILD trial in patients with PPF.
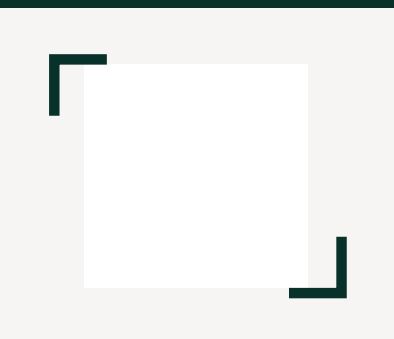
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Introduction

- Quantitative analysis enables objective assessment of the extent of ILD on CT.[1]
- More information is needed on the utility of quantitative CT measurements to assess treatment effects in large trials of drugs for pulmonary fibrosis.
- In the INBUILD trial, nintedanib reduced the rate of decline in FVC over 52 weeks compared with placebo in subjects with PPF.[2]

Methods

The INBUILD trial[2] and its sub-study

- Patients in the INBUILD trial had an ILD other than idiopathic pulmonary fibrosis, an extent of fibrosis on HRCT >10%, and met criteria for ILD progression within the prior 24 months.
- Patients were randomized to receive nintedanib or placebo, stratified by fibrotic pattern on HRCT (UIP-like fibrotic pattern or other fibrotic patterns).
- In a sub-study of the INBUILD trial, HRCT scans were taken at baseline, week 24 and week 52. Non-contrast volumetric HRCT was performed with contiguous slices with ≤1 mm thickness in supine position at full inspiration, with no iterative reconstruction.

Quantitative CT parameters

- The UCLA algorithm classifies abnormal lung tissue based on pixel density or texture.[3]
  - Quantitative lung fibrosis (QLF) score: extent of reticular patterns with architectural distortion due to fibrosis
  - Quantitative honeycomb (QHC) score: extent of honeycomb cysts
  - Quantitative ground glass opacity (QGGO) score: extent of ground glass opacities
  - The total of these scores is the quantitative ILD (QILD) score.
- e-Lung is an artificial intelligence-developed image processing module.[4] Features analyzed include:
  - Weighted Reticulovascular Score (WRVS): Measure of fibrosis combining reticular abnormalities and vascular structures
  - Total Disease Extent (TDE): Combines ground glass opacification and reticulovascular structures to provide a total ILD extent.

Analyses

- We analyzed changes from baseline in QLF, QILD, e-Lung TDE and WRVS at weeks 24 and 52 in the nintedanib and placebo groups.
- Analyses used a mixed model for repeated measures, with fixed categorical effects of treatment at each visit, sex, HRCT pattern (UIP-like pattern versus other fibrotic patterns) and fixed continuous effects of baseline value of quantitative CT at each visit, baseline FVC, age and height.
- Quantitative CT values were $\log_{10}$ transformed before analysis.

Results

Baseline characteristics of participants in INBUILD HRCT sub-study

	Nintedanib (n=236)	Placebo (n=238)
Male	125 (53.0)	132 (55.5)
Age, years	64.7 (9.6)	66.2 (10.0)
Current or former smoker	121 (51.3)	121 (50.8)
UIP-like fibrotic pattern on HRCT	141 (59.7)	151 (63.4)
Time since diagnosis of ILD, years	3.8 (3.9)	3.9 (3.6)
FVC % predicted	68.0 (15.8)	69.7 (14.8)
DLco % predicted	44.0 (11.8)	48.4 (15.7)

Data are n (%) or mean (SD).

Quantitative CT parameters at baseline of INBUILD HRCT sub-study

	Nintedanib	Placebo
UCLA algorithm		
N analyzed	197	206
QILD, %	37.5 (13.1)	35.9 (15.2)
QLF, %	17.4 (8.5)	16.5 (9.7)
e-Lung algorithm		
N analyzed	179	192
TDE, %	23.1 (9.9)	23.2 (11.7)
WRVS, %	16.1 (5.9)	16.3 (6.8)

Data are mean (SD).

Effects of nintedanib versus placebo on changes in QILD score (%)

	Week 24 Nintedanib	Week 24 Placebo	Week 52 Nintedanib	Week 52 Placebo
N	159	181	145	158
Adjusted mean (95% CI) fold change from baseline*	1.01 (0.97, 1.04)	1.08 (1.04, 1.11)	1.03 (1.00, 1.07)	1.11 (1.07, 1.15)
Absolute change from baseline	0.2	2.5	1.1	3.6
Difference vs placebo				
Adjusted ratio (95% CI) of fold changes from baseline*	0.93 (0.89, 0.98)		0.93 (0.88, 0.98)	
Absolute difference	−2.4		−2.5	
p-value	0.005		0.004	

*Analysis of $\log_{10}$ transformed data.

Effects of nintedanib versus placebo on changes in e-Lung TDE (%)

	Week 24 Nintedanib	Week 24 Placebo	Week 52 Nintedanib	Week 52 Placebo
N	150	173	135	148
Adjusted mean (95% CI) fold change from baseline*	1.00 (0.97, 1.04)	1.09 (1.06, 1.13)	1.04 (1.00, 1.08)	1.12 (1.08, 1.16)
Absolute change from baseline	0.1	1.9	0.9	2.4
Difference vs placebo				
Adjusted ratio (95% CI) of fold changes from baseline*	0.92 (0.88, 0.96)		0.93 (0.88, 0.98)	
Absolute difference	−1.8		−1.5	
p-value	<0.001		0.011	

*Analysis of $\log_{10}$ transformed data.

Effects of nintedanib versus placebo on changes in QLF score (%)

	Week 24 Nintedanib	Week 24 Placebo	Week 52 Nintedanib	Week 52 Placebo
N	159	181	145	158
Adjusted mean (95% CI) fold change from baseline*	1.07 (1.01, 1.13)	1.14 (1.08, 1.20)	1.12 (1.06, 1.18)	1.22 (1.16, 1.28)
Absolute change from baseline	1.0	1.9	1.7	3.0
Difference vs placebo				
Adjusted ratio (95% CI) of fold changes from baseline*	0.94 (0.87, 1.01)		0.92 (0.85, 0.98)	
Absolute difference	−0.9		−1.3	
p-value	0.099		0.015	

*Analysis of $\log_{10}$ transformed data.

Effects of nintedanib versus placebo on changes in e-Lung WRVS (%)

	Week 24 Nintedanib	Week 24 Placebo	Week 52 Nintedanib	Week 52 Placebo
N	150	173	135	148
Adjusted mean (95% CI) fold change from baseline*	1.04 (1.01, 1.07)	1.09 (1.06, 1.12)	1.09 (1.06, 1.13)	1.13 (1.09, 1.17)
Absolute change from baseline	0.6	1.3	1.4	1.9
Difference vs placebo				
Adjusted ratio (95% CI) of fold changes from baseline*	0.96 (0.92, 0.99)		0.97 (0.92, 1.02)	
Absolute difference	−0.7		−0.5	
p-value	0.020		0.179	

*Analysis of $\log_{10}$ transformed data.

Conclusions

- In the INBUILD trial in patients with PPF, significant effects of nintedanib versus placebo on changes in ILD extent over 24 and 52 weeks were demonstrated using both the QILD score and e-Lung TDE.
- These data add to the evidence supporting the use of quantitative CT measurements in clinical trials to assess the efficacy of drugs in slowing progression of pulmonary fibrosis.

References
1. Walsh SLF et al. Eur Respir Rev 2024;33:230055; 2. Flaherty KR et al. N Engl J Med 2019;381:1718–27; 3. Kim HG et al. Clin Exp Rheumatol 2010;28:S26–35; 4. George PM et al. ERJ Open Res 2024;10:00570-2024.