Effect of nintedanib in patients with progressive fibrosing interstitial lung diseases (ILDs): subgroup analyses from the INBUILD® trial

Martin Kolb,[1] Kevin R Flaherty,[2] Rafael S Silva,[3] Antje Prasse,[4] Nina M Patel,[5] Carlo Vancheri,[6] Manuel Quaresma,[7] Rainer-Georg Goeldner,[8] Susanne Stowasser,[7] Rozsa Schlenker-Herceg,[9] Athol U Wells[10] on behalf of the INBUILD trial investigators

[1]McMaster University and St. Joseph's Healthcare, Hamilton, Ontario, Canada; [2]University of Michigan, Ann Arbor, MI, USA; [3]Centro de Investigación del Maule, Talca, Chile; [4]MHH Hannover Medical School, Department of Respiratory Medicine, Hannover, Germany; [5]Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University College of Physicians and Surgeons/ New York-Presbyterian Hospital, New York, NY, USA; [6]Regional Referral Center for Rare Lung Diseases, University-Hospital "Policlinico G. Rodolico"; [7]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [8]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; [9]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [10]National Institute for Health Research Respiratory Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust, and National Heart and Lung Institute, Imperial College, London, UK

Introduction

- In the INBUILD trial in patients with chronic fibrosing ILDs with a progressive phenotype (other than idiopathic pulmonary fibrosis [IPF]), nintedanib slowed the rate of decline in forced vital capacity (FVC) (mL/year) versus placebo, with adverse events that were manageable for most patients.[1]

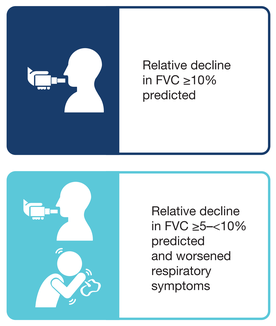
Aim

- To assess the effect of nintedanib versus placebo on the rate of FVC decline in the INBUILD trial in subgroups defined by baseline characteristics.

Methods

Trial design

- Subjects in the INBUILD trial had an ILD other than IPF, diagnosed according to the investigator's usual clinical practice; diffuse fibrosing interstitial lung disease (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT; FVC ≥45% predicted; 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 randomized 1:1 to receive nintedanib 150 mg bid or placebo, stratified by HRCT pattern (usual interstitial pneumonia [UIP]-like fibrotic pattern or other fibrotic patterns) based on central review.

Analyses

- In pre-specified analyses, we assessed the rate of decline in FVC (mL/year) over 52 weeks in subgroups based on the following baseline characteristics:
  - Sex
  - Age (<65, ≥65 years)
  - Race (White, Asian, Black/African-American)
  - FVC (≤70, >70% predicted)
  - ILD diagnosis: hypersensitivity pneumonitis; autoimmune ILDs; idiopathic non-specific interstitial pneumonia (iNSIP); unclassifiable idiopathic interstitial pneumonia (IIP); other ILDs.
- 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.

Results

Baseline characteristics of subgroups by sex, age, race and FVC

	Female (n=307)		Male (n=356)
	64.7 (9.9)	Age (years)	66.7 (9.6)
	28.6 (6.0)	BMI (kg/m²)	28.0 (4.5)
	54%	UIP-like fibrotic pattern on HRCT	69%
	68.5 (14.7)	FVC % predicted	69.4 (16.4)

	Age <65 years (n=260)		Age ≥65 years (n=403)
	47%	Male (%)	58%
	28.6 (5.7)	BMI (kg/m²)	28.0 (5.0)
	48%	UIP-like fibrotic pattern on HRCT	71%
	66.5 (14.5)	FVC % predicted	70.6 (16.1)

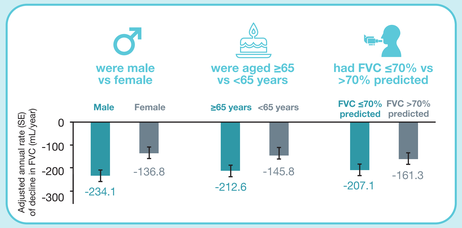
	White (n=488)	Asian (n=164)	Black/African-American (n=10)
Male (%)	55%	53%	20%
Age (years)	65.9 (9.5)	65.6 (10.4)	61.6 (9.4)
BMI (kg/m²)	29.4 (5.1)	24.5 (3.6)	31.1 (7.4)
UIP-like fibrotic pattern on HRCT	58%	74%	50%
FVC % predicted	68.7 (15.7)	69.4 (15.3)	77.5 (17.7)

	FVC ≤70% predicted (n=389)		FVC >70% predicted (n=274)
	53%	Male (%)	55%
	65.0 (9.8)	Age (years)	66.8 (9.7)
	28.5 (5.5)	BMI (kg/m²)	27.9 (5.0)
	58%	UIP-like fibrotic pattern on HRCT	68%

Mean (SD) or % of patients

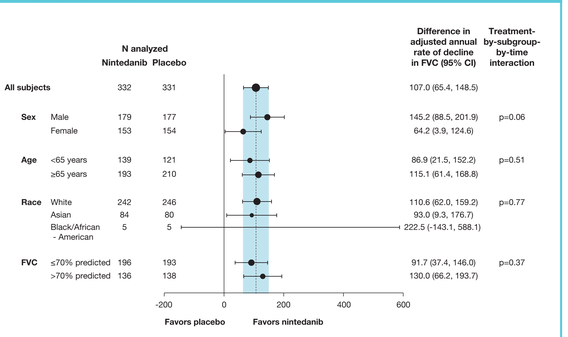
Annual rate of decline in FVC (mL/year) by sex, age, race and FVC at baseline

In the placebo group, the annual rate of decline in FVC was numerically greater in subjects who:



- The effect of nintedanib versus placebo on reducing the annual rate of decline in FVC was consistent across subgroups by sex, age, race, and FVC at baseline (Figure 1).

Figure 1. *Treatment effect of nintedanib versus placebo on annual rate of decline in FVC (mL/year) in subgroups by sex, age, race and FVC at baseline*



Subgroups by ILD diagnosis

Baseline characteristics of subgroups by ILD diagnosis

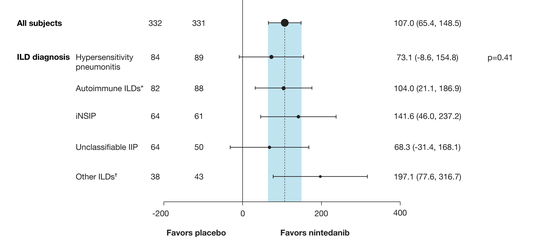
	Hypersensitivity pneumonitis (n=173)	Autoimmune ILDs* (n=170)	iNSIP (n=125)	Unclassifiable IIP (n=114)	Other ILDs† (n=81)
Male (%)	51%	47%	50%	54%	77%
Age (years)	65.5 (8.3)	64.3 (10.6)	65.4 (9.4)	68.4 (9.4)	66.2 (11.2)
BMI (kg/m²)	29.8 (5.4)	27.3 (5.1)	28.8 (5.3)	27.3 (4.8)	27.6 (5.2)
UIP-like fibrotic pattern on HRCT	52%	75%	57%	68%	58%
FVC % predicted	65.2 (14.2)	70.9 (14.9)	71.3 (17.3)	69.8 (15.4)	68.4 (16.6)

Mean (SD) or % of patients. *Included rheumatoid arthritis-associated ILD, systemic sclerosis-associated ILD, mixed connective tissue disease-associated ILD, plus subjects with an autoimmune disease noted in the "Other fibrosing ILDs" category of the case report form. †Included sarcoidosis, exposure-related ILDs and selected terms in the "Other fibrosing ILDs" category of the case report form.

Annual rate of decline in FVC (mL/year) by ILD diagnosis

- The effect of nintedanib versus placebo on reducing the rate of FVC decline was consistent across the subgroups by ILD diagnosis (Figure 2).

Figure 2. *Treatment effect of nintedanib versus placebo on annual rate of decline in FVC (mL/year) in subgroups by ILD diagnosis[2]*



*Included rheumatoid arthritis-associated ILD, systemic sclerosis-associated ILD, mixed connective tissue disease-associated ILD, plus subjects with an autoimmune disease noted in the †Other fibrosing ILDs" category of the case report form. †Included sarcoidosis, exposure-related ILDs and selected terms in the "Other fibrosing ILDs" category of the case report form.

Conclusions

- **In the INBUILD trial, nintedanib had a consistent effect on reducing the annual rate of decline in FVC in patients with progressive fibrosing ILDs, irrespective of demographic characteristics, lung function, or ILD diagnosis at baseline.**

References

1. Flaherty KR et al. N Engl J Med 2019;381:1718–27.
2. Wells AU et al. Lancet Respir Med 2020;8:453–60.

Acknowledgements

The INBUILD trial was funded by Boehringer Ingelheim. Editorial and formatting assistance, supported financially by Boehringer Ingelheim, was provided by Elizabeth Ng and Wendy Morris of FleishmanHillard Fishburn, London, UK during preparation of this poster. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. The authors received no direct compensation related to the development of this poster. Martin Kolb reports grants and personal fees from Boehringer Ingelheim, Gilead, GlaxoSmithKline, ProMetic, and Roche and personal fees from AstraZeneca, Covance, Galapagos NV, Indalo, and Third Pole Therapeutics. Athol Wells reports personal fees from Blade Therapeutics, Boehringer Ingelheim, and InterMune/Roche.

INTERACTIVE

https://www.usscicomms.com/respiratory/ATS2020

https://www.usscicomms.com/respiratory/ATS2020/kolb

Boehringer Ingelheim

Poster developed for the American Thoracic Society International Conference, 2020.