Reduced Decline in Forced Vital Capacity in Patients with Progressive Fibrosing Autoimmune Disease-Related Interstitial Lung Diseases (ILDs) Treated with Nintedanib

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Introduction

- In the INBUILD trial in subjects with chronic fibrosing ILDs with a progressive phenotype (other than idiopathic pulmonary fibrosis [IPF]), nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 57% versus placebo.[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 patients with autoimmune disease-related ILDs, nintedanib reduced the rate of decline in FVC (mL/year) by 58% versus placebo.
- A decline in FVC of >10% predicted has been associated with mortality in patients with autoimmune disease-related ILDs.[3,4]

Aim

- To analyze the effects of nintedanib on categorical changes in FVC in subjects with autoimmune disease-related ILDs in the INBUILD trial.

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

Relative decline in FVC ≥10% predicted

Relative decline in FVC ≥5%–<10% predicted and worsened respiratory symptoms

Relative decline in FVC ≥5%–<10% predicted and increased extent of fibrosis on HRCT

Worsened respiratory symptoms and increased extent of fibrosis on HRCT

- Subjects were randomized to receive nintedanib 150 mg bid or placebo, stratified by HRCT pattern (usual interstitial pneumonia [UIP]-like fibrotic pattern or other fibrotic patterns).

Analyses

- In the subgroup of subjects with autoimmune disease-related ILDs, we analyzed
  - Absolute change from baseline in FVC (mL) at week 52
  - Absolute change from baseline in FVC % predicted at week 52
  - Proportions of subjects with absolute and relative declines in FVC >5% and >10% predicted at week 52.

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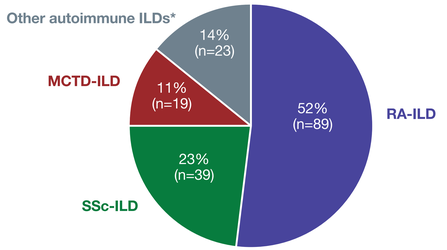
https://www.usscicomms.com/respiratory/ACR2020/Matteson

Results

Subjects

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



*Subjects 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 subjects with autoimmune disease-related ILDs

- 53% female
- Mean (SD) age 64 (11) years
- 50% former or current smokers
- 75% UIP-like fibrotic pattern on HRCT
- Mean (SD) FVC 70.9 (14.9) % predicted
- Mean (SD) DLco 48.0 (15.1) % predicted
- 77% taking DMARDs and/or glucocorticoids†

†Based on WHO standardized drug groupings, including baricitinib and excluding denosumab.

Absolute changes from baseline in FVC at week 52

Figure 1. *Absolute change from baseline in FVC (mL) over 52 weeks*

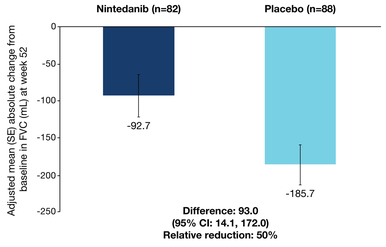
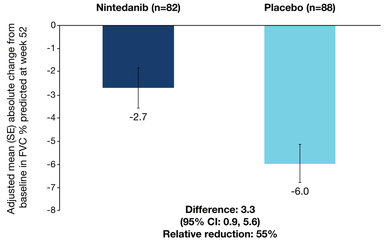


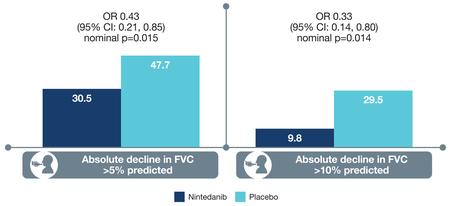
Figure 2. *Absolute change from baseline in FVC % predicted over 52 weeks*



Categorical changes in FVC % predicted at week 52

- The proportions of patients with absolute declines in FVC >5% predicted or >10% predicted at week 52 were lower in the nintedanib group than in the placebo group (Figure 3).

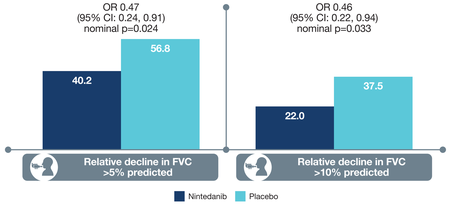
Figure 3. *Proportions of patients with absolute declines in FVC >5% predicted or >10% predicted at week 52*



Values shown are the percentages of subjects with the respective decline. Missing values were imputed using a multiple imputation approach. Based on a logistic regression model including baseline FVC % predicted and fibrotic pattern on HRCT (UIP-like fibrotic pattern or other fibrotic patterns). OR, odds ratio.

- The proportions of patients with relative declines in FVC >5% predicted or >10% predicted at week 52 were lower in the nintedanib group than in the placebo group (Figure 4).

Figure 4. *Proportions of patients with relative declines in FVC >5% predicted or >10% predicted at week 52*



Values shown are the percentages of subjects with the respective decline. Missing values were imputed using a multiple imputation approach. Based on a logistic regression model including baseline FVC % predicted and fibrotic pattern on HRCT (UIP-like fibrotic pattern or other fibrotic patterns). OR, odds ratio.

Conclusions

- **In patients with fibrosing autoimmune disease-related ILDs with a progressive phenotype, the proportions of patients with absolute and relative declines in FVC % predicted of >5% and >10% over 52 weeks were lower in patients who received nintedanib than placebo.**
- **These results support an effect of nintedanib in slowing the progression of ILD in patients with progressive fibrosing autoimmune disease-related ILDs.**

References

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Acknowledgements and Disclosures

The INBUILD trial was funded by Boehringer Ingelheim International GmbH (BI). The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment for the development of this poster. Editorial support and formatting assistance was provided by Elizabeth Ng of FleishmanHillard Fishburn, London, UK, which was contracted and funded by BI. BI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations.

ELM has served as a consultant and/or speaker for BI, Gilead, TympoBio, Arena, Simply Speaking, UpToDate. OD reports grants from Actelion, Bayer, BI, Kymera, Mitsubishi Tanabe and has served as a consultant and/or speaker for Actelion, Bayer, BI, Medscape, Novartis, Roche, Menarini, Mepha, Merck Sharp & Dohme, iQone Healthcare, Pfizer, AbbVie, Acceleron, Amgen, AnaMar, Arxx Therapeutics, Beacon Discovery, Blade Therapeutics, CSL Behring, ChemomAb, Corpus Pharma, Curzion, Ergonex, Galapagos, GlaxoSmithKline (GSK), Glenmark, Inventiva, Italfarmaco, IQVIA, Kymera, Medac, Mitsubishi Tanabe, Sanofi, UCB, Lilly, Target BioScience, Catenion. JHWD reports grants from AnaMar, Active Biotech, Array Biopharma, Arxx Therapeutics, aTyr, Bristol-Myers Squibb (BMS), Bayer, BI, Celgene, Galapagos, GSK, Inventiva, Novartis, Sanofi-Aventis, RedX, UCB; has served as a consultant for Actelion, Active Biotech, AnaMar, Arxx, Bayer, BI, Celgene, Galapagos, GlaxoSmithKline, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB and owns stock in 4D Science. MK reports grants from BI, Ono Pharmaceuticals and has served as a consultant and/or speaker for Bayer, BI, Chugai, Corbus, CSL Behring, MBL, Mochida, Reata, Actelion, Astellas, GSK, Ono, Pfizer. JP reports grants from AbbVie, BMS, Lilly, Gilead, Merck, Roche, Seattle Genetics, UCB and has served as a consultant and/or speaker for AbbVie, Actelion, Amgen, Bayer, BMS, Eicos, Lilly, Emerald Health, Gilead, Janssen, Medexus, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB. JRS has served as a consultant and/or speaker for Atlantic, BI, Blade Therapeutics, Corbus, Camarus, Guidepoint, Xenikos, Indalo and owns stock in BriaCell, Pacific Therapeutics. AJ, RSH, KBR are employees of BI. KRF has served as a consultant for BI, Respivant, Bellerophon, Blade Therapeutics.

Poster developed for the American College of Rheumatology Convergence Conference, 5–9 November 2020.