OP0115

Effect of nintedanib on progression of interstitial lung disease (ILD) in patients with autoimmune disease-related ILDs: further data from the INBUILD® trial

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Introduction

- Nintedanib is an inhibitor of tyrosine kinases that inhibits processes fundamental to the progression of pulmonary fibrosis.[1]
- The INBUILD trial investigated the efficacy and safety of nintedanib in patients with chronic fibrosing ILDs with a progressive phenotype, excluding idiopathic pulmonary fibrosis (IPF).[2]

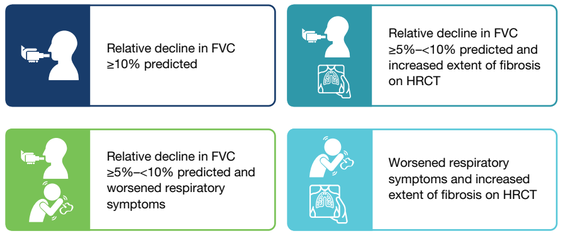
Aim

- To assess the effects of nintedanib on the risks of death, acute exacerbation of ILD or death, and disease progression or death in subjects with autoimmune disease-related ILDs in the INBUILD trial.

Methods

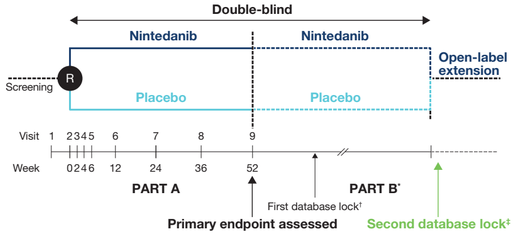
Trial design[2]

- Subjects in the INBUILD trial had a physician-diagnosed ILD other than IPF, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted and 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. The second database lock took place after all the subjects had completed the post-treatment follow-up visit or entered the open-label extension study.

The INBUILD trial



R, Randomisation 1:1, stratified by HRCT pattern (UIP-like fibrotic pattern or other fibrotic patterns).
* Visits occurred every 16 weeks until end of treatment.
† After last subject had completed week 52 visit.
‡ After all patients had completed follow-up visit or entered open-label extension study.

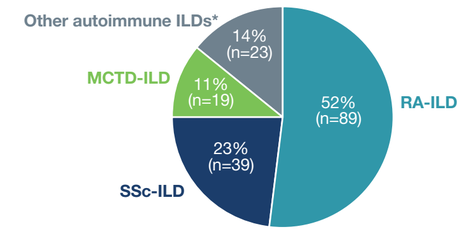
Analyses

- In the subgroup of patients with autoimmune disease-related ILDs, we assessed the following using data up to the second database lock:
  - Time to death
  - Time to first acute exacerbation of ILD or death
  - Time to disease progression (absolute decline in FVC ≥10% predicted) or death
  - Adverse events

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

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

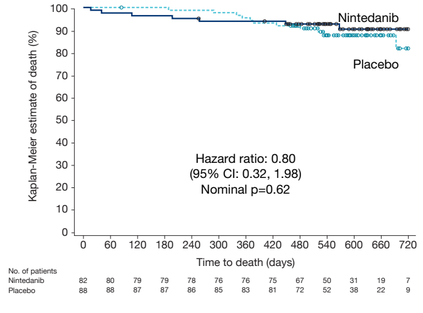
Exposure to trial medication

- Mean (SD) exposure was 15.4 (7.4) months in the nintedanib group and 16.9 (6.1) months in the placebo group.

Time to death

- 8 patients (9.8%) in the nintedanib group and 11 patients (12.5%) in the placebo group died.

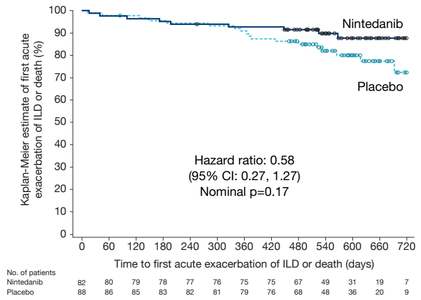
Time to death



Time to first acute exacerbation of ILD or death

- 10 patients (12.2%) in the nintedanib group and 18 patients (20.5%) in the placebo group had an acute exacerbation of ILD or died.

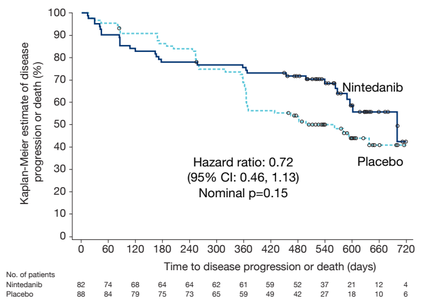
Time to first acute exacerbation of ILD or death



Time to disease progression or death

- 33 patients (40.2%) in the nintedanib group and 47 patients (53.4%) in the placebo group had an absolute decline in FVC ≥10% predicted or died.

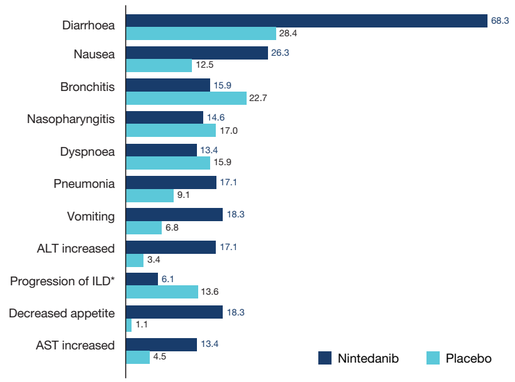
Time to disease progression or death



Disease progression was defined as an absolute decline in FVC ≥10% predicted.

Adverse events

Most frequent adverse events (reported irrespective of causality)

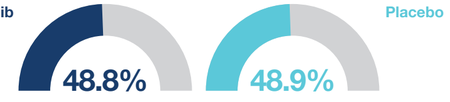


Adverse events (reported irrespective of causality) were coded using preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of subjects with ≥1 such adverse event reported between first trial drug intake and 28 days after the last trial drug intake in >10% of patients in either treatment group. *Corresponded to the MedDRA preferred term "interstitial lung disease". ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Adverse events leading to permanent discontinuation of trial drug

Data are % of subjects with ≥1 such adverse event.

Serious adverse events



Data are % of subjects with ≥1 such adverse event reported between first trial drug intake and 28 days after the last trial drug intake. Serious adverse events were defined as events that resulted in death, were life-threatening, resulted in hospitalisation or prolonged hospitalisation, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed serious for any other reason.

Conclusions

- **Data from the INBUILD trial suggest that nintedanib has a clinically meaningful effect on slowing the progression of ILD in patients with chronic fibrosing autoimmune disease-related ILDs with a progressive phenotype, with adverse events that are manageable for most patients.**

References

1. Wollin L, et al. Eur Respir J 2019;54. doi: 10.1183/13993003.00161-2019.
2. Flaherty KR et al. N Engl J Med 2019;381:1718-1727.

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. The authors received no direct compensation related to the development of this poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations.

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Authors' disclosures:
ELM has received a grant from Pfizer and has served as a consultant/speaker for Boehringer Ingelheim (BI), Gilead, TympoBio, Arena Pharmaceuticals and Simply Speaking. CK has served as a consultant/speaker for BI. JHWD reports grants from BI and has served as a consultant/speaker for BI. AMHV reports grants from BI and has served as a consultant/speaker for BI, Actelion, Bayer, GlaxoSmithKline (GSK) and Roche. JRS owns shares in BriaCell, Pacific and has served as a consultant/speaker for Atlantic, Blade, Eicos, Eiger, Indalo, Mitsubishi Tanabe, Xenikos, Bayer, BI, Camurus, Corbus, EMD Serono. SM reports grants from Pfizer and has served as a consultant for Novartis, Abbvie, Pfizer. OD reports grants from Actelion, Bayer, BI, Kymera Therapeutics, Mitsubishi Tanabe and consultancy relationship and/or research funding from Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Baecon Discovery, Blade Therapeutics, Bayer, BI, Catenion, Competitive Corpus, Drug Development International Ltd, CSL Behring, ChemomAb, Ergonex, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, Italfarmaco, iQone, iQvia, Kymera Therapeutics, Lilly, medac, Medscape, Mitsubishi Tanabe Pharma, Merck Sharp & Dohme (MSD), Novartis, Pfizer, Roche, Sanofi, Target BioScience, UCB; he has a patent mir-29 for the treatment of SSc (US8247389, EP2331143). PFD reports grants from Genentech and has served as a consultant for BI. AJ, RSH, SS and MQ are employees of BI. KRF reports grants from BI and has served as a consultant for BI, Veracyte, Genentech, Bellerophon, Blade.

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Poster developed for the Annual European Congress of Rheumatology, 2020.