Effects of nintedanib in patients with progressive fibrosing interstitial lung diseases (ILDs) taking anti-acid therapy

Michael Kreuter,[1] Craig Glazer,[2] Hideya Kitamura,[3] Dirk Koschel,[4] Teng Moua,[5] Heiko Mueller,[6] Susanne Stowasser,[6] Klaus B Rohr,[6] Kevin K Brown[7] on behalf of the INBUILD trial investigators

[1]Center for Interstitial and Rare Lung Diseases, Pneumology and Respiratory Care Medicine, Thoraxklinik, University of Heidelberg, Member of the German Center for Lung Research, Heidelberg, Germany; [2]Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, USA; [3]Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Kanazawa-ku, Yokohama, Japan; [4]Fachkrankenhaus Coswig, Coswig, Germany; [5]Division of Pulmonary and Critical Care Medicine, Mayo Clinic Rochester, Rochester, MN, USA; [6]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [7]Department of Medicine, National Jewish Health, Denver, CO, USA.

INTRODUCTION

- In the INBUILD trial in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib slowed the rate of decline in FVC (mL/year) over 52 weeks by 57% compared with placebo, with adverse events that were manageable for most patients.[1]
- Previous studies have suggested a possible association between gastroesophageal reflux disease and progression of ILD,[2,3] but it remains unclear whether anti-acid therapy has any impact on the progression of ILD.[4]

AIM

- To evaluate the efficacy and safety of nintedanib in subgroups by use of anti-acid therapy at baseline in the INBUILD trial.

METHODS

Trial design

- Patients in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted, and DLco ≥30%–<80% predicted. Patients with IPF were excluded.
- Patients met ≥1 of the following criteria for ILD progression within the 24 months before screening, despite management deemed appropriate in clinical practice:

- Patients were randomized to receive nintedanib or placebo, stratified by HRCT pattern (usual interstitial pneumonia [UIP]-like fibrotic pattern or other fibrotic patterns).
- The primary endpoint was the rate of decline in FVC (mL/year) over 52 weeks. Patients continued to receive blinded randomized treatment until all subjects had completed the follow-up visit or entered the open-label extension study (INBUILD-ON).

Analyses

- Use of anti-acid therapy at baseline (yes/no) was determined based on whether an anti-acid therapy was reported as a concomitant medication.
- In subgroups by use of anti-acid therapy at baseline, we analyzed *post-hoc* the rate of FVC decline (mL/year) over 52 weeks and the time to absolute decline in FVC ≥10% predicted or death over the whole trial in the overall population and in patients with a UIP-like fibrotic pattern on HRCT.
- Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo between subgroups. No adjustment for multiplicity was made.

CONCLUSIONS

- In the INBUILD trial, the rate of decline in FVC, and the effect of nintedanib on slowing the decline in FVC, were consistent between patients with progressive fibrosing ILDs who were and were not taking anti-acid therapy at baseline.

RESULTS

Patients

380 (57.3%) taking anti-acid therapy

283 (42.7%) not taking anti-acid therapy

Baseline characteristics

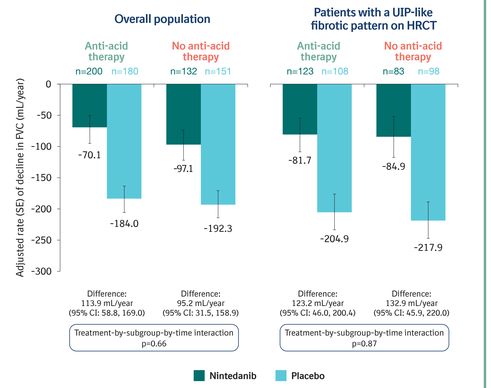
	Overall population: Anti-acid therapy (n=380)	Overall population: No anti-acid therapy (n=283)	Patients with a UIP-like fibrotic pattern on HRCT: Anti-acid therapy (n=231)	Patients with a UIP-like fibrotic pattern on HRCT: No anti-acid therapy (n=181)
Mean age (years)	66.2	65.1	68.2	67.7
Male, %	55.8	50.9	64.1	54.7
Former or current smoker, %	55.8	44.5	63.2	49.7
Mean FVC % predicted	67.4	71.1	68.5	73.2
Mean DLco % predicted	44.5	48.3	44.8	48.9
GERD*, %	40.8	7.8	38.5	10.5

*Gastroesophageal reflux disease, based on preferred term in Medical Dictionary for Regulatory Activities.

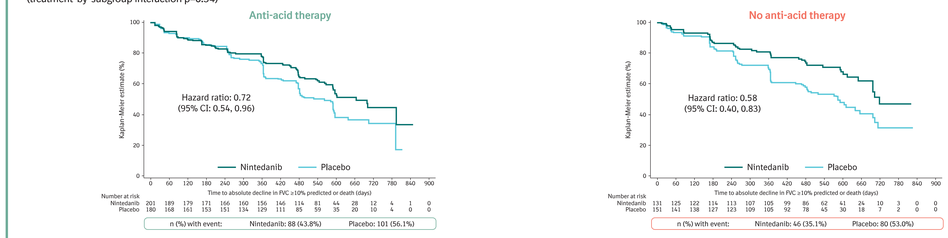
Rate of decline in FVC (mL/year) over 52 weeks

- The rate of FVC decline in the placebo group, and the treatment effect of nintedanib on reducing the rate of FVC decline, were similar between patients taking versus not taking anti-acid therapy at baseline.

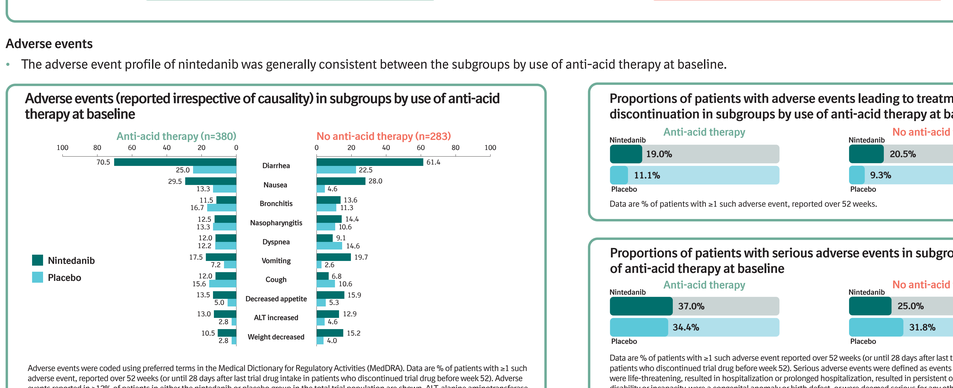
Rate of decline in FVC (mL/year) over 52 weeks in subgroups by use of anti-acid therapy at baseline



Time to absolute decline in FVC ≥10% predicted or death in the overall population in subgroups by use of anti-acid therapy at baseline
(treatment-by-subgroup interaction p=0.34)



Time to absolute decline in FVC ≥10% predicted or death in patients with a UIP-like fibrotic pattern on HRCT in subgroups by use of anti-acid therapy at baseline
(treatment-by-subgroup interaction p=0.15)



Adverse events

- The adverse event profile of nintedanib was generally consistent between the subgroups by use of anti-acid therapy at baseline.

Adverse events (reported irrespective of causality) in subgroups by use of anti-acid therapy at baseline

Adverse events were coded using preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of patients with ≥1 such adverse event, reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Adverse events reported in >12% of patients in either the nintedanib or placebo group in the total trial population are shown. ALT, alanine aminotransferase.

Proportions of patients with adverse events leading to treatment discontinuation in subgroups by use of anti-acid therapy at baseline

Data are % of patients with ≥1 such adverse event, reported over 52 weeks.

Proportions of patients with serious adverse events in subgroups by use of anti-acid therapy at baseline

Data are % of patients with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Serious adverse events were defined as events that resulted in death, were life-threatening, resulted in hospitalization or prolonged hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed serious for any other reason.

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