Characteristics of patients with progressive fibrosing interstitial lung diseases (ILDs) in the INBUILD® trial of nintedanib

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Introduction

A proportion of patients with fibrosing interstitial lung diseases (ILDs) are at risk of developing a progressive phenotype characterized by decline in lung function, worsening respiratory symptoms and early mortality.1 These progressive ILD (pILD) patients are similar to idiopathic pulmonary fibrosis (IPF) in longitudinal disease behavior and pathogenic mechanisms.2,3 Nintedanib slows the rate of disease progression in patients with IPF and is an approved treatment for IPF.4 Pre-clinical data suggest that nintedanib inhibits pathologic processes responsible for the progression of lung fibrosis irrespective of the cause.5,6 This provides a rationale for the investigation of nintedanib as a treatment for progressive fibrosing ILDs other than IPF.7

Aim

The aim of the INBUILD trial (NCT02999776) is to evaluate the efficacy and safety of nintedanib in patients with non-IPF chronic fibrosing ILDs with a progressive phenotype.

Methods

Trial design

Eligible patients had diffuse fibrosing lung disease of ≥10% extent on high-resolution computed tomography (HRCT) (confirmed by central review). Pre-clinical data suggested that nintedanib inhibited pathologic processes responsible for the progression of lung fibrosis irrespective of the cause. This provided a rationale for the investigation of nintedanib as a treatment for progressive fibrosing ILDs other than IPF.7

Endpoints

- The primary endpoint is the annual rate of decline in FVC (mL/year) assessed over 52 weeks. There will be no primary analysis populations: all patients and patients with a UIP-like fibrotic pattern only on HRCT.

- The main secondary endpoints are the change from baseline in King’s Brief Interstitial Lung Disease Questionnaire (K-BILD) total score over 52 weeks, time to first vital capacity (VC) exacerbation predicted, and predicted capacity of the lungs for carbon monoxide (DLco) ≥30–<80% predicted.

- Other secondary endpoints are listed in Table 1.

- Safety will be assessed by the recording of adverse events and clinical and laboratory evaluations.

Primary and secondary efficacy endpoints

- Annual rate of decline in FVC (mL/year) assessed over 52 weeks
- Change from baseline in DLco total score at week 52
- Time to death or death ≤30 days after randomization

Other secondary endpoints

- Time to death due to respiratory cause over 52 weeks
- Time to progression (absolute decline from baseline in FVC ≥10% predicted or death) over 52 weeks
- Proportion of patients with a relative decline from baseline in FVC ≥15% predicted at week 52
- Propensity score estimators from baseline in FVC ≥15% predicted at week 52

Results

- Patients: A total of 663 subjects from 15 countries (Figure 2) were randomized and received ≥1 dose of trial medication.

- Baseline characteristics are shown in Table 2.

- Based on central review of HRCT scans, 411 (62%) patients had a UIP-like fibrotic pattern only and 252 (39%) had other fibrotic patterns.

- The most common ILD diagnoses are shown in Table 3.

- Table 3: ILD diagnoses (N=663)

- Hypersensitivity pneumonitis
- Idiopathic non-protective interstitial pneumonia
- Unclassifiable idiopathic interstitial pneumonia
- Rheumatoid arthritis-associated ILD
- Systemic sclerosis-associated ILD
- Exposure-related ILD
- Mixed connective tissue disease ILD
- Sarcoidosis
- Other fibrosis

Table 4: Criteria for FVC progression in 24 months before screening (N=663)

- Relative decline in FVC ≥10% predicted 330 (49.8)
- Relative decline in FVC ≥5%–<10% predicted and increased extent of fibrotic changes on imaging 182 (27.5)
- Relative decline in FVC ≥5%–<10% predicted and worsened respiratory symptoms and increased extent of fibrotic changes on imaging 89 (13.4)

Conclusions

- The INBUILD trial will provide insights into the natural history of non-IPF chronically fibrosing ILDs with a progressive phenotype and the role of nintedanib in treating patients with these diseases.

- Results will be presented in September 2019.

References

- Posters presented at the American Thoracic Society International Conference, Dallas, TX, USA 17–22 May 2019.

*Visits to occur every 16 weeks until end of treatment.

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