**ARTICLE**


**CLINICAL QUESTION**

Can nintedanib, an intracellular inhibitor of tyrosine kinases, slow progression of lung fibrosis across a broad range of fibrosing lung diseases much like it does in idiopathic pulmonary fibrosis (IPF)?

**SUMMARY**

Many patients with interstitial lung disease (ILD) have a progressive fibrosing phenotype characterized by an increasing extent of fibrosis on high-resolution computed tomography (HRCT), decline in lung function, and worsening of clinical symptoms such as breathlessness. The most well know progressive fibrosing lung disease is IPF. ILD with a progressive phenotype likely has a common pathobiologic mechanism regardless of the cause of the initial ILD and therefore may respond similarly to therapy.

In IPF and systemic sclerosis associated interstitial lung disease, treatment with nintedanib, an intracellular inhibitor of tyrosine kinases, slows progression of pulmonary fibrosis.\(^1,2\) The INBUILD trial was designed to investigate the safety and efficacy of nintedanib in slowing progression in all patients with progressive fibrotic ILD.

INBUILD is a double-blind, placebo-controlled, phase-3 trial conducted in 15 countries. Patients with fibrosing lung disease affecting more than 10% of lung volume on HRCT, who met criteria for progression of ILD in the last 24 months, were randomly assigned to receive nintedanib at 150mg twice daily or placebo. Patients had to have a forced vital capacity (FVC) of at least 45% of the predicted value and a diffusing capacity of the lung for carbon monoxide (DLCO) ranging from 30 to 80% of the predicted value. Patients who were treated with azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids at more than 20mg daily were excluded. The primary end point was the annual rate of decline in FVC as assessed over a 52-week period.

A total of 663 patients were treated. The adjusted rate of decline in FVC was 80.8 ml per year in the nintedanib group and 187.8 ml per year in the placebo group. The annual rate of decline in the FVC was significatinly lower among patients who received nintedanib than among those who received placebo.
Patients who received nintedanib had a slower rate of decline than those who received placebo independent of the fibrotic pattern on HRCT. This study supports the idea that progressive fibrosing ILD likely has a similar mechanism regardless of clinical diagnosis. Thus, suggesting that once fibrosis develops it leads to additional fibrosis regardless of the initial insult or pathway that led to the development of fibrosis initially. Finally, the safety and side-effect profile of nintedanib in patients with progressive fibrosing interstitial lung disease is similar to that observed in patients with IPF and systemic sclerosis associated interstitial lung disease.


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