
Nineteen years ago, Dr. Michael Holroyd-Carling published an artfully written discussion of his review of the INBUILD trial, which at that time was the largest international trial ever conducted in patients with idiopathic pulmonary fibrosis (IPF) (1). Since then, we have gained much additional knowledge about pulmonary fibrosis and the clinical characteristics of patients with idiopathic pulmonary fibrosis. In the INBUILD trial, the international team led by Dr. Grant and colleagues (2) demonstrated that nintedanib, a multitargeted tyrosine kinase inhibitor, significantly reduced the decline in forced vital capacity (FVC) in patients with IPF compared with placebo, thereby confirming the potential for a treatment that could slow the progression of IPF.

In this issue of the Annals of the Rheumatic Diseases, Gérard Cribeau et al. (3) published a study of the INBUILD trial in patients with autoimmune disease-related ILDs. These investigators included patients with autoimmune disease-related ILDs (89 RA-ILD, 39 SSc-ILD, 19 MCTD-ILD, 23 other autoimmune ILDs including Sjogren's disease-related ILD [n=7], interstitial pneumonia with autoimmune features [n=5] and undifferentiated CTD-ILD [n=3]). Over the whole trial in patients with autoimmune disease-related ILDs, incidence rates of adverse events per 100 patient-years were calculated based on events that occurred with onset between the first trial drug intake and the last intake plus 28 days. Analyses were descriptive.

## Methods

### Patients

Patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF) were randomised to receive nintedanib 150 mg bid or placebo. Time to i) death, ii) first acute exacerbation of ILD or death, and iii) disease progression (absolute decline in FVC ≥10% predicted) or death, were the primary outcome analyses in patients with autoimmune disease-related ILDs. Incidence rates of adverse events per 100 patient-years were calculated based on events that occurred with onset between the first trial drug intake and the last intake plus 28 days. Analyses were descriptive.

### Results

Of 663 patients, 170 (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSC-ILD, 19 MCTD-ILD, 23 other autoimmune ILDs including Sjogren's disease-related ILD [n=7], interstitial pneumonia with autoimmune features [n=5] and undifferentiated CTD-ILD [n=3]). Over the whole trial, in the nintedanib and placebo groups, respectively, mean (SD) exposure to drug was 15.4 (7.4) and 16.9 (6.1) months and maximum exposure was 26.0 and 25.2 months; 62 (75.6%) and 68 (77.3%) patients in these groups, respectively, completed the planned observation time. Over the whole trial, in the nintedanib and placebo groups, respectively, 9.8% and 12.5% of patients died, 12.2% and 20.5% of patients had ≥1 acute exacerbation of ILD or died, and 40.2% and 53.4% of patients had disease progression or died (Table). Diazoxide was the most common adverse event, with incidence rates of 139.2 and 26.3 events per 100 patient-years in the nintedanib and placebo groups, respectively. Adverse events led to treatment discontinuation in 20.7% of patients in the nintedanib group and 25.2% of patients in the placebo group.

### Conclusion

Data from the INBUILD trial suggest that nintedanib has a clinically meaningful effect on slowing the progression of ILD in patients with progressive fibrosing autoimmune disease-related ILDs, with adverse events that can be tolerated by most patients.