Addition of Nerandomilast May Slow the Progression of IPF

Glenview, IL – Nerandomilast is a preferential inhibitor of phosphodiesterase 4B that has antifibrotic and immunomodulatory effects. In the phase III FIBRONEER-IPF trial in patients with idiopathic pulmonary fibrosis (IPF), nerandomilast 9 mg twice daily (bid) and 18 mg bid reduced the decline in forced vital capacity (FVC) over 52 weeks versus placebo (the primary end point), with acceptable safety and tolerability. Researchers investigated the effect of nerandomilast in the subgroup of US patients.

In the study, patients with IPF were randomized to receive nerandomilast 9 mg bid, nerandomilast 18 mg bid, or placebo, stratified by use of nintedanib/pirfenidone vs neither. Analyses were descriptive and assessed: changes from baseline in FVC (mL) at week 52; time to first acute exacerbation, hospitalization for respiratory cause, or death, up to the first database lock (which took place after the last patient had completed the week 52 visit); and adverse events over 52 weeks.

Of 1,177 patients who received trial medication, 196 were from the US (70 placebo, 70 nerandomilast 9 mg bid, 56 nerandomilast 18 mg bid). In these patients, at baseline, mean (SD) age was 73.1 (6.9) years; 81.6% were male; FVC was 76.5% (17.5) predicted; DLco was 50.9% (16.2) predicted; 53.6% took nintedanib; 30.1% took pirfenidone. Adjusted mean (SE) changes in FVC (mL) at week 52 were -257.9 (33.6) in the placebo group, -152.7 (32.9) in the nerandomilast 9 mg bid group (difference vs placebo, 105.2 [95% CI: 13.0, 197.4]) and -126.2 (36.9) in the nerandomilast 18 mg group (difference vs placebo, 131.7 [95% CI: 33.8, 229.6]). Mean exposure to trial medication until first database lock was 13.2 months. Up to first database lock, the composite end point of acute exacerbation, hospitalization for respiratory cause, or death was experienced by 30.0% of the placebo group, 21.4% of the nerandomilast 9 mg bid group (HR vs placebo, 0.86 [95% CI: 0.44, 1.69]) and 19.6% of the nerandomilast 18 mg bid group (HR vs placebo, 0.74 [95% CI: 0.36, 1.54]). The most frequent adverse event was diarrhea, reported in 14.3%, 34.3%, and 42.9% of patients in the placebo, nerandomilast 9 mg bid and nerandomilast 18 mg bid groups, respectively, over 52 weeks. Adverse events led to discontinuation of trial medication in 15.7% of the placebo group, 12.9% of the nerandomilast 9 mg bid group, and 10.7% of the nerandomilast 18 mg bid group.

"In US patients in our FIBRONEER-IPF trial, nerandomilast 9 miligrams bid and 18 miligrams bid slowed the decline in forced vital capacity over 52 weeks and had acceptable safety and tolerability," said Toby Maher, MD, CHEST 2025 presenter.

Based on the findings of this research, adding nerandomilast to a treatment regimen for patients receiving standard of care therapy for IPF may slow disease progression.

Further results will be shared at the CHEST Annual Meeting 2025 as part of the Innovations in Assessment and Treatment of Fibrosing Lung Diseases Rapid Fire Original Investigation presentations, titled *Effect of Nerandomilast in US Patients With Idiopathic Pulmonary Fibrosis: Subgroup Analysis of The FIBRONEER-IPF Trial.* The study abstract can be viewed on the journal *CHEST*® website.