Nerandomilast in Patients with Idiopathic Pulmonary Fibrosis

FIRST REPORT MANAGED CARE

Results From the FIBRONEER-IPF Trial

In the FIBRONEER-IPF Phase 3 trial, nerandomilast met the primary endpoint, achieving a smaller decline in FVC than placebo over a period of 52 weeks

Background

- IPF is a chronic, progressive ILD characterized by altered lung function, with a high symptom burden, including progressive dyspnea, that increases as patients near end of life[1,2]
- Only two therapies have been approved for IPF in the past decade—pirfenidone and nintedanib—both of which offer modest clinical benefit but are associated with side effects that may impact treatment persistence and adherence[2,3]
- A critical treatment gap remains, underscoring the need for more effective and better-tolerated options for patients with IPF

Abbreviations

AE = adverse event

BID = twice-daily dosing

DLCO = diffusing capacity (of lung) for carbon monoxide

FEV1 = forced expiratory volume in 1 second

FVC = forced vital capacity

IPF = idiopathic pulmonary fibrosis

ILD = interstitial lung disease

PDE = phosphodiesterase

Nerandomilast: An oral preferential inhibitor of PDE4B

Preclinical
Antifibrotic and immunomodulatory effects; anticipated improved tolerability in humans[4]

Phase 1
Acceptable safety profile among healthy volunteers and patients with IPF, supporting further development[5]

Phase 2
Slowed decline in FVC over 12 weeks vs placebo while maintaining a comparable AE profile to placebo[6]

FIBRONEER-IPF Phase 3 Trial Design[7]

1177 Patients randomized

915 Taking background therapy

262 Not taking background therapy

305 Nerandomilast 18 mg BID + background therapy

87 Nerandomilast 18 mg BID

304 Nerandomilast 9 mg BID + background therapy

88 Nerandomilast 9 mg BID

306 Placebo + background therapy

87 Placebo only

- Primary Endpoint: Absolute change from baseline in FVC at week 52
- Key Secondary Endpoint: First acute exacerbation, hospitalization for a respiratory cause, or death
- Patients who completed the trial were eligible to receive open-label nerandomilast in an extension study

Selected Eligibility Criteria[8]

Inclusion Criteria	Exclusion Criteria
≥40 years old	Prebronchodilator FEV1 / FVC <0.7
Diagnosis of IPF	Clinically significant pulmonary abnormalities
Either 1) on stable background therapy for ≥12 weeks and planning to stay on it after randomization, or 2) not on background therapy for ≥8 weeks prior to Visit 1	Acute IPF exacerbation within 3 months prior to Visit 1 and/or during the screening period
FVC ≥45% of predicted normal	Relevant chronic or acute infections
DLCO ≥25% of predicted normal corrected for hemoglobin	Major surgery within 6 weeks prior to Visit 2 or planned during trial

Characteristics of Patients at Baseline[7]

Characteristic	Nerandomilast 18 mg	Nerandomilast 9 mg	Placebo
Male sex	82.4%	80.9%	85.8%
Age (years)	70.3 ± 7.8	70.5 ± 7.8	69.9 ± 7.5
Time since IPF diagnosis (years)	3.6 ± 2.8	3.5 ± 2.6	3.5 ± 2.7
Current / former smoker	72.2%	69.7%	71.3%
FVC (mL)	2827 ± 758	2837 ± 781	2864 ± 805
FVC, % predicted	78.4 ± 16.8	79.0 ± 16.7	77.3 ± 18.3
DLCO, % predicted	51.5 ± 17.5	51.7 ± 15.5	49.4 ± 15.8
Supplemental oxygen therapy	23.0%	17.3%	22.9%

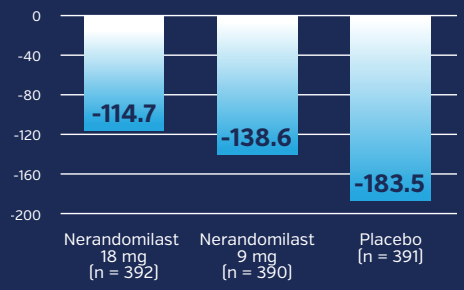
Nerandomilast is an investigational agent and has not been approved for use; its efficacy and safety have not been established.

Efficacy[7]

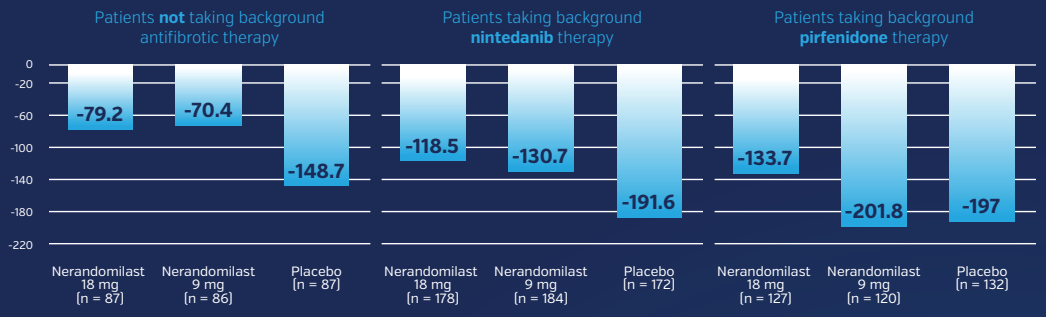
68.8 mL
Adjusted difference in FVC decline for nerandomilast **18 mg** [95% CI, 30.3 to 107.4] *P*<0.001

44.9 mL
Adjusted difference in FVC decline for nerandomilast **9 mg** [95% CI, 6.4 to 83.3] *P*=0.02

Mean Change From Baseline in FVC (mL) for Overall Trial Population

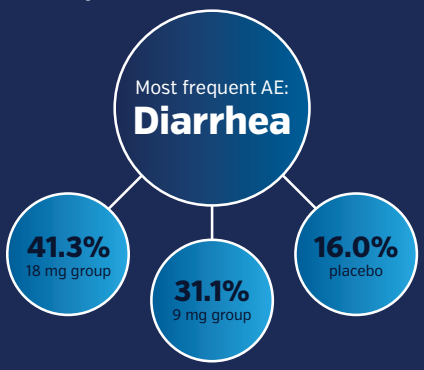


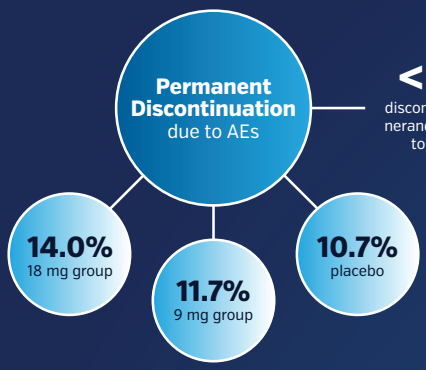
Mean Change From Baseline in FVC (mL) Across Subgroups*



*Trial was not powered to show a difference between subgroups.

Safety[7]





<4%
discontinuation of nerandomilast due to diarrhea

No imbalances between groups for:

Depression

Suicidality

Vasculitis

Liver Injury

Note: Incidence was higher among those taking background nintedanib therapy.

Limitations[7]

- Not powered to evaluate nerandomilast in subgroups
- Acute exacerbations and hospitalizations for a respiratory cause were not adjudicated
- Discontinuations, initiations, and changes in background therapy may have affected efficacy between treatment groups

Conclusions[7]

- Nerandomilast was associated with a significantly smaller decline in FVC than placebo over 52 weeks, which indicates a slowing of disease progression
- Nerandomilast's safety and tolerability profile showed similar rates of permanent treatment discontinuation to placebo and low rates of discontinuation due to diarrhea
- These positive results represent a statistically significant difference in primary endpoint following over a decade of unsuccessful IPF trials

Nerandomilast is an investigational agent and has not been approved for use; its efficacy and safety have not been established.

References

1. Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. Marked deterioration in the quality of life of patients with idiopathic pulmonary fibrosis during the last two years of life. *BMC Pulm Med*. 2018; 18[1]:172.
2. Zhao R, Xie B, Wang X, et al. The tolerability and efficacy of antifibrotic therapy in patients with idiopathic pulmonary fibrosis: results from a real-world study. *Pulm Pharmacol Ther*. 2024;84:102287.
3. Kou M, Jiao Y, Li Z, et al. Real-world safety and effectiveness of pirfenidone and nintedanib in the treatment of idiopathic pulmonary fibrosis: a systematic review and meta-analysis. *Eur J Clin Pharmacol*. 2024; 80[10]:1445-1460.
4. Herrmann FE, Hesslinger C, Wollin L, Nickolaus P. BI 1015550 is a PDE4B inhibitor and a clinical drug candidate for the oral treatment of idiopathic pulmonary fibrosis. *Front Pharmacol*. 2022;13:838449.
5. Maher TM, Schlecker C, Luedtke D, Bossert S, Zoz DF, Schultz A. Phase I studies of BI 1015550, a preferential phosphodiesterase 4B inhibitor, in healthy males and patients with idiopathic pulmonary fibrosis. *ERJ Open Res*. 2022;8[4]:00240-2022.
6. Richeldi L, Azuma A, Cottin V, et al. Trial of a preferential phosphodiesterase 4B inhibitor for idiopathic pulmonary fibrosis. *N Engl J Med*. 2022;386[23]:2178-2187.
7. Richeldi L, Azuma A, Cottin V, et al. Nerandomilast in patients with idiopathic pulmonary fibrosis. *N Engl J Med*. 2025;392[22]:2193-2202.
8. ClinicalTrials.gov. A Study to Find Out Whether BI 1015550 Improves Lung Function in People With Idiopathic Pulmonary Fibrosis (IPF) (FIBRONEER-IPF) (NCT05321069). U.S. National Library of Medicine. Updated 2025. Accessed June 13, 2025. https://clinicaltrials.gov/study/NCT05321069