Initiation of supplemental oxygen in the FIBRONEER-IPF trial of nerandomilast in patients with idiopathic pulmonary fibrosis.

Marlies S Wijsenbeek,[1] Arata Azuma,[2] Vincent Cottin,[3] Michael Kreuter,[4] Toby M Maher,[5] Fernando J Martinez,[6] Justin M Oldham,[7] Claudia Valenzuela,[8] Yi Liu,[9] Susanne Stowasser,[10] Donald F Zoz,[11] Luca Richeldi.[12]

1. Center of Expertise for Interstitial Lung Diseases, Department of Respiratory Medicine, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands; 2. Clinical Research Center, Mihara General Hospital, Saitama, Japan; 3. National Reference Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Hospices Civils de Lyon, Claude Bernard University Lyon 1, UMR 754, ERN-LUNG, Lyon, France; 4. Center for Pulmonary Medicine, Department of Pneumology, Mainz University Medical Center and Pulmonary, Critical Care & Sleep Medicine, Marienhaus Clinic Mainz, Mainz, Germany; 5. Department of Pulmonary, Critical Care and Sleep Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA; 6. University of Massachusetts (UMass) Chan Medical School/UMass Memorial Health System, Worcester, Massachusetts, USA; 7. Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, Michigan, USA; 8. Pulmonology Department, Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain; 9. Department of Biostatistics and Data Sciences, Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Connecticut, USA; 10. Therapy Area Inflammation Medicine, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 11. Global Clinical Development and Medical Affairs, Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Connecticut, USA; 12. Unità Operativa Complessa di Pneumologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy.

Objectives

To evaluate the effect of nerandomilast on supplemental oxygen use in patients with IPF in the FIBRONEER-IPF trial.

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Introduction

- Nerandomilast is a preferential inhibitor of phosphodiesterase 4B that has antifibrotic and immunomodulatory properties.[1,2]
- In the placebo-controlled FIBRONEER-IPF trial, both nerandomilast 9 mg bid and 18 mg bid reduced the decline in FVC at week 52 (primary endpoint) in patients with IPF.[3]
- The initiation of supplemental oxygen places physical limitations on patients and can have a psychological impact.[4]

Methods

- Eligible patients were aged ≥40 years, had IPF with a UIP or probable UIP pattern on HRCT, FVC ≥45% predicted and DLco ≥25% predicted. Patients had taken stable nintedanib or pirfenidone for ≥12 weeks or had not taken nintedanib or pirfenidone for ≥8 weeks.
- Patients were randomised 1:1:1 to receive nerandomilast 9 mg bid, nerandomilast 18 mg bid, or placebo, stratified by use of background therapy (nintedanib/pirfenidone vs neither). Patients continued to take randomised blinded treatment until the end of the trial. The final database lock took place after all patients had completed an end-of-treatment visit.
- The L-PF questionnaire[5] was completed at baseline, weeks 12, 26, 36, 44 and 52, and every 12 weeks thereafter.
- The 5 oxygen questions in the L-PF questionnaire assess whether and when a patient uses supplemental oxygen and the flow rate used in different situations.
- Time to initiation of supplemental oxygen and time to increase in oxygen use (initiation or increase in flow rate) were assessed using a Cox proportional hazards model based on the final database lock.

Results

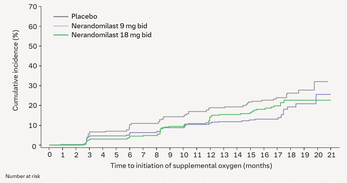
Supplemental oxygen use at baseline

248 (21.1%) patients were using supplemental oxygen at baseline

Type of oxygen use			
121 (10.3%) only when performing physical activity	38 (3.2%) only when sleeping	44 (3.7%) when sleeping and performing physical activity	44 (3.7%) all the time

N=1177. Overall, 17 patients (1.4%) had missing data on oxygen use.

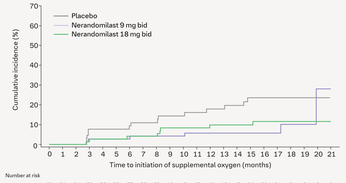
Time to initiation of supplemental oxygen



	Initiated oxygen, n (%)	HR (95% CI) vs placebo
Placebo (n=297)	67 (22.6)	
Nerandomilast 9 mg bid (n=315)	47 (14.9)	0.67 (0.46, 0.98)
Nerandomilast 18 mg bid (n=300)	56 (18.7)	0.92 (0.64, 1.32)

Mean exposure to trial medication was 14.8 months.

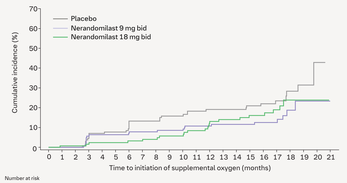
Time to initiation of supplemental oxygen in patients not taking background therapy



	Initiated oxygen, n (%)	HR (95% CI) vs placebo
Placebo (n=68)	14 (20.6)	
Nerandomilast 9 mg bid (n=75)	6 (8.0)	0.39 (0.15, 1.05)
Nerandomilast 18 mg bid (n=73)	8 (11.0)	0.53 (0.22, 1.29)

Mean exposure to trial medication was 14.8 months.

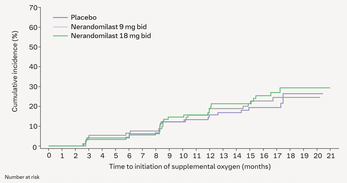
Time to initiation of supplemental oxygen in patients taking background nintedanib



	Initiated oxygen, n (%)	HR (95% CI) vs placebo
Placebo (n=133)	32 (24.1)	
Nerandomilast 9 mg bid (n=147)	21 (14.3)	0.61 (0.35, 1.06)
Nerandomilast 18 mg bid (n=128)	22 (17.2)	0.75 (0.43, 1.28)

Mean exposure to trial medication was 14.8 months.

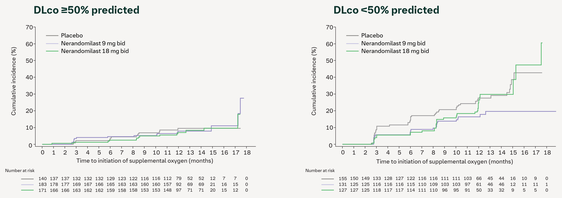
Time to initiation of supplemental oxygen in patients taking background pirfenidone



	Initiated oxygen, n (%)	HR (95% CI) vs placebo
Placebo (n=96)	21 (21.9)	
Nerandomilast 9 mg bid (n=93)	20 (21.5)	0.96 (0.52, 1.77)
Nerandomilast 18 mg bid (n=99)	26 (26.3)	1.49 (0.84, 2.67)

Mean exposure to trial medication was 14.8 months.

Time to initiation of supplemental oxygen by baseline DLco % predicted



Nerandomilast 9 mg bid vs placebo: HR 0.97 (95% CI: 0.46, 2.05)

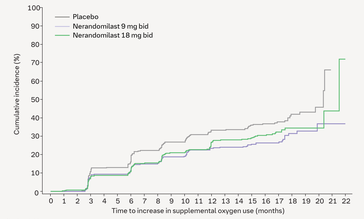
Nerandomilast 18 mg bid vs placebo: HR 0.92 (95% CI: 0.42, 1.99)

Nerandomilast 9 mg bid vs placebo: HR 0.52 (95% CI: 0.31, 0.87)

Nerandomilast 18 mg bid vs placebo: HR 0.93 (95% CI: 0.60, 1.46)

Mean exposure to trial medication was 13.3 months. DLco was corrected for haemoglobin.

Time to increase in supplemental oxygen use (initiation or increase in flow rate)



	Initiated/ increased oxygen, n (%)	HR (95% CI) vs placebo
Placebo (n=393)	141 (35.9)	
Nerandomilast 9 mg bid (n=392)	102 (26.0)	0.73 (0.56, 0.94)
Nerandomilast 18 mg bid (n=392)	118 (30.1)	0.84 (0.65, 1.07)

Mean exposure to trial medication was 14.8 months.

Conclusions

In the FIBRONEER-IPF trial in patients with IPF:

- 21% of patients used supplemental oxygen at baseline
- Patients with DLco <50% predicted at baseline had a greater risk of initiating oxygen than patients with higher DLco
- There was a numerical reduction in the risk of initiation of supplemental oxygen in patients who received nerandomilast as monotherapy or as add-on to nintedanib
- There was a numerical reduction in the risk of initiation/increase in supplemental oxygen use in patients who received nerandomilast versus placebo.

Abbreviations
bid, twice daily. CI, confidence interval. DLco, diffusing capacity of the lungs for carbon monoxide. FVC, forced vital capacity. HR, hazard ratio. HRCT, high-resolution computed tomography. IPF, idiopathic pulmonary fibrosis. L-PF, Living with Pulmonary Fibrosis. UIP, usual interstitial pneumonia.

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