ILD Collaborative

Project ECHO

New and Emerging Treatments for Pulmonary Fibrosis

Barry Shea, MD

MGH Interstitial Lung Disease Program

January 21, 2026

Disclosures

- Consulting (Radius Health, Contineum Therapeutics, United Therapeutics)
- Clinical trial site principal investigator (Boehringer Ingelheim, Bristol Myers Squibb, Mediar Therapeutics)

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FDA News Release

FDA approves Esbriet to treat idiopathic pulmonary fibrosis

For Immediate Release October 15, 2014

A to Z Index

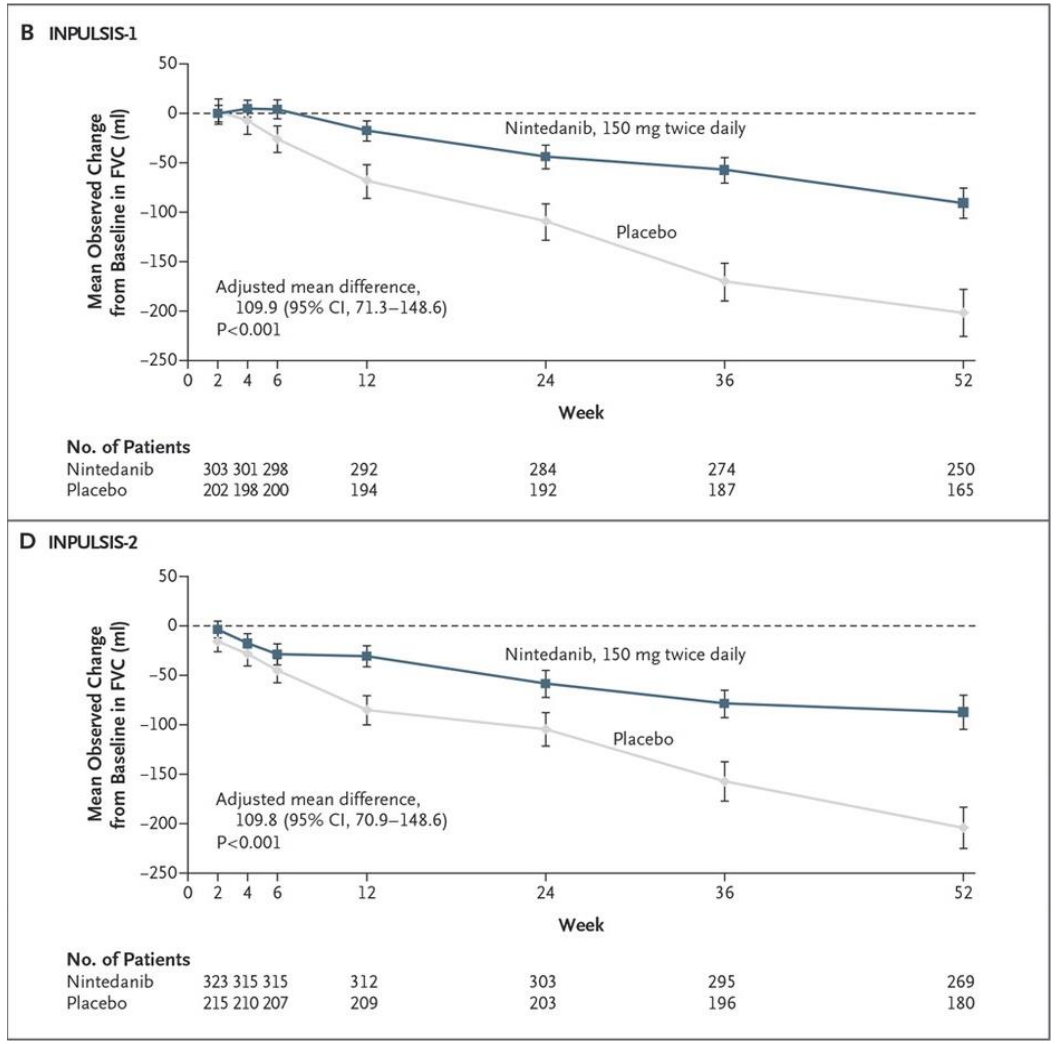
accines, Blood & Biologics | Animal & Veterinary

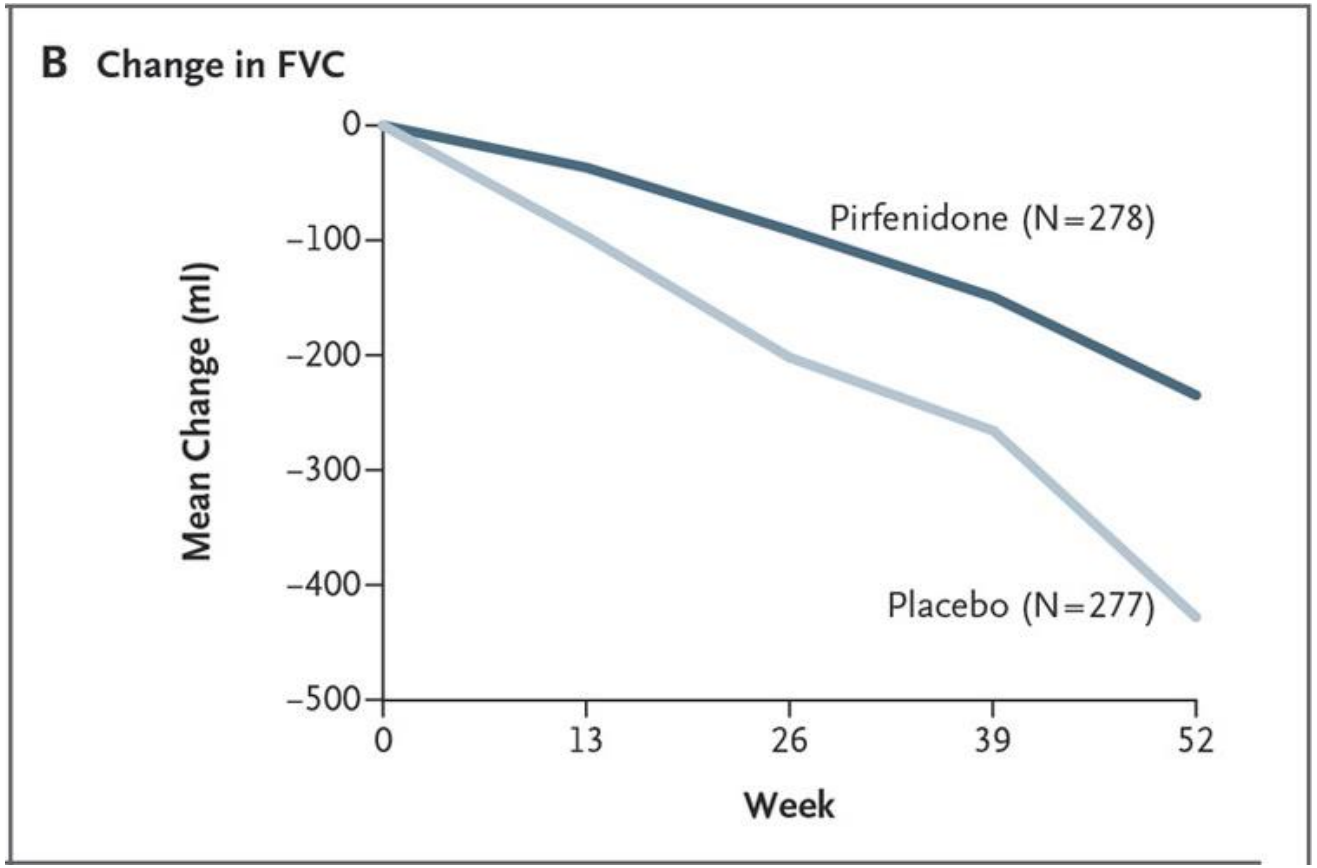
FDA News Release

FDA approves Ofev to treat idiopathic pulmonary fibrosis

For Immediate Release October 15, 2014

Existing "Legacy" Antifibrotic Therapy: INPULSIS and ASCEND Trials

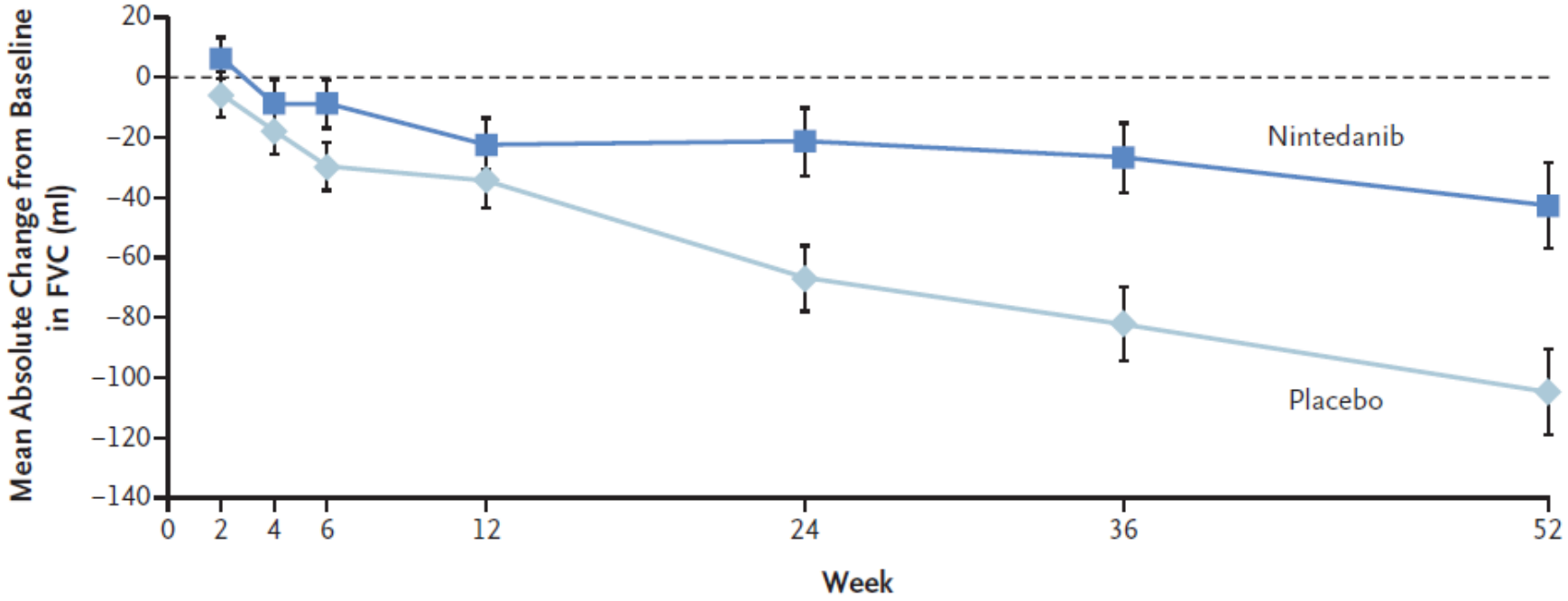




Richeldi L et al. N Engl J Med 2014;370:2071-2082
King TE et al. N Engl J Med 2014;370:2083-2092

SENSCIS Trial: Antifibrotics for SSc-ILD

RCT of Nintedanib vs. placebo for SSc-ILD (n = 576)

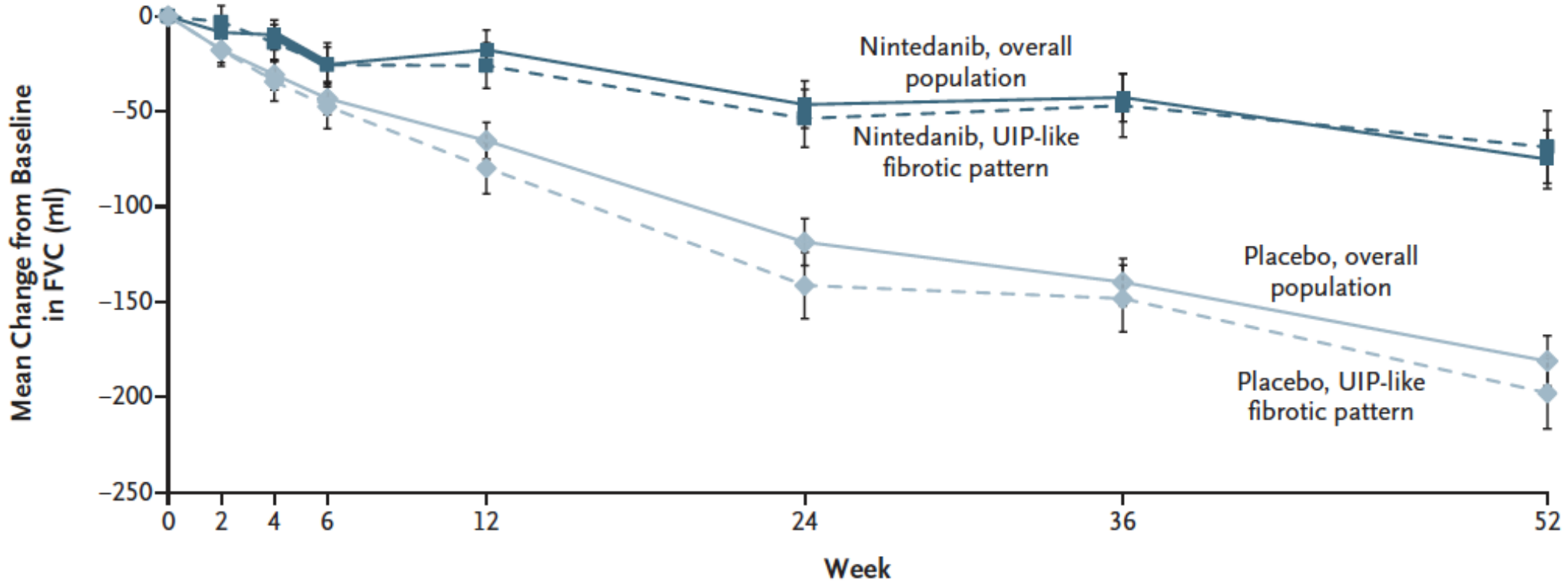


No. of Patients							
Nintedanib	288	283	281	273	278	265	262	241
Placebo	288	283	281	280	283	280	268	257

Distler O et al. *NEJM*. 2019

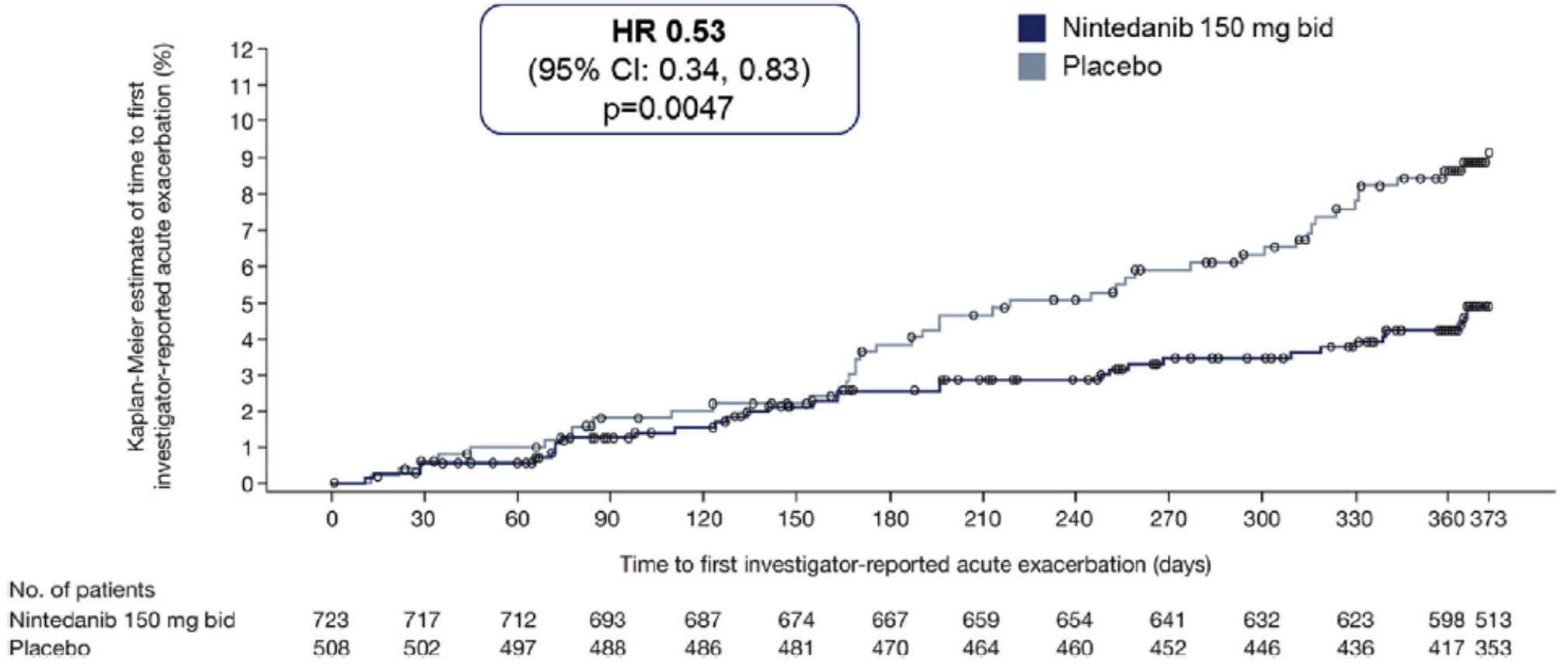
INBUILD Trial: Antifibrotics for progressive fibrosing ILDs

RCT of Nintedanib vs. placebo for **progressive fibrosing** ILD (n = 663)



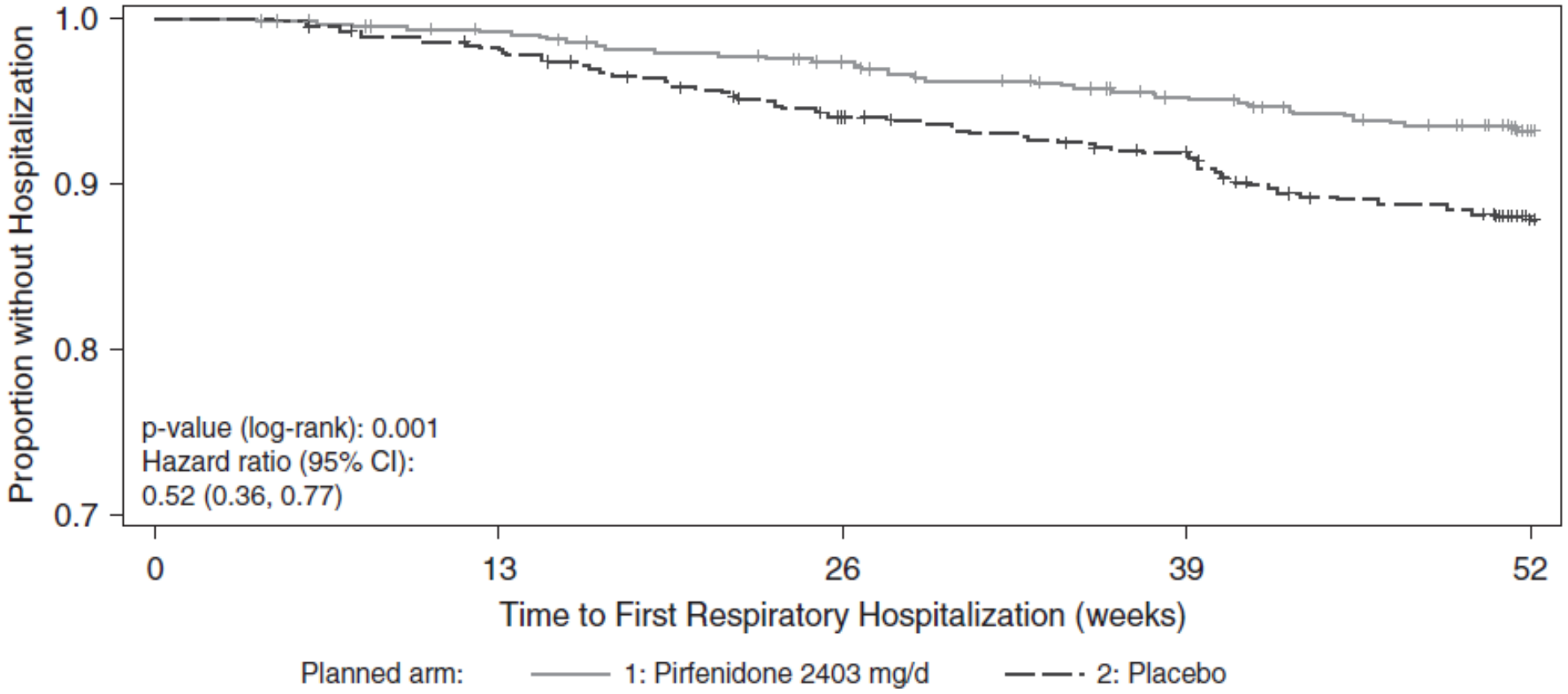
Flaherty KR et al. *NEJM*. 2019

Effects of Nintedanib on Acute Exacerbations in IPF



Richeldi L et al. *Respir Med*. 2016;113:74-79.

Effects of Pirfenidone on Respiratory Hospitalizations in IPF



Ley B et al. *Am J Respir Crit Care Med*. 2017;196:756-761.

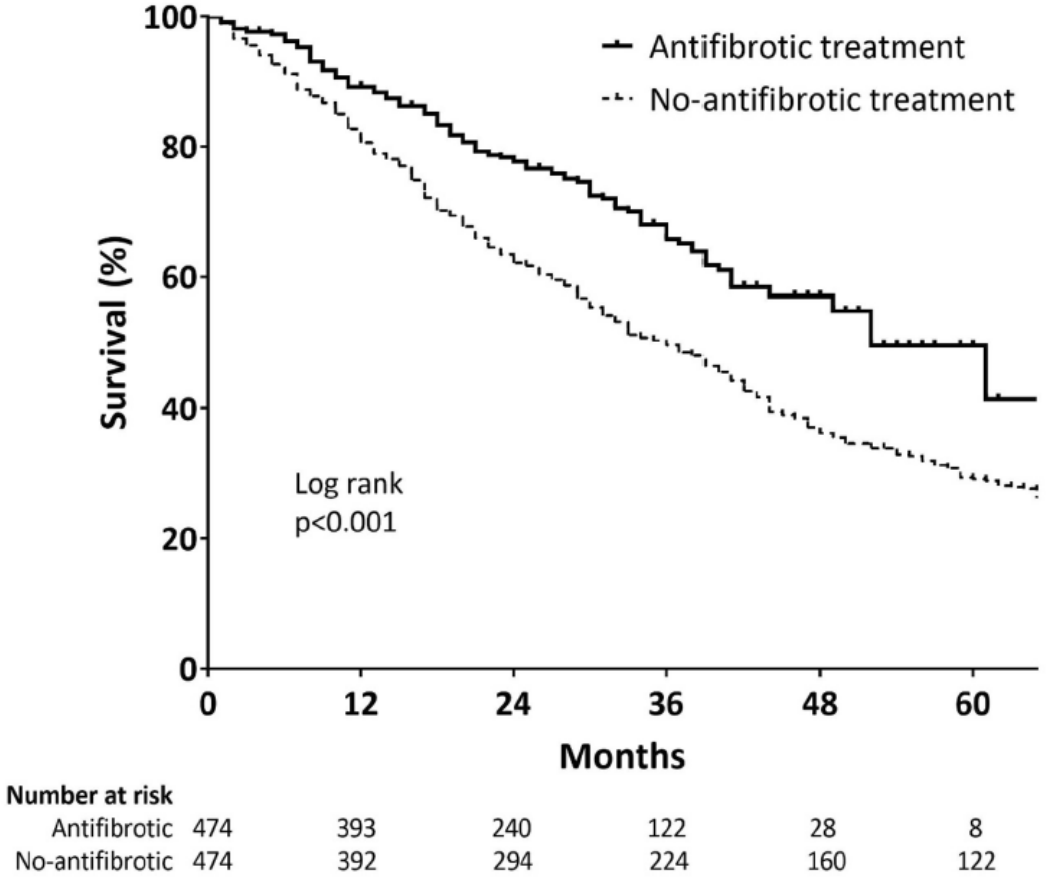
Effects of Antifibrotic Therapy on Mortality

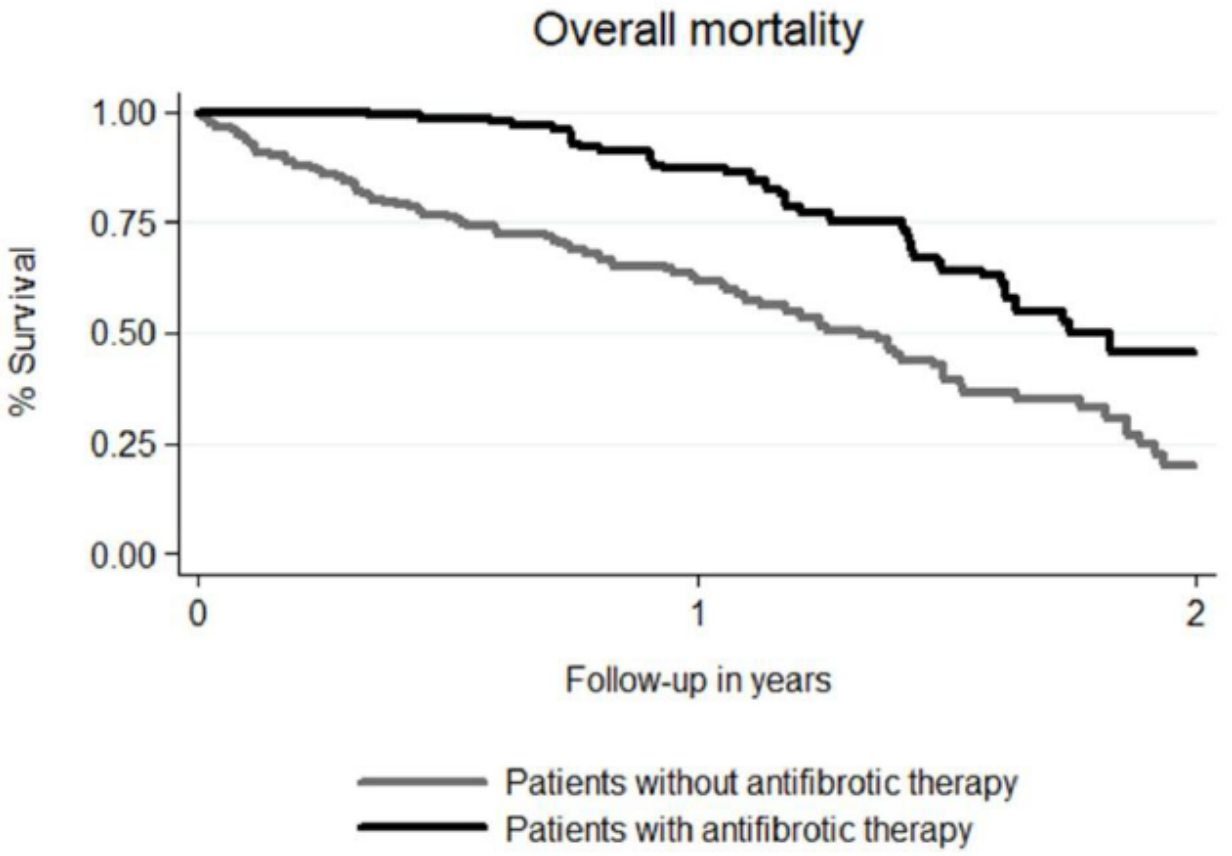
Nintedanib vs Placebo *Pooled data* from 3 trials (N=1231); 52 weeks*			
Mortality Outcome	Hazard Ratio (95% CI)	Deaths, %	
		Nintedanib	Placebo
On-treatment	0.57 (0.34–0.97) *P*=0.0274	3.5	6.7
All-cause	0.70 (0.46–1.08) *P*=0.0954	5.8	8.3
Respiratory-related	0.62 (0.37–1.06) *P*=0.0779	3.6	5.7

Pirfenidone vs Placebo *Pooled data* from 3 trials (N=1247); 52 weeks†*			
Mortality Outcome	Hazard Ratio (95% CI)	Deaths, %	
		Pirfenidone	Placebo
Treatment-emergent all-cause	0.45 (0.24–0.83) *P*=0.0094	2.2	5.1
All-cause	0.52 (0.31–0.87) *P*=0.0107	3.5	6.7
IPF-related	0.35 (0.17–0.72) *P*=0.0029	1.6	4.5

Richeldi L et al. *Respir Med*. 2016;113:74-79
Nathan SD et al. *Lancet Respir Med.* 2017;5:33-41.

Do antifibrotics improve survival in IPF in the real world?





Kang J et al. *Scientific Reports.* 2020.
Behr J et al. E*ur Respir J*. 2020;1902279

Antifibrotic Therapy – the Good and the Bad

Efficacy

Nintedanib	Pirfenidone
~ 50% reduction in FVC decline at 1 year	~ 50% reduction in FVC decline at 1 year
Fewer acute exacerbations?	Fewer respiratory hospitalizations?
Prolongs survival?	Prolongs survival?

Safety/tolerability

Nintedanib	Pirfenidone
Diarrhea (>60%), nausea (24%), vomiting (12%), anorexia (11%), weight loss (10%)	Nausea (35%), vomiting (13%), dyspepsia (18%), anorexia (16%), weight loss (13%)
Thrombosis? MI in 1.6% vs. 0.5%	Photosensitivity rash (28%)
Bleeding?	
GI perforation?	
Transaminitis	Transaminitis

A new era in antifibrotic therapy?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nerandomilast in Patients with Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D.,[1] Arata Azuma, M.D.,[2,3] Vincent Cottin, M.D.,[4] Michael Kreuter, M.D.,[5,6] Toby M. Maher, M.D.,[7,8] Fernando J. Martinez, M.D.,[9] Justin M. Oldham, M.D.,[10] Claudia Valenzuela, M.D.,[11] Emmanuelle Clerisme-Beaty, M.D.,[12] Maud Gordat, M.Sc.,[13] Daniel Wachtlin, M.Sc.,[14] Yi Liu, Ph.D.,[15] Christina Schlecker, M.D.,[16] Susanne Stowasser, M.D.,[12] Donald F. Zoz, M.D.,[17] and Marlies S. Wijsenbeek, M.D.,[18] for the FIBRONEER-IPF Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nerandomilast in Patients with Progressive Pulmonary Fibrosis

Toby M. Maher, M.D.,[1,2] Shervin Assassi, M.D.,[3] Arata Azuma, M.D.,[4,5] Vincent Cottin, M.D.,[6] Anna-Maria Hoffmann-Vold, M.D.,[7,8] Michael Kreuter, M.D.,[9,10] Justin M. Oldham, M.D.,[11] Luca Richeldi, M.D.,[12] Claudia Valenzuela, M.D.,[13] Marlies S. Wijsenbeek, M.D.,[14] Emmanuelle Clerisme-Beaty, M.D.,[15] Carl Coeck, M.D.,[16] Hui Gu, Ph.D.,[17] Ivana Ritter, M.D.,[15] Arno Schlosser, M.Sc.,[18] Susanne Stowasser, M.D.,[15] Florian Voss, Ph.D.,[19] Gerrit Weimann, M.D.,[15] Donald F. Zoz, M.D.,[20] and Fernando J. Martinez, M.D.,[21] for the FIBRONEER-ILD Trial Investigators*

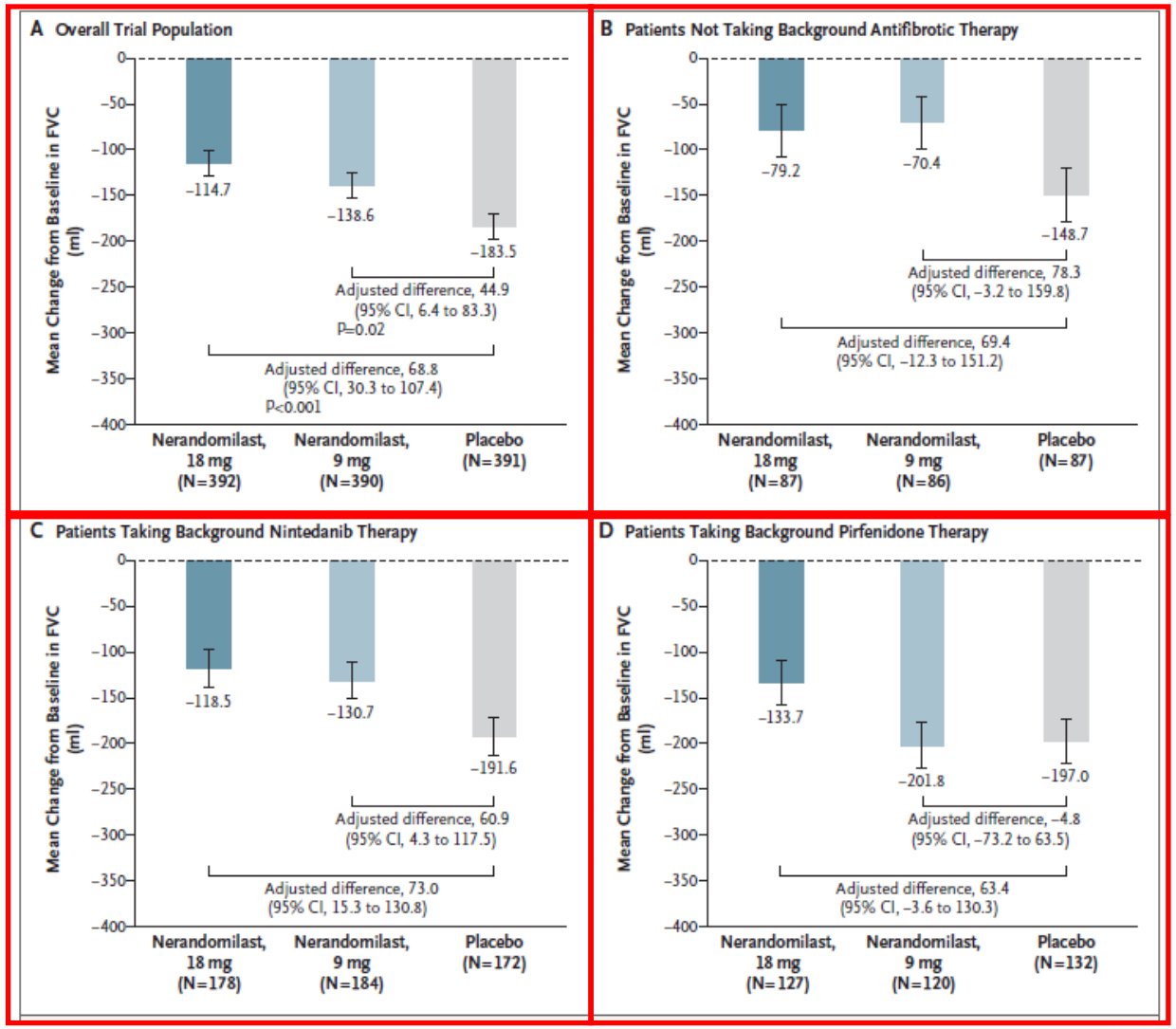
Nerandomilast: PDE4B inhibitor → increases intracellular cAMP

- *In vitro:* inhibits fibroblast proliferation, myofibroblast activity, and lung microvascular permeability
- PDE4 inhibition attenuates experimental lung fibrosis in mice

Richeldi L et al. *N Engl J Med.* 2025;392:2193-2202.
Maher T et al. N Engl J Med. 2025:392:2203-2214.

Reininger D et al. *AJRCMB*. 2025;73:700-712
Sisson TH et al. Phys Rep. 2018;6:e13753

FIBRONEER-IPF: Nerandomilast slows FVC decline in IPF



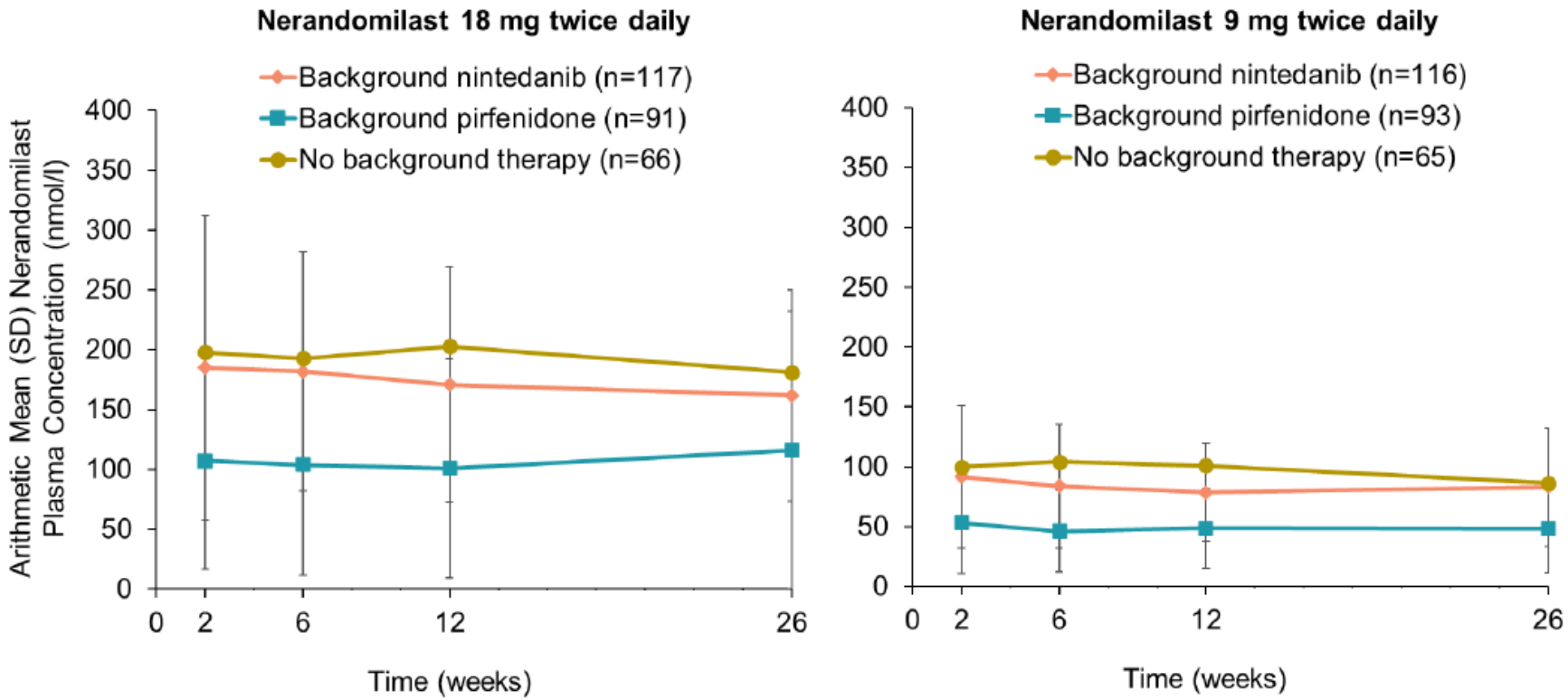
Nerandomilast 18 mg vs. 9 mg. vs placebo PO BID (n = 1177)

- 9 mg and 18 mg both reduced FVC decline at 52 weeks
  - 9 mg vs. placebo 45 ml (p = 0.02)
  - 18 mg vs. placebo 69 ml (p < 0.001)
- No background Rx (22%) or background nintedanib (45%)
  - 9 mg ≈ 18 mg
- Background pirfenidone (32%)
  - Only 18 mg dose was effective!

Richeldi L et al. *N Engl J Med.* 2025;392:2193-2202.

Pirfenidone lowers nerandomilast plasma levels ~50%

Figure S12. Plasma concentration–time profiles of nerandomilast after oral administration of nerandomilast 18 mg twice daily or 9 mg twice daily in patients taking nintedanib, pirfenidone, or no background therapy.



Richeldi L et al. *N Engl J Med.* 2025;392:2193-2202.

FIBRONEER-IPF: Secondary endpoints

Table 2. Time-to-Event End Points up to First Database Lock.*

End Point	Nerandomilast, 18 mg (N=392)	Nerandomilast, 9 mg (N=392)	Placebo (N=393)	Hazard Ratio (95% CI)	
				Nerandomilast, 18 mg, vs. Placebo	Nerandomilast, 9 mg, vs. Placebo
	number with event (percent)				
Key secondary end point					
First acute exacerbation, hospitalization for a respiratory cause, or death	85 (21.7)	79 (20.2)	80 (20.4)	1.17 (0.86–1.59)†	1.03 (0.75–1.41)‡
Other secondary end points					
Acute exacerbation or death	50 (12.8)	51 (13.0)	49 (12.5)	1.11 (0.75–1.65)	1.12 (0.76–1.67)
Hospitalization for a respiratory cause or death	75 (19.1)	68 (17.3)	73 (18.6)	1.13 (0.82–1.56)	0.98 (0.70–1.36)
Death	21 (5.4)	26 (6.6)	28 (7.1)	0.81 (0.46–1.43)	1.03 (0.60–1.76)
Absolute decline in percentage of predicted value of FVC of >10 percentage points from baseline or death	94 (24.0)	107 (27.3)	111 (28.2)	0.84 (0.64–1.10)	0.96 (0.74–1.25)
Absolute decline in percentage of predicted value of DLco of >15 percentage points from baseline or death	59 (15.1)	59 (15.1)	66 (16.8)	0.88 (0.62–1.26)	0.98 (0.69–1.41)

- No significant differences in secondary endpoints

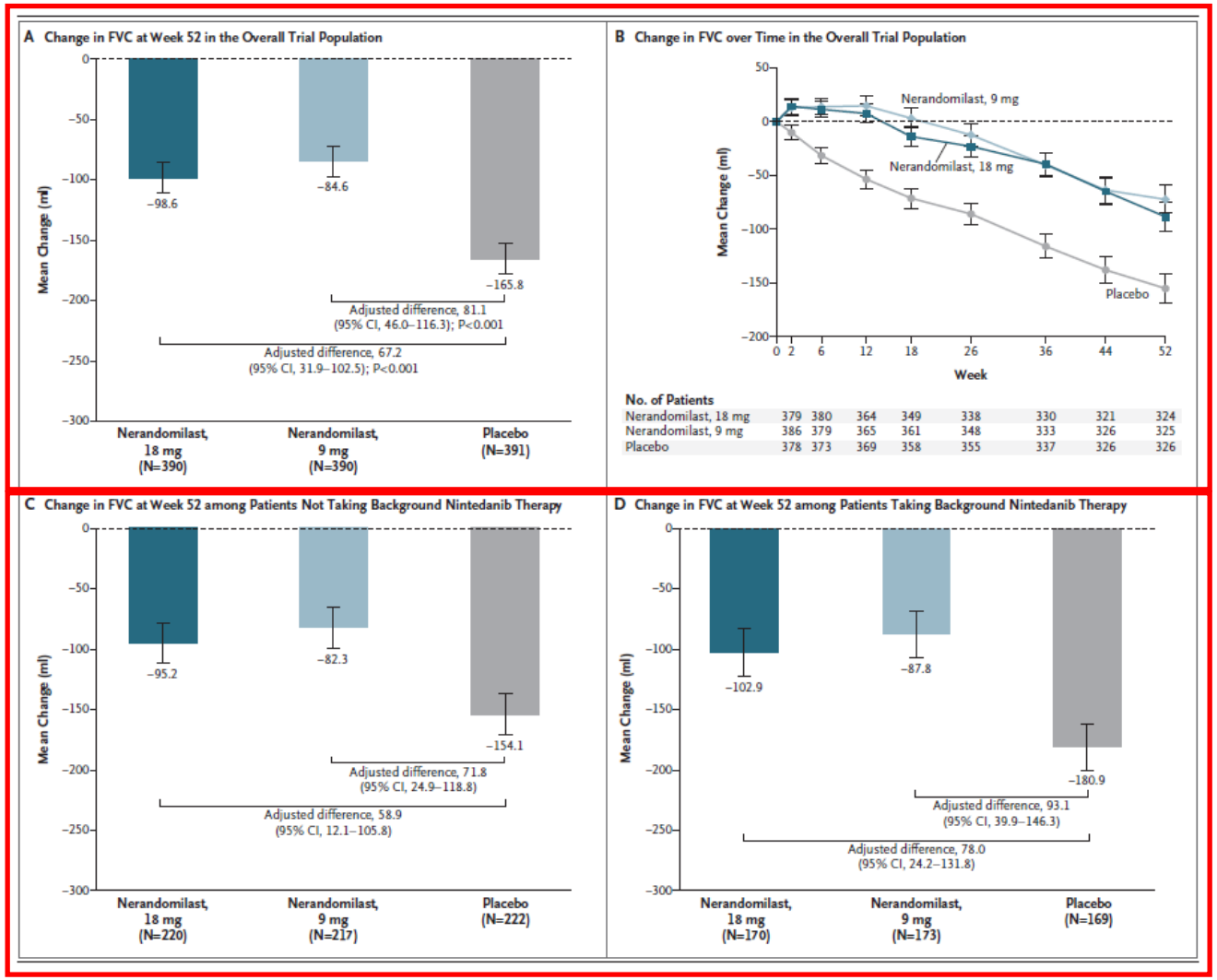
FIBRONEER-IPF: Adverse Events

Table 3. Adverse Events over a Period of 52 Weeks.*

Event Category	All Patients			No Background Antifibrotic Therapy			Background Nintedanib Therapy			Background Pirfenidone Therapy		
	Nerandomilast		Placebo (N=393)	Nerandomilast		Placebo (N=87)	Nerandomilast		Placebo (N=173)	Nerandomilast		Placebo (N=133)
	18 mg (N=392)	9 mg (N=392)		18 mg (N=87)	9 mg (N=88)		18 mg (N=178)	9 mg (N=184)		18 mg (N=127)	9 mg (N=120)	
	number of patients (percent)											
Any event	372 (95)	364 (93)	371 (94)	79 (91)	77 (88)	83 (95)	174 (98)	175 (95)	163 (94)	119 (94)	112 (93)	125 (94)
Most frequent events†												
Diarrhea	162 (41)	122 (31)	63 (16)	23 (26)	15 (17)	7 (8)	110 (62)	91 (49)	46 (27)	29 (23)	16 (13)	10 (8)
Cough	55 (14)	65 (17)	65 (17)	9 (10)	12 (14)	4 (5)	21 (12)	28 (15)	31 (18)	25 (20)	25 (21)	30 (23)
Covid-19	51 (13)	59 (15)	45 (11)	14 (16)	8 (9)	5 (6)	17 (10)	30 (16)	21 (12)	20 (16)	21 (18)	19 (14)
URT infection	49 (12)	39 (10)	40 (10)	13 (15)	10 (11)	8 (9)	24 (13)	17 (9)	14 (8)	12 (9)	12 (10)	18 (14)
Dyspnea	35 (9)	39 (10)	50 (13)	6 (7)	2 (2)	12 (14)	14 (8)	21 (11)	23 (13)	15 (12)	16 (13)	15 (11)
Nasopharyngitis	35 (9)	40 (10)	44 (11)	8 (9)	9 (10)	12 (14)	17 (10)	19 (10)	19 (11)	10 (8)	12 (10)	13 (10)
Condition aggravated	38 (10)	32 (8)	40 (10)	7 (8)	3 (3)	10 (11)	18 (10)	16 (9)	17 (10)	13 (10)	13 (11)	13 (10)
Weight decreased	40 (10)	35 (9)	30 (8)	6 (7)	1 (1)	5 (6)	28 (16)	24 (13)	19 (11)	6 (5)	10 (8)	6 (5)
Events leading to discontinuation of trial regimen												
Any	55 (14)	46 (12)	42 (11)	6 (7)	7 (8)	7 (8)	38 (21)	31 (17)	22 (13)	11 (9)	8 (7)	13 (10)
Diarrhea	24 (6)	7 (2)	2 (1)	1 (1)	0	0	23 (13)	4 (2)	2 (1)	0	3 (2)	0
Event leading to interruption of trial regimen	76 (19)	72 (18)	56 (14)	11 (13)	12 (14)	13 (15)	48 (27)	45 (24)	21 (12)	17 (13)	15 (12)	22 (17)
Serious events‡												
Any	117 (30)	121 (31)	131 (33)	20 (23)	22 (25)	28 (32)	56 (31)	62 (34)	50 (29)	41 (32)	37 (31)	53 (40)
Fatal event	6 (2)	16 (4)	18 (5)	0	3 (3)	7 (8)	4 (2)	9 (5)	5 (3)	2 (2)	4 (3)	6 (5)

Richeldi L et al. *N Engl J Med.* 2025;392:2193-2202.

FIBRONEER-ILD: Nerandomilast slows FVC decline in PPF



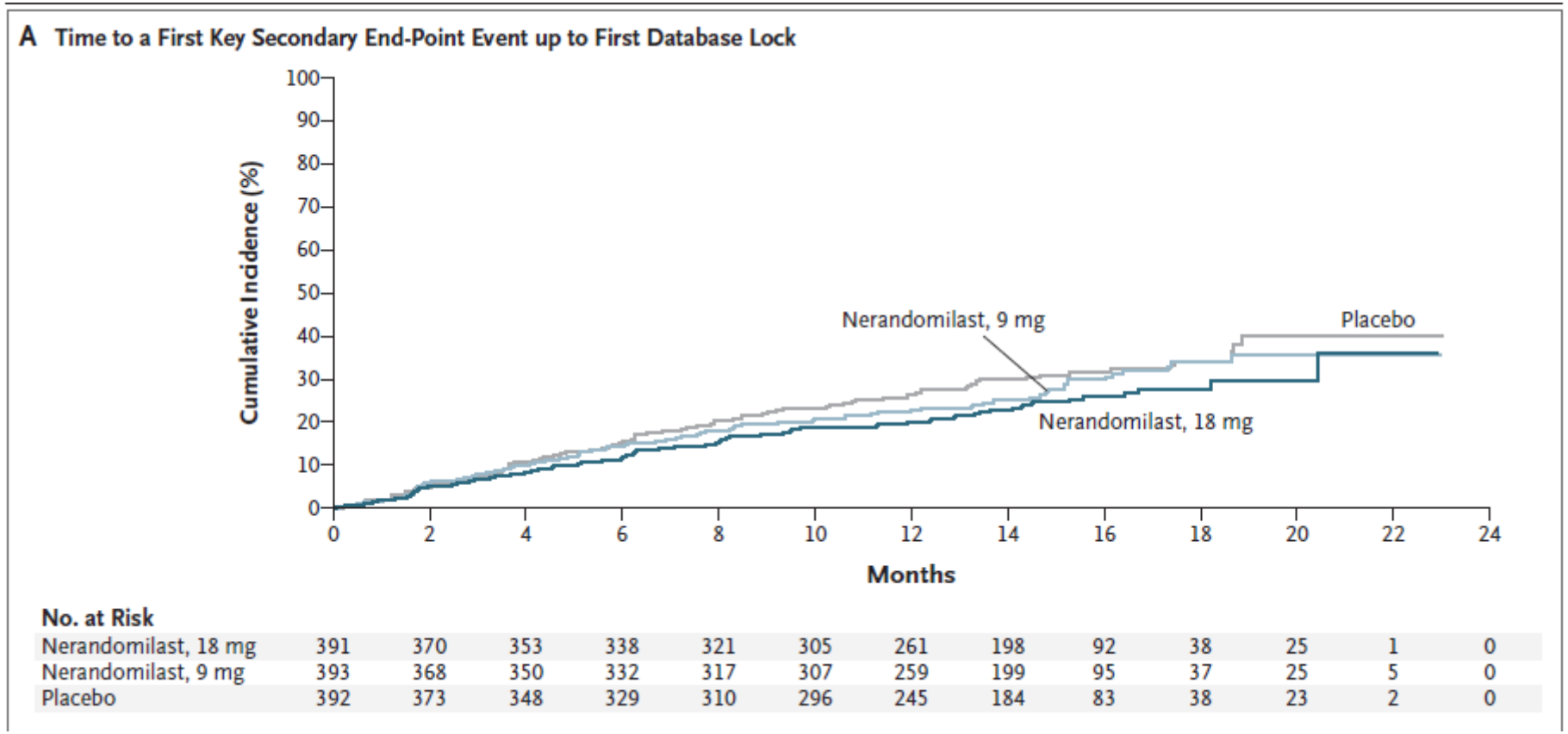
Nerandomilast 18 mg vs. 9 mg. vs placebo PO BID (n = 1176)

- 9 mg and 18 mg both reduced FVC decline at 52 weeks
  - 9 mg vs. placebo 81 ml ($p < 0.001$)
  - 18 mg vs. placebo 67 ml ($p < 0.001$)

- Similar results with (44%) and without (56%) background nintedanib

Maher T et al. N Engl J Med. 2025:392:2203-2214.

FIBRONEER-ILD: Secondary endpoints



No. at Risk

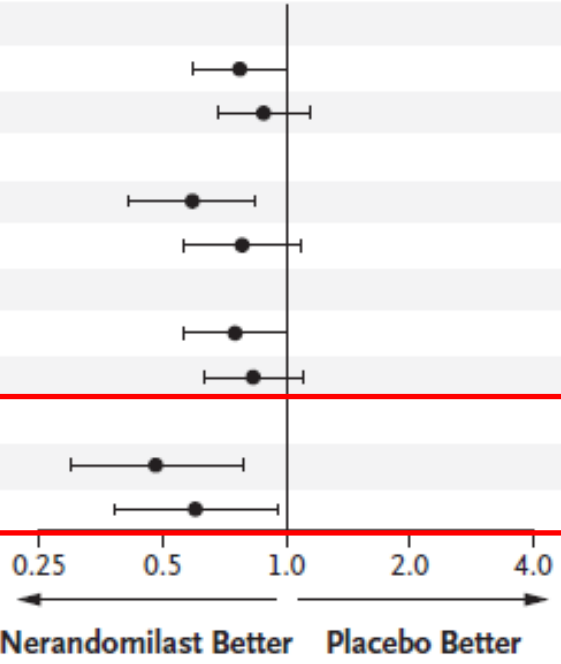
Nerandomilast, 18 mg	391	370	353	338	321	305	261	198	92	38	25	1	0
Nerandomilast, 9 mg	393	368	350	332	317	307	259	199	95	37	25	5	0
Placebo	392	373	348	329	310	296	245	184	83	38	23	2	0

Maher T et al. N Engl J Med. 2025:392:2203-2214.

FIBRONEER-ILD: Secondary endpoints

B Analyses of Key Secondary End Point and Related Secondary End Points up to First Database Lock

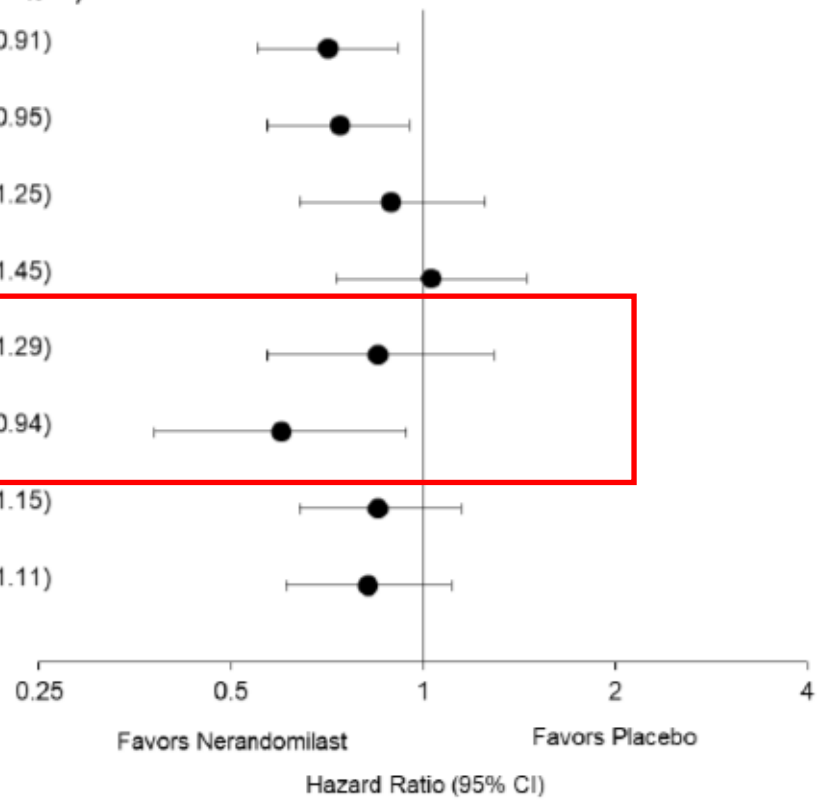
End Point	Nerandomilast	Placebo	Hazard Ratio (95% CI)	P Value
	no. with event/no. of patients			
Key secondary end point				
Nerandomilast, 18 mg	95/391	122/392	0.77 (0.59–1.01)	0.06
Nerandomilast, 9 mg	110/393	122/392	0.88 (0.68–1.14)	0.34
Acute exacerbation of ILD or death				
Nerandomilast, 18 mg	48/391	83/392	0.59 (0.41–0.84)	
Nerandomilast, 9 mg	65/393	83/392	0.78 (0.56–1.08)	
Hospitalization for respiratory cause or death				
Nerandomilast, 18 mg	84/391	110/392	0.75 (0.56–1.00)	
Nerandomilast, 9 mg	97/393	110/392	0.83 (0.63–1.10)	
Death				
Nerandomilast, 18 mg	24/391	50/392	0.48 (0.30–0.79)	
Nerandomilast, 9 mg	33/393	50/392	0.60 (0.38–0.95)	



Maher T et al. N Engl J Med. 2025:392:2203-2214.

FIBRONEER-ILD: Secondary endpoints

		Placebo	Nerandomilast	Hazard ratio (95% CI)
Absolute decline in FVC >10% of predicted value from baseline or death	Nerandomilast 9 mg twice daily	142/392	109/393	0.71 (0.55, 0.91)
	Nerandomilast 18 mg twice daily	142/392	107/391	0.74 (0.57, 0.95)
Absolute decline in DLco >15% of predicted value from baseline or death	Nerandomilast 9 mg twice daily	73/392	68/393	0.89 (0.64, 1.25)
	Nerandomilast 18 mg twice daily	73/392	61/391	1.03 (0.73, 1.45)
Acute exacerbation	Nerandomilast 9 mg twice daily	52/392	42/393	0.85 (0.57, 1.29)
	Nerandomilast 18 mg twice daily	52/392	30/391	0.60 (0.38, 0.94)
Hospitalization for respiratory cause	Nerandomilast 9 mg twice daily	95/392	86/393	0.85 (0.64, 1.15)
	Nerandomilast 18 mg twice daily	95/392	79/391	0.82 (0.61, 1.11)



Maher T et al. N Engl J Med. 2025:392:2203-2214.

FIBRONEER-ILD: Adverse Events

Table 2. Adverse Events over a Period of 52 Weeks.*

Event Category	All Patients			No Background Nintedanib Therapy			Background Nintedanib Therapy†		
	Nerandomilast		Placebo	Nerandomilast		Placebo	Nerandomilast		Placebo
	18 mg (N=391)	9 mg (N=393)	(N=392)	18 mg (N=220)	9 mg (N=220)	(N=222)	18 mg (N=171)	9 mg (N=173)	(N=170)
	number of patients (percent)								
Any event	362 (92.6)	362 (92.1)	360 (91.8)	202 (91.8)	200 (90.9)	202 (91.0)	160 (93.6)	162 (93.6)	158 (92.9)
Most frequent events‡									
Diarrhea	143 (36.6)	116 (29.5)	97 (24.7)	59 (26.8)	33 (15.0)	35 (15.8)	84 (49.1)	83 (48.0)	62 (36.5)
Cough	58 (14.8)	49 (12.5)	55 (14.0)	35 (15.9)	24 (10.9)	31 (14.0)	23 (13.5)	25 (14.5)	24 (14.1)
URT infection	46 (11.8)	39 (9.9)	60 (15.3)	31 (14.1)	26 (11.8)	44 (19.8)	15 (8.8)	13 (7.5)	16 (9.4)
Covid-19	42 (10.7)	41 (10.4)	58 (14.8)	26 (11.8)	20 (9.1)	27 (12.2)	16 (9.4)	21 (12.1)	31 (18.2)
Condition aggravated	28 (7.2)	46 (11.7)	57 (14.5)	12 (5.5)	24 (10.9)	34 (15.3)	16 (9.4)	22 (12.7)	23 (13.5)
Depression	40 (10.2)	38 (9.7)	44 (11.2)	23 (10.5)	21 (9.5)	24 (10.8)	17 (9.9)	17 (9.8)	20 (11.8)
Nasopharyngitis	34 (8.7)	45 (11.5)	39 (9.9)	16 (7.3)	21 (9.5)	18 (8.1)	18 (10.5)	24 (13.9)	21 (12.4)
Anxiety	37 (9.5)	40 (10.2)	37 (9.4)	22 (10.0)	20 (9.1)	20 (9.0)	15 (8.8)	20 (11.6)	17 (10.0)
Nausea	40 (10.2)	30 (7.6)	26 (6.6)	13 (5.9)	9 (4.1)	8 (3.6)	27 (15.8)	21 (12.1)	18 (10.6)
Weight decreased	42 (10.7)	27 (6.9)	23 (5.9)	23 (10.5)	11 (5.0)	9 (4.1)	19 (11.1)	16 (9.2)	14 (8.2)
Event leading to discontinuation of trial regimen									
Any	39 (10.0)	32 (8.1)	40 (10.2)	19 (8.6)	16 (7.3)	23 (10.4)	20 (11.7)	16 (9.2)	17 (10.0)
Diarrhea	10 (2.6)	5 (1.3)	2 (0.5)	3 (1.4)	0	0	7 (4.1)	5 (2.9)	2 (1.2)
Event leading to interruption of trial regimen	69 (17.6)	68 (17.3)	59 (15.1)	28 (12.7)	31 (14.1)	30 (13.5)	41 (24.0)	37 (21.4)	29 (17.1)
Serious events§									
Any	130 (33.2)	125 (31.8)	138 (35.2)	65 (29.5)	68 (30.9)	82 (36.9)	65 (38.0)	57 (32.9)	56 (32.9)
Fatal event	8 (2.0)	14 (3.6)	20 (5.1)	5 (2.3)	10 (4.5)	11 (5.0)	3 (1.8)	4 (2.3)	9 (5.3)

Maher T et al. N Engl J Med. 2025:392:2203-2214.

FDA U.S. FOOD & DRUG
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October 7, 2025

FDA approves drug to treat idiopathic pulmonary fibrosis

First new treatment in more than a decade for rare lung condition

News & Events for Human Drugs

Meetings, Conferences, & Workshops

Action

Today, the U.S. Food and Drug Administration (FDA) approved Jascayd (nerandomilast) tablets to treat idiopathic pulmonary fibrosis (IPF), a rare, serious, and progressive disease with no cure and limited treatments. This is the first new therapy approved in more than 10 years for IPF.

FDA U.S. FOOD & DRUG
A FDA Homepage

← Home / Drugs / News & Events for Human Drugs / FDA approves drug to treat idiopathic pulmonary fibrosis

October 7, 2025

FDA U.S. FOOD & DRUG ADMINISTRATION

← Home / Drugs / News & Events for Human Drugs / FDA Approves Drug to Treat Chronic, Progressive Lung Disease

December 19, 2025

FDA Approves Drug to Treat Chronic, Progressive Lung Disease

News & Events for Human Drugs

Meetings, Conferences, & Workshops

Action

Today, the U.S. Food and Drug Administration (FDA) approved Jascayd (nerandomilast) tablets to treat adults with progressive pulmonary fibrosis (PPF). Jascayd was previously approved to treat idiopathic pulmonary fibrosis (IFP) in adults.

Incorporating nerandomilast into IPF and PPF treatment algorithms

On existing Rx and tolerating well:

- Pirfenidone → add nerandomilast 18 mg BID
- Nintedanib → add nerandomilast 9* or 18 mg BID

On existing Rx with tolerability issues:

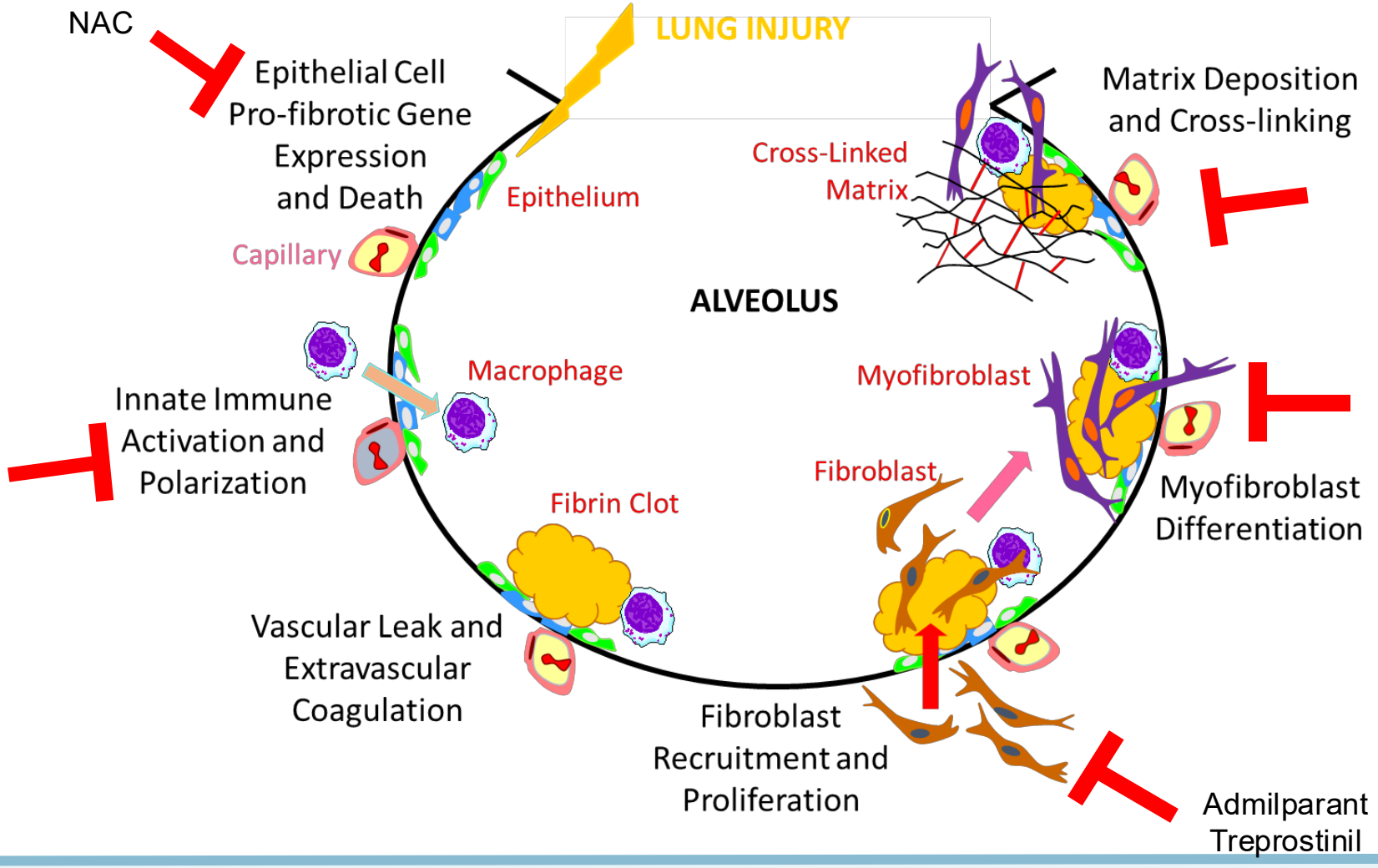
- Switch to alternative legacy antifibrotic or nerandomilast 9 or 18 mg

Treatment naïve:

- Pirfenidone/Nintedanib or Nerandomilast first line?
- Nera 9 vs 18 mg depending on plans for combination Rx, concerns for AE's, etc.

*preferred based on tolerability profile?

More PF treatments on the horizon?



Inhaled Treprostinil for PF?

INCREASE Trial: Phase 3 RCT of inhaled Treprostinil for PH-ILD)

Variable Visit Treatment	N	LS Mean	Contrast: Inhaled treprostinil - Placebo Estimated Difference (95% CI)	P-value
FVC (mL)				
Week 8				
Inhaled treprostinil	142	5.49	28.47	
Placebo	141	-22.98	(-30.81, 87.74)	0.35
Week 16				
Inhaled treprostinil	130	9.77	44.40	
Placebo	126	-34.63	(-25.25, 114.05)	0.21
FVC (% predicted)				
Week 8				
Inhaled treprostinil	142	0.77	1.79	
Placebo	141	-1.02	(0.37, 3.21)	0.01
Week 16				
Inhaled treprostinil	130	1.07	1.80	
Placebo	126	-0.72	(0.20, 3.39)	0.03

TETON-1 and TETON-2:

- Phase 3 RCTs of inhaled treprostinil in IPF

TETON-PPF

- Phase 3 RCT of inhaled treprostinil in PPF
- Results expected 2026/2027

Waxman A et al. NEJM. 2021;384:325-334

Inhaled Treprostinil for PF?

INCREASE Trial: Phase 3 RCT of inhaled Treprostinil for PH-ILD)

Variable Visit Treatment	N	LS M
FVC (mL)		
Week 8		
Inhaled treprostinil	142	5.4
Placebo	141	-22.9
Week 16		
Inhaled treprostinil	130	9.7
Placebo	126	-34.(
FVC (% predicted)		
Week 8		
Inhaled treprostinil	142	0.7
Placebo	141	-1.0
Week 16		
Inhaled treprostinil	130	1.0
Placebo	126	-0.7

TETON-1 and TETON-2:

- Phase 3 RCTs of inhaled treprostinil in IPF

For Immediate Release

United Therapeutics Corporation Announces *TETON-2* Pivotal Study of Tyvaso® Meets Primary Endpoint for the Treatment of Idiopathic Pulmonary Fibrosis

Positive results were observed across all subgroups

Study meets several key secondary endpoints with statistical significance

Waxman A et al. NEJM. 2021;384:325-334

Evolving landscape of PF treatment