호흡기내과 의사를 위한 Respiratory Review of 2026
Interstitial lung disease

2026-04-18
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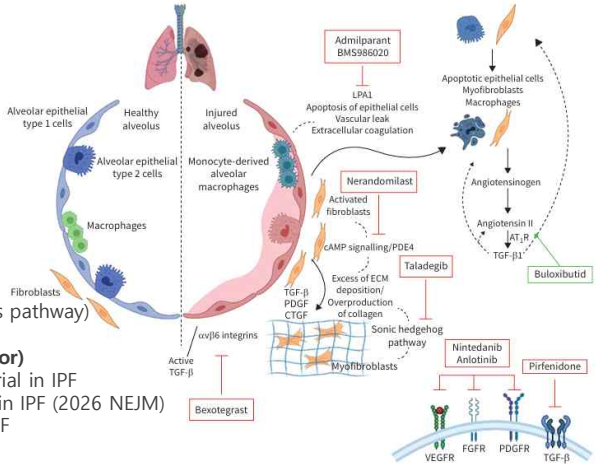

Breathe (Sheff) 2025; 21(2): 240259.

1. Nerandomilast : FIBRONEER-IPF

The NEW ENGLAND JOURNAL of MEDICINE
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Nerandomilast in Patients with Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D.,[1] Arata Azuma, M.D.,[2] Vincent Cottin, M.D.,[3] Michael Kreuter, M.D.,[4] Toby M. Maher, M.D.,[5]
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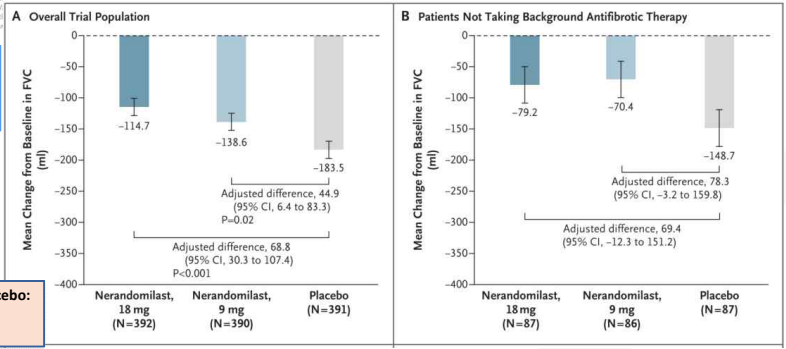
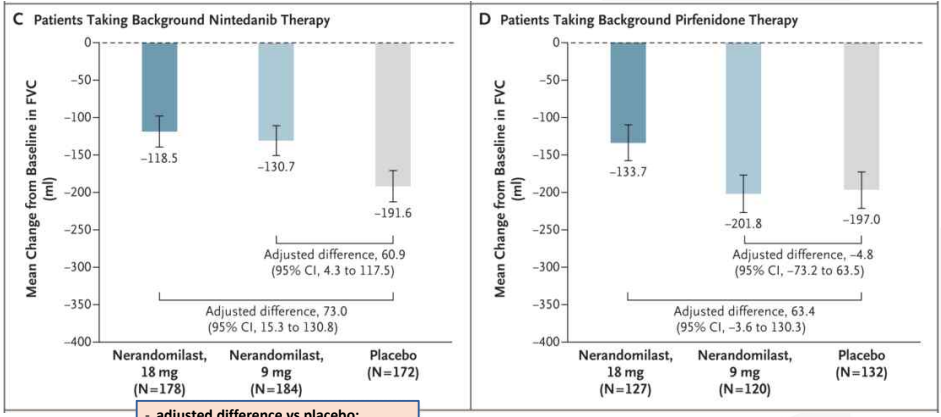
for the FIBRONEER-IPF Trial Investigators*

- **double-blind, placebo-controlled, phase 3 trial**
- **1,177 IPF patients**
- **randomized 1:1:1 to nerandomilast 18 mg BID, nerandomilast 9 mg BID, or placebo**
- **background antifibrotic therapy allowed**
- **primary endpoint: absolute change in FVC over 52 weeks**

selective PDE4B inhibitor
- elevation of intracellular cAMP
- inhibition of inflammatory responses
- inhibition of fibrotic pathways



- **adjusted difference vs placebo:**
- **18 mg: +68.8 mL (P<0.001)**
- **9 mg: +44.9 mL (P=0.02)**



- **adjusted difference vs placebo:**
- **18 mg: +73.0 mL (95% CI, 15.3 to 130.8)**
- **9 mg: +60.9 mL (95% CI, 4.3 to 117.5)**

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 DL_{CO} 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)

1. Nerandomilast (PDE4B inhibitor) - FIBRONEER-PPF

- **double-blind, placebo-controlled, phase 3 trial**
- **1,176 PPF patients**
- **randomized 1:1:1 to nerandomilast 18 mg BID, nerandomilast 9 mg BID, or placebo**
- **stratified by background nintedanib use and HRCT pattern**
- **primary endpoint: absolute change in FVC over 52 weeks**

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]
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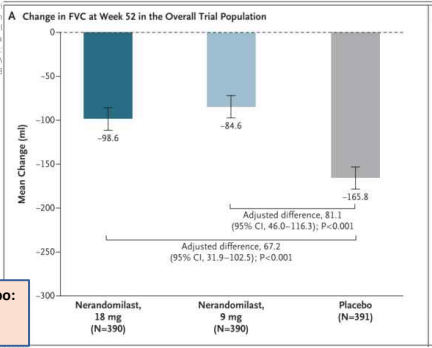
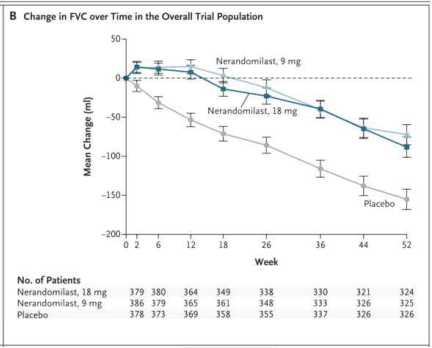
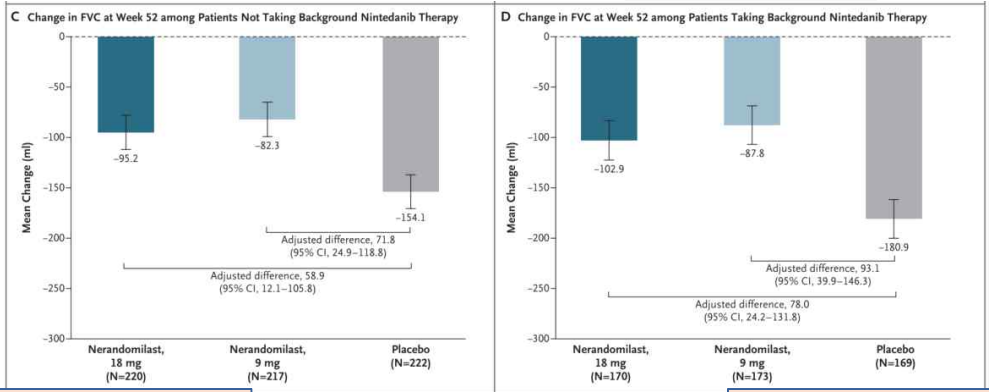
Michael Kreuter, M.D.,[9,10] Justin M. Oldh
Claudia Valenzuela, M.D.,[17] Mari
Emmanuelle Clerisme-Beaty, M.D.,[21] Ca
Ivana Ritter, M.D.,[24] Arno Schlosser, M.
Florian Voss, Ph.D.,[28] Gerrit Weimann, M
Fernando J. Martinez, M.D.,[31] for the FIB





- **adjusted difference vs placebo:**
- **18 mg: +67.2 mL, P<0.001**
- **9 mg: +81.1 mL, P<0.001**

N Engl J Med 2025;392:2203-2214.



- **adjusted difference vs placebo:**
- **18 mg: +58.9 mL (95% CI, 12.1 to 105.8)**
- **9 mg: +71.8 mL (95% CI, 24.9 to 118.8)**

- **adjusted difference vs placebo:**
- **18 mg: +78.0 mL (95% CI, 24.2 to 131.8)**
- **9 mg: +93.1 mL (95% CI, 39.9 to 146.3)**

N Engl J Med 2025;392:2203-2214.

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)	

2. Admilparant (LPA1 antagonist)

- phase 2, randomized, placebo-controlled trial
- parallel 273 IPF and 125 PPF cohorts
- randomized to admilparant 30 mg BID, 60 mg BID, or placebo
- primary endpoint (IPF): rate of change in ppFVC over 26 weeks

ORIGINAL ARTICLE

Efficacy and Safety of Admilparant, an LPA$_1$ Ant
Pulmonary Fibrosis
A Phase 2 Randomized Clinical Trial

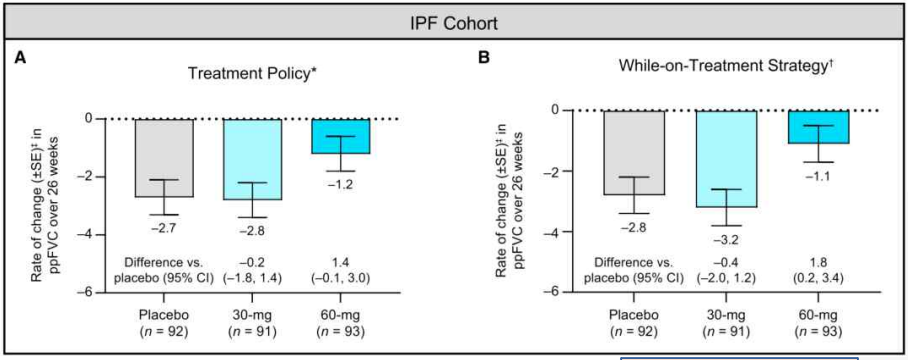
Tamera J. Corte[1,2], Juergen Behr[3], Vincent Cottin[4], Marilyn K. Glassberg[5], Michae Takashi Ogura[9], Takafumi Suda[10], Marlies Wijsenbeek[11], Elchonon Berkowitz[12] Hideaki Watanabe[12], Aryeh Fischer[12], and Toby M. Maher[13,14]

LPA1 antagonist

- LPA: lipid signaling molecule involved in fibrotic pathways
- blocks LPA-mediated profibrotic signaling
- reduces fibroblast recruitment and activation

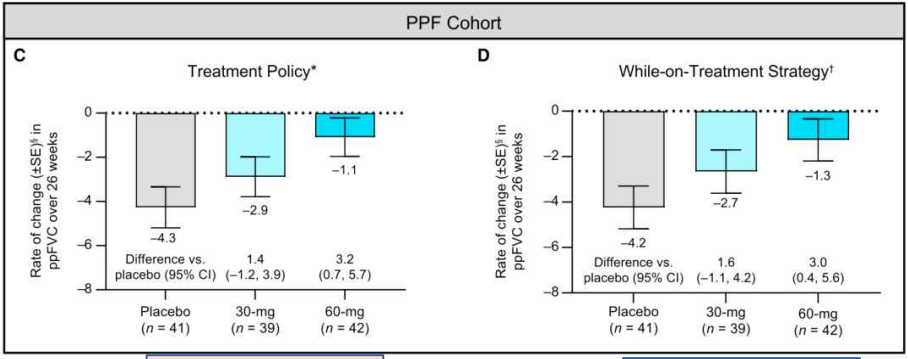
Parameter	IPF Cohort			PPF Cohort		
	Placebo ($n = 92$)	30 mg Admilparant ($n = 91$)	60 mg Admilparant ($n = 93$)	Placebo ($n = 41$)	30 mg Admilparant ($n = 40$)	60 mg Admilparant ($n = 42$)
Demographics						
Age, yr	69.0 ± 6.7	69.5 ± 7.3	68.8 ± 7.9	68.8 ± 8.1	71.4 ± 7.9	67.9 ± 8.4
Male sex	76 (82.6)	77 (84.6)	69 (74.2)	20 (48.8)	23 (57.5)	22 (52.4)
Race						
White	65 (70.7)	64 (70.3)	64 (68.8)	31 (75.6)	27 (67.5)	32 (76.2)
Asian	25 (27.2)	25 (27.5)	27 (29.0)	8 (19.5)	9 (22.5)	6 (14.3)
Other	2 (2.2)	2 (2.2)	2 (2.2)	2 (4.9)	4 (10.0)	4 (9.5)
Clinical characteristics						
Weight, kg	76.5 ± 15.0	76.5 ± 14.1	75.8 ± 15.6	71.9 ± 16.2	73.5 ± 17.3	74.9 ± 19.4
BMI, kg/m^2	27.2 ± 4.1	26.9 ± 4.0	27.1 ± 4.5	26.9 ± 4.7	26.3 ± 5.0	27.0 ± 4.8
Cigarette smoking history						
Never	32 (34.8)	30 (33.0)	31 (33.3)	19 (46.3)	19 (47.5)	24 (57.1)
Current	1 (1.1)	1 (1.1)	2 (2.2)	0	0	0
Former	59 (64.1)	60 (65.9)	60 (64.5)	22 (53.7)	21 (52.5)	18 (42.9)
Concurrent background antifibrotic treatment*						
Pirfenidone	26 (28.3)	26 (28.6)	25 (26.9)	3 (7.3)	4 (10.0)	6 (14.3)
Nintedanib	36 (39.1)	36 (39.6)	37 (39.8)	12 (29.3)	11 (27.5)	9 (21.4)
None†	30 (32.6)	29 (31.9)	31 (33.3)	26 (63.4)	25 (62.5)	27 (64.3)
Time since diagnosis, yr	2.7 ± 1.7	2.8 ± 1.6	2.8 ± 1.7	2.8 ± 2.6	3.1 ± 2.7	3.9 ± 2.7
No.	89	82	84	39	36	39
FVC, ml	2,741 ± 810	2,768 ± 770	2,641 ± 768	2,126 ± 616	2,246 ± 728	2,113 ± 723
FVC, percentage of predicted	77 ± 19	77 ± 19	76 ± 17	68 ± 18	67 ± 16	65 ± 17
No.	92	91	93	41	40	42
D_{LCO}, percentage of predicted, hemoglobin corrected	51.1 ± 17.4	50.9 ± 16.2	50.8 ± 18.0	48.0 ± 16.0	48.7 ± 18.7	46.1 ± 12.4
No.	80	81	82	41	40	42
6MWT, m	380.5 ± 112.1	391.6 ± 108.8	396.2 ± 116.1	339.6 ± 108.8	326.6 ± 108.0	340.2 ± 107.5
No.	89	88	90	39	39	42
Quantitative lung fibrosis (HRCT), %	17.3 ± 11.0	17.3 ± 10.8	17.2 ± 10.4	18.1 ± 11.1	19.1 ± 11.9	23.9 ± 12.4

Am J Respir Crit Care Med 2025; 211(2): 230-238



- **Difference vs placebo:**
- **30 mg: -0.4 (95% CI, -2.0 to 1.2)**
- **60 mg: +1.8 (95% CI, 0.2 to 3.4)**

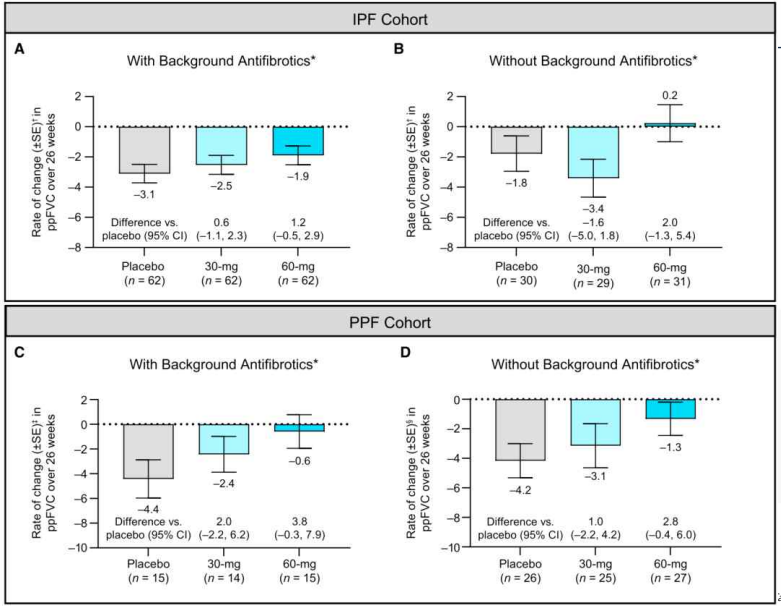
Am J Respir Crit Care Med 2025; 211(2): 230-238



- **Difference vs placebo:**
- **30 mg: +1.4 (95% CI, -1.2 to 3.9)**
- **60 mg: +3.2 (95% CI, 0.7 to 5.7)**

- **Difference vs placebo:**
- **30 mg: +1.6 (95% CI, -1.1 to 4.2)**
- **60 mg: +3.0 (95% CI, 0.4 to 5.6)**

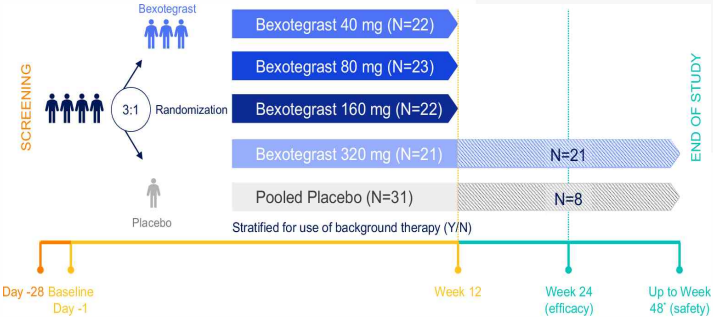
Am J Respir Crit Care Med 2025; 211(2): 230-238


IPF Cohort
A
With Background Antifibrotics*
Rate of change (±SE)† in ppFVC over 26 weeks
2
0
−2
−4
−6
−8
−3.1
−2.5
−1.9
Difference vs. placebo (95% CI)
0.6 (−1.1, 2.3)
1.2 (−0.5, 2.9)
Placebo (n = 62)
30-mg (n = 62)
60-mg (n = 62)
B
Without Background Antifibrotics*
Rate of change (±SE)† in ppFVC over 26 weeks
2
0
−2
−4
−6
−8
0.2
−1.8
−3.4
−1.6 (−5.0, 1.8)
Difference vs. placebo (95% CI)
2.0 (−1.3, 5.4)
Placebo (n = 30)
30-mg (n = 29)
60-mg (n = 31)
PPF Cohort
C
With Background Antifibrotics*
Rate of change (±SE)† in ppFVC over 26 weeks
2
0
−2
−4
−6
−8
−10
−0.6
−2.4
−4.4
Difference vs. placebo (95% CI)
2.0 (−2.2, 6.2)
3.8 (−0.3, 7.9)
Placebo (n = 15)
30-mg (n = 14)
60-mg (n = 15)
D
Without Background Antifibrotics*
Rate of change (±SE)† in ppFVC over 26 weeks
0
−2
−4
−6
−8
−10
−1.3
−3.1
−4.2
Difference vs. placebo (95% CI)
1.0 (−2.2, 4.2)
2.8 (−0.4, 6.0)
Placebo (n = 26)
30-mg (n = 25)
60-mg (n = 27)

3. Bexotegrast (αvβ6/αvβ1 integrin inhibitor)

Dual αvβ6/αvβ1 integrin inhibitor
- inhibition of latent TGF-β activation
- reduction of profibrotic signaling

The INTEGRIS-IPF Clinical Trial - Phase-2a



- **phase 2a, multicenter, randomized, double-blind, placebo-controlled trial**
- **119 IPF**
- **bexotegrast 40, 80, 160, or 320 mg once daily vs pooled placebo**
- **with 320 mg and placebo: extension follow-up**
- **primary endpoint: treatment-emergent adverse event**
- **Exploratory efficacy: change in FVC, quantitative lung fibrosis**

Am J Respir Crit Care Med 2024, 210.4: 424-434.

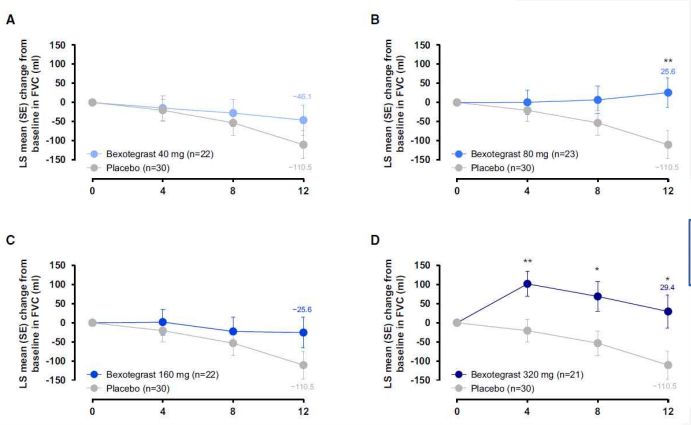
3. Bexotegrast (αvβ6/αvβ1 integrin inhibitor)

- Safe and well tolerated
- TEAEs similar to placebo

Nature of TEAE	Participants, *n* (%)					
	Bexotegrast					
	40 mg (*n* = 22)	80 mg (*n* = 23)	160 mg (*n* = 22)	320 mg (*n* = 22)	Pooled (*n* = 89)	Placebo (*n* = 31)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	17 (77.3)	62 (69.7)	21 (67.7)
TEAE related to study drug	4 (18.2)	7 (30.4)	4 (18.2)	4 (18.2)	19 (21.3)	10 (32.3)
TEAE ⩾Grade 3	2 (9.1)	0 (0.0)	2 (9.1)	2 (9.1)	6 (6.7)	2 (6.5)
TEAE ⩾Grade 3 related to study drug	0 (0.0)	0 (0.0)	1 (4.5)*	0 (0.0)	1 (1.1)	0 (0.0)
SAE	1 (4.5)	0 (0.0)	2 (9.1)	1 (4.5)	4 (4.5)	3 (9.7)
SAE related to study drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE leading to interruption of study drug	0 (0.0)	0 (0.0)	1 (4.5)†	1 (4.5)‡	2 (2.2)	0 (0.0)
TEAE leading to withdrawal of study drug	0 (0.0)	0 (0.0)	0 (0.0)	3 (13.6)‡,§,‖	3 (3.4)	3 (9.7)
TEAE leading to early termination from the study	0 (0.0)	0 (0.0)	0 (0.0)	3 (13.6)‡,§,‖	3 (3.4)	2 (6.5)
TEAE leading to death	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)¶	1 (1.1)	0 (0.0)
TEAEs occurring in ⩾5% of participants in any group (any causality)						
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	3 (13.6)	15 (16.9)	3 (9.7)
Fatigue	2 (9.1)	2 (8.7)	1 (4.5)	2 (9.1)	7 (7.9)	2 (6.5)
Nausea	1 (4.5)	1 (4.3)	2 (9.1)	0 (0.0)	4 (4.5)	2 (6.5)
Dyspnea	0 (0.0)	1 (4.3)	2 (9.1)	1 (4.5)	4 (4.5)	0 (0.0)
Atrioventricular block, first degree	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.1)	2 (2.2)	2 (6.5)
Vomiting	0 (0.0)	0 (0.0)	2 (9.1)	0 (0.0)	2 (2.2)	0 (0.0)
COVID-19	0 (0.0)	0 (0.0)	2 (9.1)	0 (0.0)	2 (2.2)	0 (0.0)
Cough	1 (4.5)	1 (4.3)	1 (4.5)	1 (4.5)	4 (4.5)	2 (6.5)
Headache	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	1 (1.1)	2 (6.5)
IPF/pulmonary fibrosis	1 (4.5)	0 (0.0)	1 (4.5)	0 (0.0)	2 (2.3)	3 (9.7)
Hyperkalemia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (6.5)
Skin abrasion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (6.5)

Am J Respir Crit Care Med 2024, 210.4: 424-434.

3. Bexotegrast (αvβ6/αvβ1 integrin inhibitor)

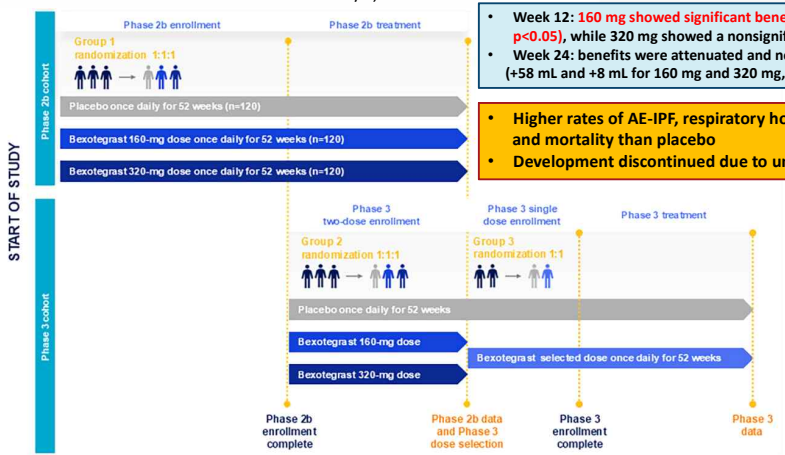


- **dose-dependent signals for preserving FVC, with the clearest effect at 320 mg**

Am J Respir Crit Care Med 2024, 210.4: 424-434.

3. Bexotegrast (αvβ6/αvβ1 integrin inhibitor)

The BEACON-IPF Clinical Trial - Phase-2b/3, 52wks



- **Week 12: 160 mg showed significant benefit in FVC decline (+72 mL, p<0.05), while 320 mg showed a nonsignificant trend (+46 mL).**
- **Week 24: benefits were attenuated and no significant (+58 mL and +8 mL for 160 mg and 320 mg, respectively).**

- **Higher rates of AE-IPF, respiratory hospitalization, and mortality than placebo**
- **Development discontinued due to unfavorable risk–benefit**

BMJ Open Respir Res 2026;13:e002937.

prostacyclin analogue
- vasodilatory effects
- increased intracellular cAMP
- inhibition of smooth muscle and fibroblast proliferation

-> potential antifibrotic activity

4. Inhaled Treprostinil (Prostacyclin vasodilator)

- TETON-2

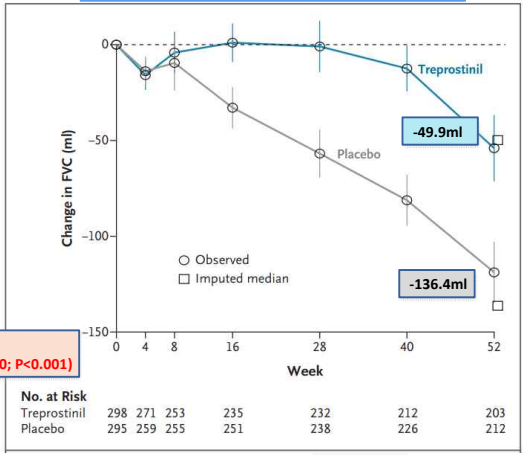
ORIGINAL ARTICLE

Inhaled Treprostinil for Idiopathic Pulmonary Fibrosis

S.D. Nathan,[1] P. Smith,[2] C. Deng,[2] M. De Salvo,[3] W. Wuyts,[4] J. Pavie-Gallegos,[5] J.W. Song,[6] M.R. Kramer,[7] C.S. King,[1] J.A. Mackintosh,[8] D. Chambers,[9] G.V. Miranda,[10] N. Breytenbach,[2] L. Peterson,[2] H. Bell,[2] K.R. Flaherty,[11] J. Behr,[12-14] and V. Cottin,[15,16] for the TETON-2 Trial Investigators*

- **phase 3, randomized, double-blind, placebo-controlled trial**
- **593 IPF**
- **inhaled treprostinil vs placebo for 52 weeks**
- **primary endpoint: absolute change in FVC at week 52**

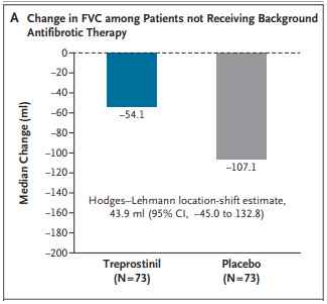
- **Difference vs placebo:**
95.6 ml (95% CI, 52.2 to 139.0; P<0.001)

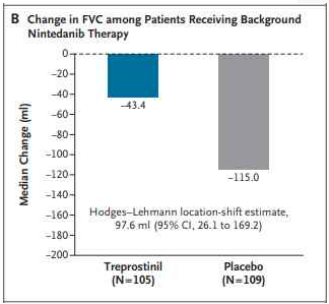


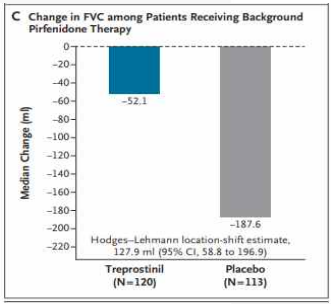
N Engl J Med. 2026 Mar 11. doi: 10.1056/NEJMoa2512911.

4. Inhaled Treprostinil (Prostacyclin vasodilator)

- TETON-2







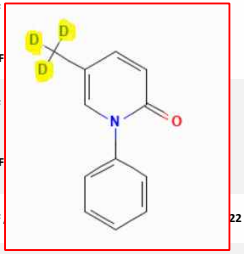
- **Difference vs placebo:**
  +97.6 mL (95% CI, 26.1 to 169.2)

- **Difference vs placebo:**
  +127.9 mL (95% CI, 58.8 to 196.9)

N Engl J Med. 2026 Mar 11. doi: 10.1056/NEJMoa2512911.

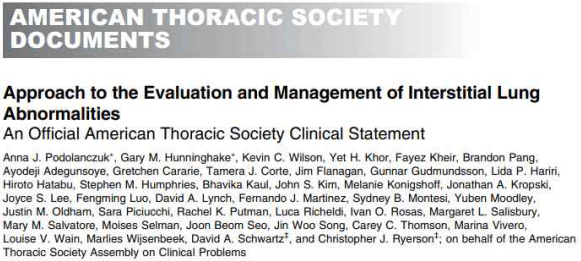
Future perspectives

Treatment / Pathway	Molecule	Disease	Trial name / identifier	Status	Phase / Type	Duration / Patients	Primary endpoint / focus
Prostacyclin vasodilator	Inhaled treprostinil	IPF		confirmatory readout awaited	Phase 3	52 weeks/598 patients	Absolute change from baseline in FVC, confirmatory study
Prostacyclin vasodilator	Inhaled treprostinil	PPF		Recruiting	Phase 3	52 weeks / 698 patients	Absolute change from baseline in FVC
LPA1 antagonism	Admilparant	IPF		Ongoing	Phase 3	≥52 weeks/~1032 patients	FVC, disease progression, safety, quality of life
LPA1 antagonism	Admilparant	PPF		Ongoing	Phase 3	≥52 weeks/~1032 patients	Absolute change in FVC, disease progression, safety, quality of life
PDE4B inhibition	Nerandomilast	IPF	22	Ongoing	Open-label extension	Long-term follow-up/ /~1700 patients	Long-term safety, tolerability, efficacy durability
deuterated form pirfenidone	Deupirfenidone	IPF	SURPASS-IPF / NCT07284602	Starting plan	Phase 3	52 weeks	Lung function and safety vs pirfenidone
IL-11 targeting	BI 765423	IPF	NCT07036523	Recruiting	Phase 2a	8–10 months (primary endpoint at 3 months)	Effect on lung function and safety
Epithelial-restorative inhaled therapy	LTI-03	IPF	NCT06968845	Recruiting	Phase 2	24 weeks/~120 patines	Safety, tolerability, exploratory efficacy/biologic effects



2. Interstitial Lung Abnormalities (ILA)

- 2025년 ATS Clinical Statement


AMERICAN THORACIC SOCIETY DOCUMENTS

Approach to the Evaluation and Management of Interstitial Lung Abnormalities

An Official American Thoracic Society Clinical Statement

Anna J. Podolanczuk*, Gary M. Hunninghake*, Kevin C. Wilson, Yet H. Khor, Fayez Kheir, Brandon Pang, Ayodeji Adegunsoye, Gretchen Cararie, Tamera J. Corte, Jim Flanagan, Gunnar Gudmundsson, Lida P. Hariri, Hiroto Hatabu, Stephen M. Humphries, Bhavika Kaul, John S. Kim, Melanie Konigshoff, Jonathan A. Kropski, Joyce S. Lee, Fengming Luo, David A. Lynch, Fernando J. Martinez, Sydney B. Montesi, Yuben Moodley, Justin M. Oldham, Sara Piciucchi, Rachel K. Putman, Luca Richeldi, Ivan O. Rosas, Margaret L. Salisbury, Mary M. Salvatore, Moises Selman, Joon Beom Seo, Jin Woo Song, Carey C. Thomson, Marina Vivero, Louise V. Wain, Marlies Wijsenbeek, David A. Schwartz‡, and Christopher J. Ryerson‡; on behalf of the American Thoracic Society Assembly on Clinical Problems

Am J Respir Crit Care Med 2025; 211(7): 1132-1155.

✓ Definition of ILA

HHS Public Access

Author manuscript

Lancet Respir Med. Author manuscript; available in PMC 2021 July 01.

Published in final edited form as:

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Interstitial lung abnormalities detected incidentally on CT: a Position Paper from the Fleischner Society

- Incidental identification of non-dependent abnormalities, including ground-glass or reticular abnormalities, lung distortion, traction bronchiectasis, honeycombing, and non-emphysematous cysts
- Involving at least 5% of a lung zone (upper, middle, and lower lung zones are demarcated by the levels of the inferior aortic arch and right inferior pulmonary vein
- In individuals in whom interstitial lung disease is not suspected

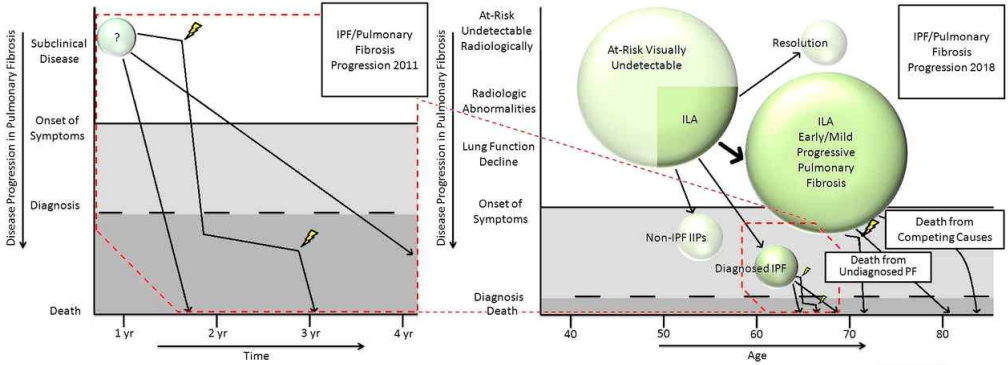
Lancet Respir Med. 2020 July ; 8(7): 726–737

Table 1. Definition of ILA

Chest CT showing bilateral and nondependent ground-glass opacities, reticular abnormalities, lung distortion, traction bronchiectasis, and/or honeycombing involving ⩾5% of a lung zone*
• Nonemphysematous cysts, centrilobular nodularity, and features of pleuroparenchymal fibroelastosis can be present but do not contribute to the volume of affected lung needed to satisfy the definition of ILA
• Bilaterality may not be necessary in some high-risk cases (i.e., with a family history of familial pulmonary fibrosis or known ILD-associated genetic variants)
• The need for findings to be incidental and exclusion of high-risk populations has purposefully been removed from the definition
• Mild abnormalities occurring exclusively in dependent locations on supine imaging should be confirmed to persist on prone imaging

Definition of abbreviations: CT = computed tomography; ILA = interstitial lung abnormality; ILD = interstitial lung disease.
*Upper, middle, and lower lung zones are demarcated by the levels of the inferior aortic arch and right inferior pulmonary vein, creating a total of six zones (three zones per lung).

✓ Clinical course of ILA



Thorax, 74(5), 506-511.

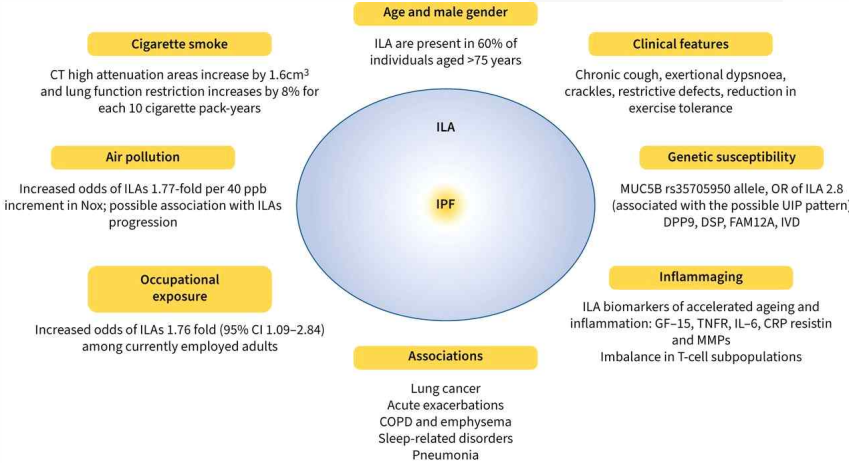
✓ Clinical course of ILA -> ILD

Table 3. Definition of ILD

Definition of interstitial lung disease for those with ILAs
In a person with CT features of ILAs, at least one of the following criteria must be present to define ILD* • Symptoms: Any amount of dyspnea and/or cough that a clinician attributes to ILD • Physiology (any of) ○ Any abnormality in FVC, TLC, or D_{LCO} that a clinician attributes to ILD (defined as a value or z-score below the lower limit of normal) ○ Satisfies physiologic criteria for progressive pulmonary fibrosis that a clinician attributes to ILD (10) • Imaging (any of the following on chest CT) ○ Fibrotic abnormalities (honeycombing and/or reticulation with traction bronchiectasis) involving ⩾5% of total lung volume by visual estimate ○ Progressive fibrotic abnormality on serial chest CT ○ Presence of a major fibrotic ILD pattern on chest CT (i.e., UIP/probable UIP, fibrotic HP, or fibrotic NSIP) • Pathology: Presence of a major fibrotic ILD pattern (i.e., UIP/probable UIP, fibrotic HP, or fibrotic NSIP)

Thorax, 74(5), 506-511.

✓ Risk factor of ILA

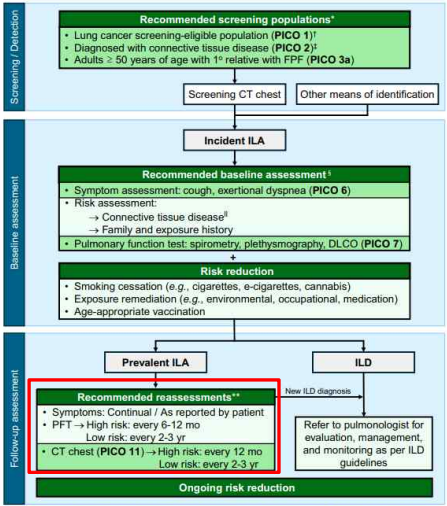


✓ Risk factor of ILA

Table 4. Features Associated with Increased Risk of ILA Progression

High-risk ILA features
Demographic and clinical factors
• Family history of pulmonary fibrosis
• Older age
• Smoking history
• Other inhaled exposures (e.g., occupational vapors, gases, dusts, and fumes; air pollution)
• Connective tissue disease
Genetic
• *MUC5B* promoter variant
• Leukocyte telomere length below age-adjusted 10th percentile
Imaging
• Definite fibrosis on CT (i.e., honeycombing, traction bronchiectasis or architectural distortion)
• Subpleural fibrotic and subpleural nonfibrotic subtypes
• Subpleural reticulation
• Greater extent of abnormalities (e.g., involvement of multiple lung zones)
Physiologic
• Abnormal or borderline FVC, TLC, and D_{LCO}

✓ Follow up strategy of ILA

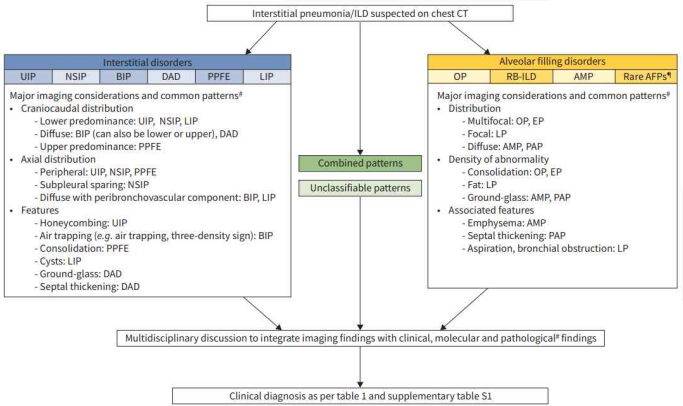


Respir Crit Care Med 2025; 211(7): 1132-1155.

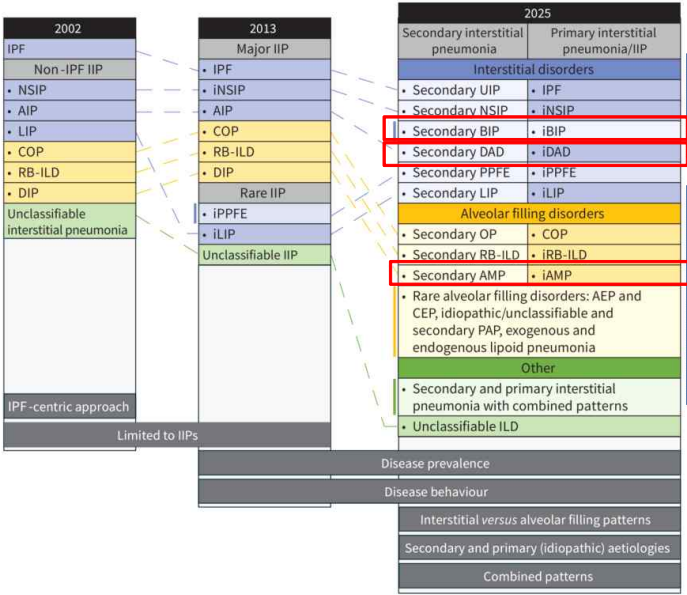
3. Classification of IIP -ERS/ATS 2025 IIP Classification Update

Update of the international multidisciplinary classification of the interstitial pneumonias: an ERS/ATS statement

Christopher J. Ryerson[1,42], Ayodeji Adegunsoye[2,42], Sara Piciucchi[3,4,42], Yet H. Khor[5,6,7,8,9], Marlies S. Wijsenbeek[10], Athol U. Wells[11], Amita Sharma[12], Katerina Antoniou[13], Raphael Borie[14,15], Aurelie Fabre[16,17], Yoshikazu Inoue[18], Takeshi Johkoh[19], Leticia Kawano-Dourado[20,21,22,24], Ella Kazerooni[23,25], Toby M. Maher[26], Philip L. Molyneaux[27,28], Raymond Procter[29], Claudia Ravaglia[3,30], Elisabetta Renzoni[31], Ryoko Saito-Koyama[32], Nicola Sverzellati[33,34], Simon L.F. Walsh[35,36,37], Paul White[38], William Travis[40,42] and Andrew G. Nicholson[27,41,42]



European Respiratory Journal 2025; 66(6).



- from **disease** label to **pattern-based framework**
- **idiopathic + secondary** causes
- **interstitial** vs **alveolar filling** disorders
- combined patterns / unclassifiable ILD

- acute interstitial pneumonia → **idiopathic diffuse alveolar damage**

- desquamative interstitial pneumonia → **alveolar macrophage pneumonia**

+) bronchiolocentric interstitial pneumonia (BIP) :
-airway-centered interstitial pneumonia pattern.
-overlaps with HP

European Respiratory Journal 2025; 66(6).

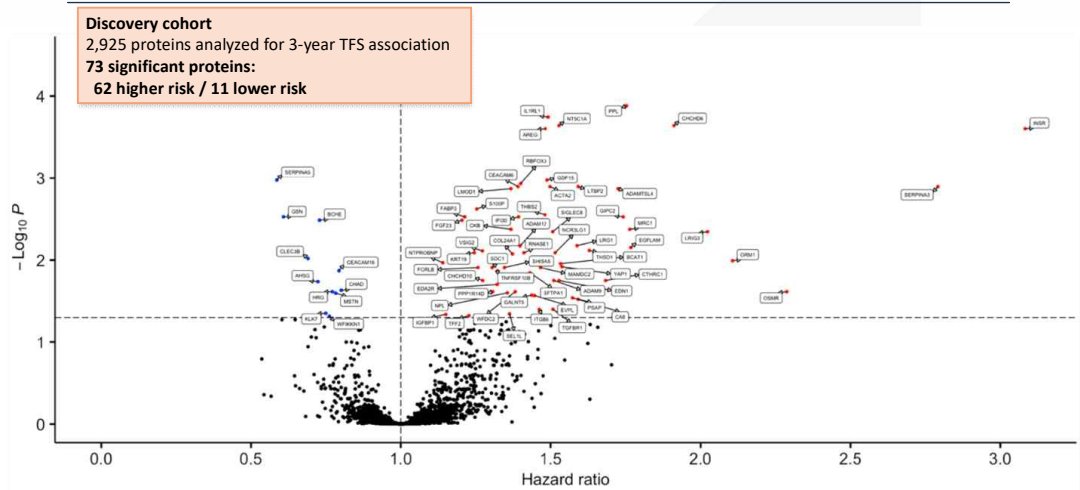
4. Biomarkers for ILD -Protemoics

Proteomic Biomarkers of Survival in Non–Idiopathic Pulmonary Fibrosis Interstitial Lung Disease

Shehabaldin Alqalyoobi[1], Jennifer A. Smith[2], Manoj V. Maddali[5,6], Janelle Vu Pugashetti[3], Chad A. Newton[7], John S. Kim[8], Angela L. Linderholm[9], Ching-Hsien Chen[9], Shwu-Fan Ma[8], Swaraj Bose[4], Susan Murray[4], Ayodeji Adegunsoye[10], Mary E. Strek[10], Christine Kim Garcia[11], Paul J. Wolters[12], Fernando J. Martinez[13], Imre Noth[7], Justin M. Oldham[2,3]

- **Non-IPF ILD**
  - 676 discovery group/ 616 validation group
- **Olink explore 3072 panel**
  - Semiquantitative proteomic platform
  - Relative normalized protein signal, not absolute concentration

Am J Respir Crit Care Med 2025; 211(8): 1452-1462.



Am J Respir Crit Care Med 2025; 211(8): 1452-1462.

Validated Protein Biomarkers of 3-Year Transplant-Free Survival in Discovery and Validation Cohorts

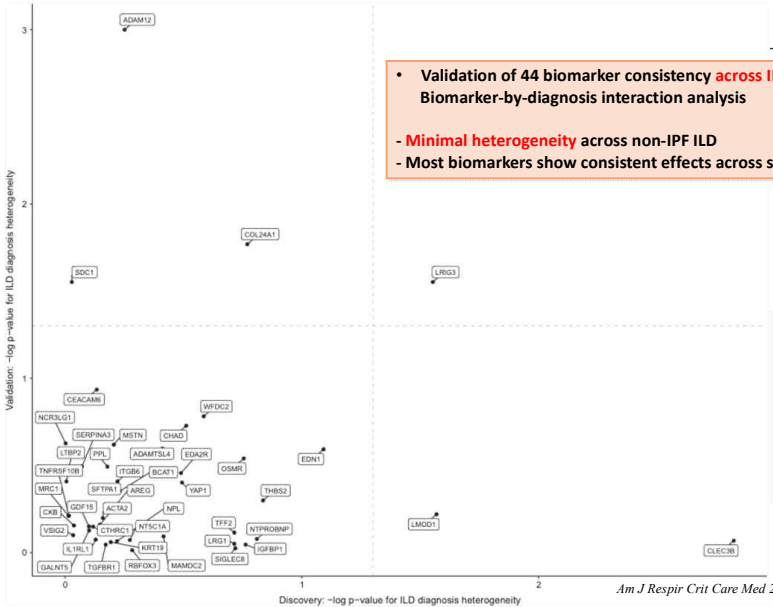
Gene	Protein	Discovery Cohort (n = 676)			Validation Cohort (n = 616)		
		HR	95% CI	FDR *P* Value	HR	95% CI	FDR *P* Value
ACTA2	Actin, aortic smooth muscle	1.498	1.259–1.783	1.277E-03	1.380	1.098–1.735	1.283E-02
ADAM12	Disintegrin and metalloproteinase domain-containing protein 12	1.397	1.186–1.647	6.726E-03	1.389	1.074–1.796	2.246E-02
ADAMTSL4	ADAMTS-like protein 4	1.725	1.361–2.188	1.354E-03	1.987	1.420–2.780	2.277E-04
AREG	Amphiregulin	1.482	1.271–1.729	2.497E-04	2.508	2.069–3.039	4.711E-19
BCAT1	Branched-chain-amino-acid aminotransferase, cytosolic	1.533	1.229–1.913	1.105E-02	1.919	1.495–2.462	3.160E-06
CEACAM6	Carcinoembryonic antigen-related cell adhesion molecule 6	1.390	1.207–1.601	1.277E-03	1.309	1.130–1.516	9.084E-04
CHAD	Chondrodherin	0.800	0.707–0.906	2.331E-02	0.781	0.664–0.918	6.570E-03
CKB	Creatine kinase B-type	1.367	1.178–1.585	4.224E-03	1.423	1.153–1.757	2.506E-03
CLEC3B	Tetranectin	0.690	0.571–0.833	9.577E-03	0.526	0.326–0.847	1.681E-02
COL3A1	Collagen α−1(XXIV) chain	1.372	1.17–1.61	8.433E-03	1.825	1.484–2.244	1.433E-07
CTHRC1	Collagen triple helix repeat-containing protein 1	1.683	1.269–2.231	1.771E-02	2.150	1.543–2.996	3.773E-05
EDA2R	Tumor necrosis factor receptor superfamily member 27	1.321	1.133–1.539	1.978E-02	1.753	1.371–2.242	3.960E-05
EDN1	Endothelin-1	1.528	1.215–1.923	1.771E-02	1.965	1.450–2.664	6.105E-05
GALNT5	Polypeptide N-acetylgalactosaminyltransferase 5	1.436	1.169–1.765	2.667E-02	1.767	1.329–2.351	3.188E-04
GDF15	Growth/differentiation factor 15	1.488	1.259–1.757	1.063E-03	1.667	1.370–2.030	3.122E-06
IGFBP1	Insulin-like growth factor-binding protein 1	1.150	1.057–1.25	4.573E-02	1.132	1.024–1.252	2.746E-02
IL1RL1	Interleukin-1 receptor-like 1	1.492	1.287–1.731	1.804E-04	1.553	1.269–1.900	8.361E-05
ITGB6	Integrin β−6	1.461	1.167–1.829	3.987E-02	2.458	1.950–3.098	9.224E-13
KRT19	Keratin, type I cytoskeletal 19	1.245	1.116–1.39	8.142E-03	1.704	1.469–1.976	4.168E-11
LMOD1	Leiomodin-1	1.367	1.193–1.567	1.354E-03	1.519	1.219–1.892	6.212E-04
LRG1	Leucine-rich α−2-glycoprotein	1.588	1.266–1.992	6.677E-03	1.731	1.195–2.507	8.418E-03
LRIG3	Leucine-rich repeats and immunoglobulin-like domains protein 3	2.024	1.445–2.834	4.521E-03	1.785	1.073–2.971	4.269E-02
LTBP2	Latent transforming growth factor-β binding protein 2	1.592	1.302–1.946	1.277E-03	2.497	1.917–3.251	2.066E-10
MAMDC2	MAM domain-containing protein 2	1.465	1.199–1.79	1.234E-02	1.804	1.396–2.331	3.673E-05
MRC1	Macrophage mannose receptor 1	1.764	1.347–2.309	4.224E-03	1.936	1.261–2.755	7.215E-04
MSTN	Growth/differentiation factor 8	0.782	0.68–0.899	2.526E-02	0.801	0.666–0.963	3.176E-02
NCR3LG1	Natural cytotoxicity triggering receptor 3 ligand 1	1.515	1.229–1.867	8.142E-03	1.499	1.099–2.044	2.015E-02
NPL	N-acetylneuraminate lyase	1.355	1.142–1.609	2.502E-02	1.267	1.065–1.507	1.644E-02
NT5C1A	5′(3′)-deoxyribonucleotidase, cytosolic type	1.528	1.299–1.798	2.289E-04	1.234	1.036–1.471	3.183E-02
NTPROBNP	N-terminal pro-B-type natriuretic peptide	1.140	1.066–1.22	1.077E-02	1.192	1.088–1.306	5.207E-04
OSMR	Oncostatin-M-specific receptor subunit β	2.288	1.457–3.641	2.422E-02	2.153	1.220–3.801	1.707E-02
PPL	Periplakin	1.753	1.454–2.144	1.316E-04	1.672	1.308–2.138	1.579E-04
RBPJ3	RNA binding protein fox-1 homolog 3	1.399	1.214–1.613	1.173E-03	1.423	1.157–1.749	2.148E-03
SDC1	Syndecan-1	1.304	1.134–1.499	1.234E-02	1.644	1.389–1.946	1.053E-07
SERPINA3	α−1-antichymotrypsin	2.792	1.794–4.344	1.277E-03	4.071	2.189–7.571	4.473E-05
SFTPA1	Pulmonary surfactant-associated protein A1	1.430	1.182–1.731	1.428E-02	1.293	1.112–1.504	2.075E-03
SIGLEC8	Sialic acid-binding Ig-like lectin 8	1.507	1.238–1.833	4.521E-03	1.626	1.296–2.039	1.050E-04
TFF3	Trefoil factor 3	1.227	1.085–1.388	4.739E-02	1.278	1.060–1.541	2.032E-02
TGFBR1	TGF-β receptor type-1	1.508	1.183–1.923	3.969E-02	1.872	1.191–2.941	1.766E-03
THBS2	Thrombospondin-2	1.481	1.259–1.77	2.812E-03	1.689	1.353–2.107	2.323E-05
TNFRSF10B	Tumor necrosis factor receptor superfamily member 10B	1.322	1.14–1.533	1.348E-02	2.018	1.539–2.648	5.167E-06
VSIG2	V-set and immunoglobulin domain-containing protein 2	1.272	1.128–1.433	7.737E-03	1.217	1.043–1.421	2.375E-02
WFDC2	WAP four-disulfide core domain protein 2	1.381	1.152–1.655	2.422E-02	1.790	1.404–2.283	1.966E-05
YAP1	Yes1-associated transcriptional regulator	1.538	1.229–1.926	1.206E-02	1.876	1.333–2.639	8.760E-04

Validation cohort
44 significant proteins:
41 higher risk / 3 lower risk

Am J Respir Crit Care Med 2025; 211(8): 1452-1462.

- **Validation of 44 biomarker consistency across ILD subtypes**
  Biomarker-by-diagnosis interaction analysis

- **Minimal heterogeneity across non-IPF ILD**
- **Most biomarkers show consistent effects across subtypes**



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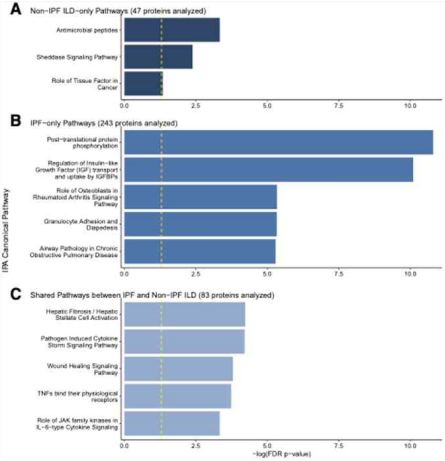

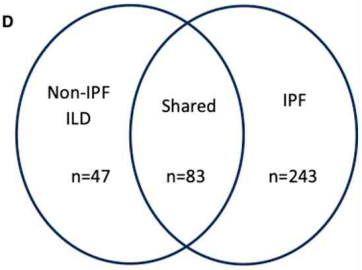

Shared pathway :**inflammation–wound healing–fibrosis axis**

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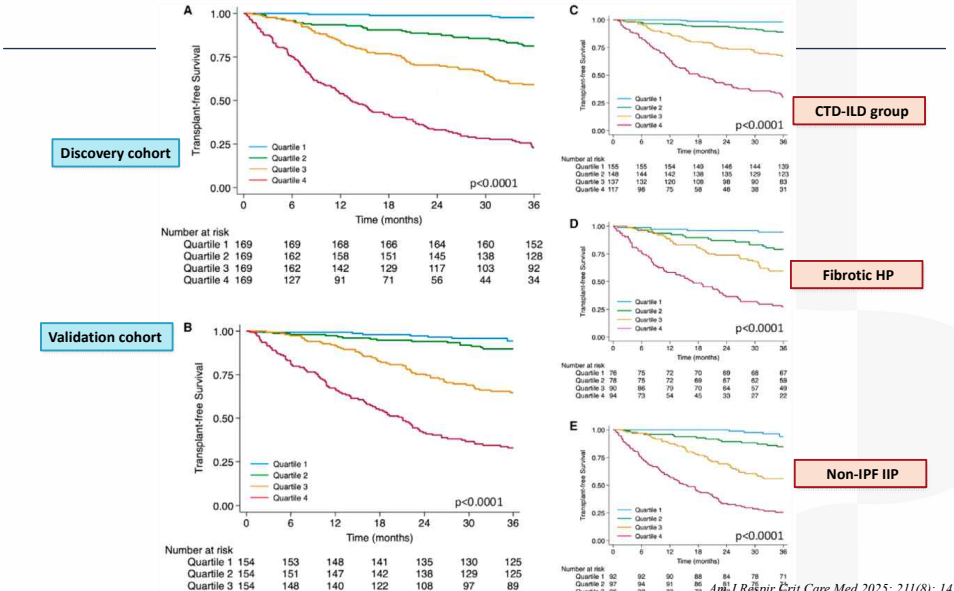

Am J Respir Crit Care Med 2025; 211(8): 1452-1462.

Summary

- ✓ Antifibrotic treatment strategies are evolving beyond nintedanib and pirfenidone.
- ✓ ILA is increasingly recognized as a clinically relevant entity that warrants appropriate evaluation and follow-up.
- ✓ The updated IIP classification highlights the importance of a more practical and integrated approach to the diagnosis of IIP.
- ✓ Proteomics is advancing the field toward biomarker-driven precision medicine in ILD.

Thank you for listening

아주대학교의료원
Ajou University Medical Center