SNUH 분당서울대학교병원
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Pulmonary hypertension associated with interstitial lung diseases

Byoung Soo Kwon
Division of Pulmonary and Critical Care Medicine
Department of Internal Medicine, Seoul National University Bundang Hospital

Disclosure of Conflict of Interest

- None to declare

Classification of Pulmonary hypertension (PH)

TABLE 2 Updated clinical classification of pulmonary hypertension (PH)

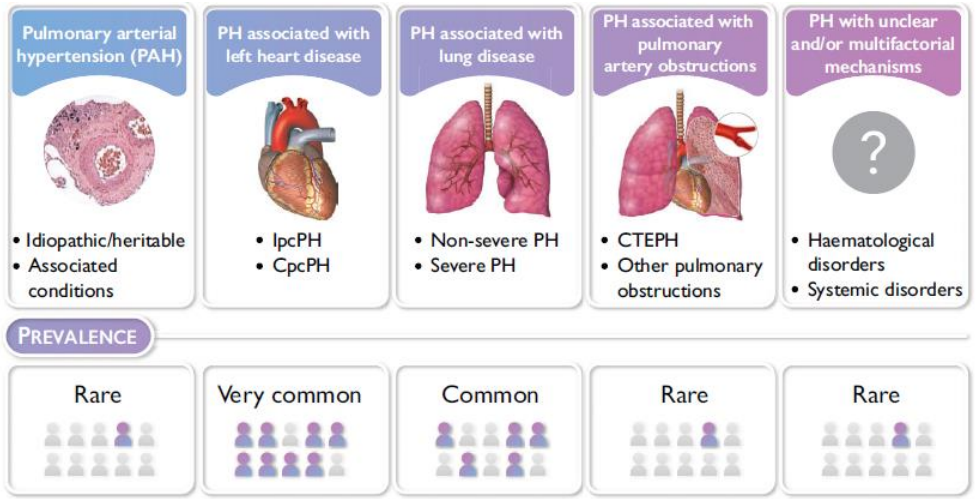
1 PAH
- 1.1 Idiopathic PAH
- 1.2 Heritable PAH
- 1.3 Drug- and toxin-induced PAH (table 3)
- 1.4 PAH associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease
  - 1.4.5 Schistosomiasis
- 1.5 PAH long-term responders to calcium channel blockers (table 4)
- 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement (table 5)
- 1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
- 2.1 PH due to heart failure with preserved LVEF
- 2.2 PH due to heart failure with reduced LVEF
- 2.3 Valvular heart disease
- 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

4 PH due to pulmonary artery obstructions (table 6)
- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions

5 PH with unclear and/or multifactorial mechanisms (table 7)
- 5.1 Haematological disorders
- 5.2 Systemic and metabolic disorders
- 5.3 Others
- 5.4 Complex congenital heart disease



3 PH due to lung diseases and/or hypoxia
- 3.1 Obstructive lung disease
- 3.2 Restrictive lung disease
- 3.3 Other lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoxia without lung disease
- 3.5 Developmental lung disorders

- Nomenclature: _____-PH

ERJ 2019 53: 1801913

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

PH in ILDs

- Early stage: 14%

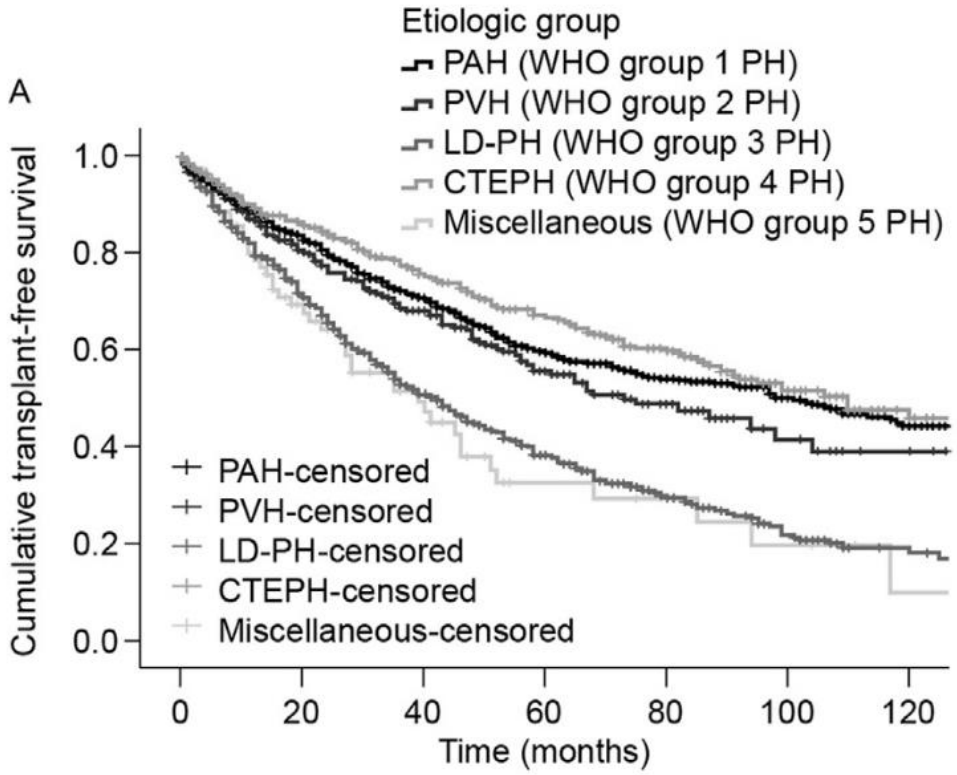
→ advanced: 50%

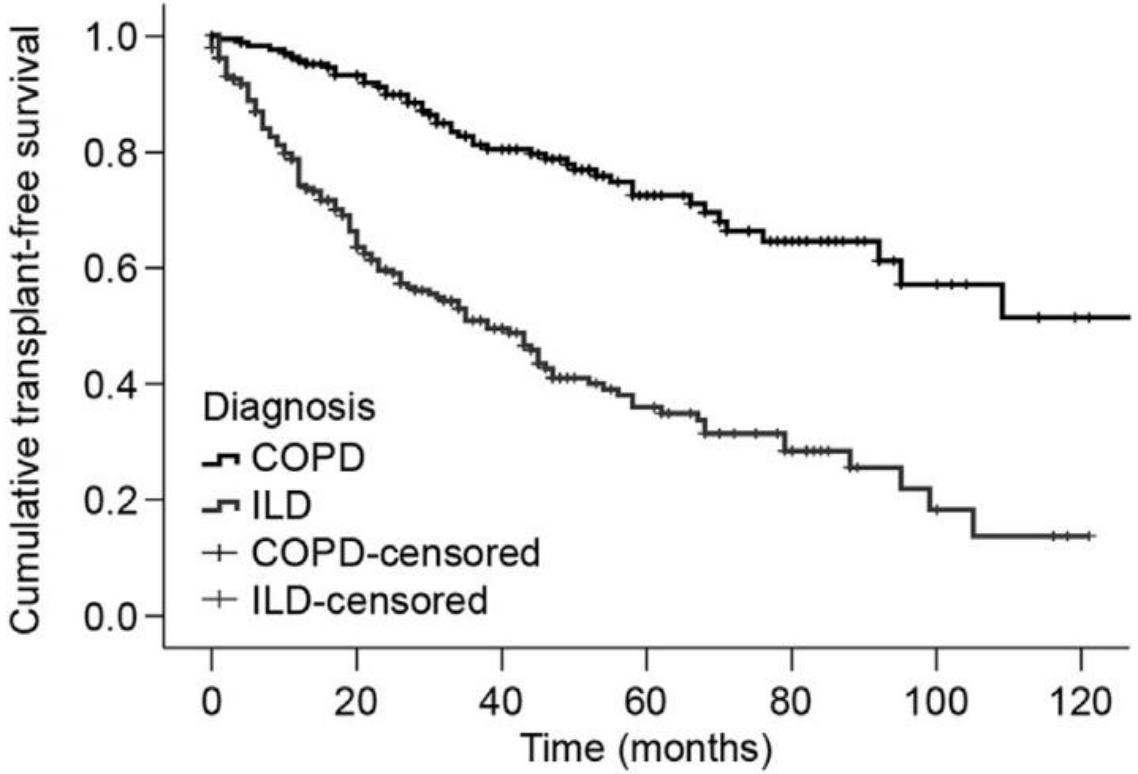
→ terminal: 80%

- Decreased exercise / functional capacity
- Oxygen requirement
- Increased risk of hospitalization
- High mortality (median survival time 0.7 yrs)

Pulmonary Circulation. 2022;12:e12127

PH in ILDs



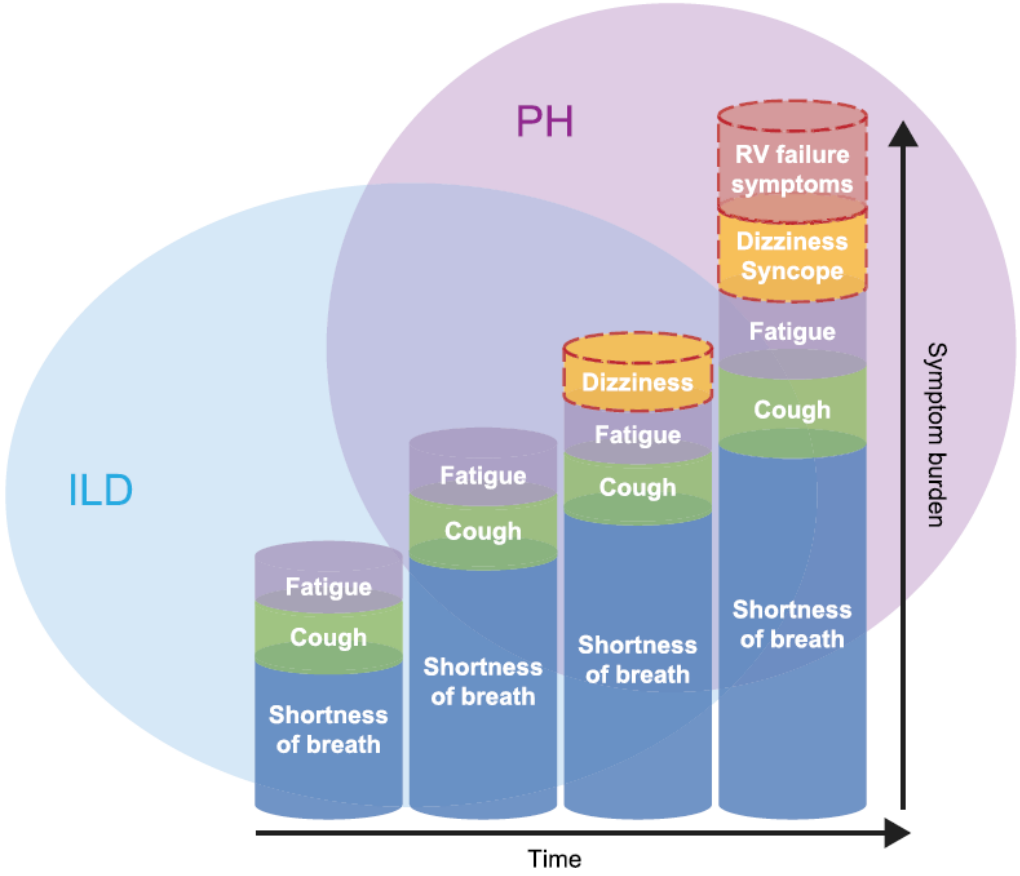


J Heart Lung Transplant 2017;36:957-967

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Overlap in symptoms

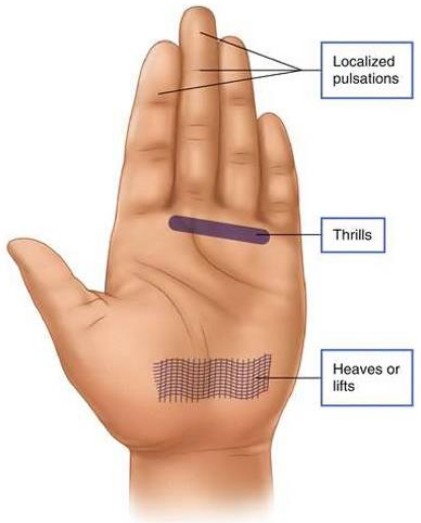


Pulmonary Circulation. 2022;12:e12127

SNUH

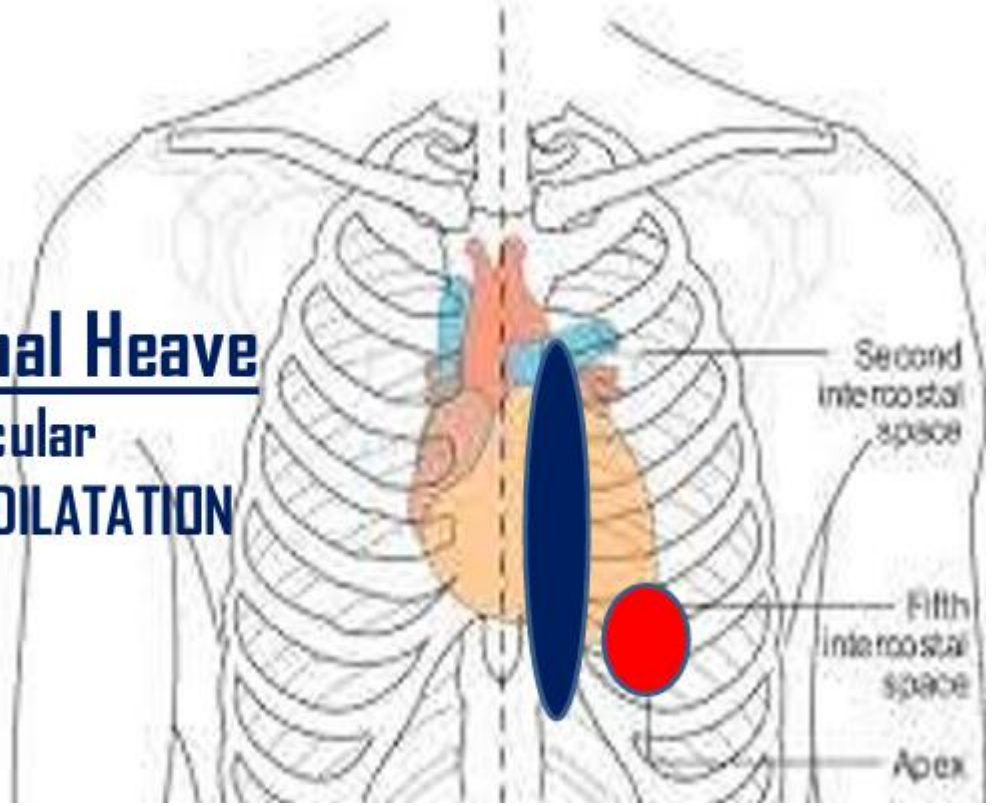
대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Physical examination



Left parasternal Heave

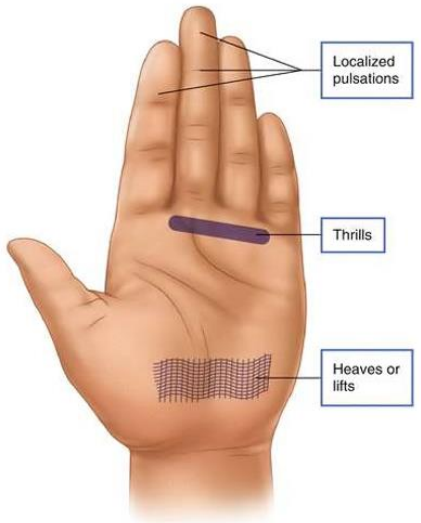
* For Right Ventricular HYPERTROPHY or DILATATION
* Pulmonary HTN



https://doctor2019.jumedicine.com/wp-content/uploads/sites/10/2022/06/Precordiumupdated.pdf

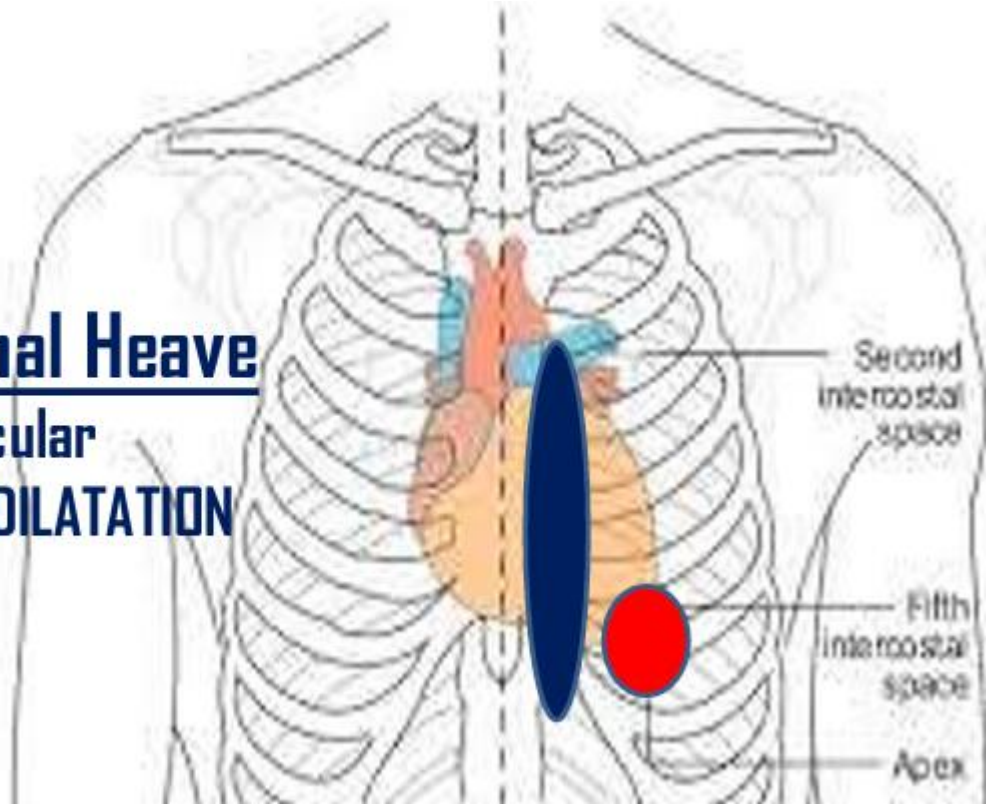
Physical examination

- Jugular venous di
  galy
  edema



Left parasternal Heave

* For Right Ventricular HYPERTROPHY or DILATATION
* Pulmonary HTN



https://doctor2019.jumedicine.com/wp-content/uploads/sites/10/2022/06/Precordiumupdated.pdf

High index of suspicion

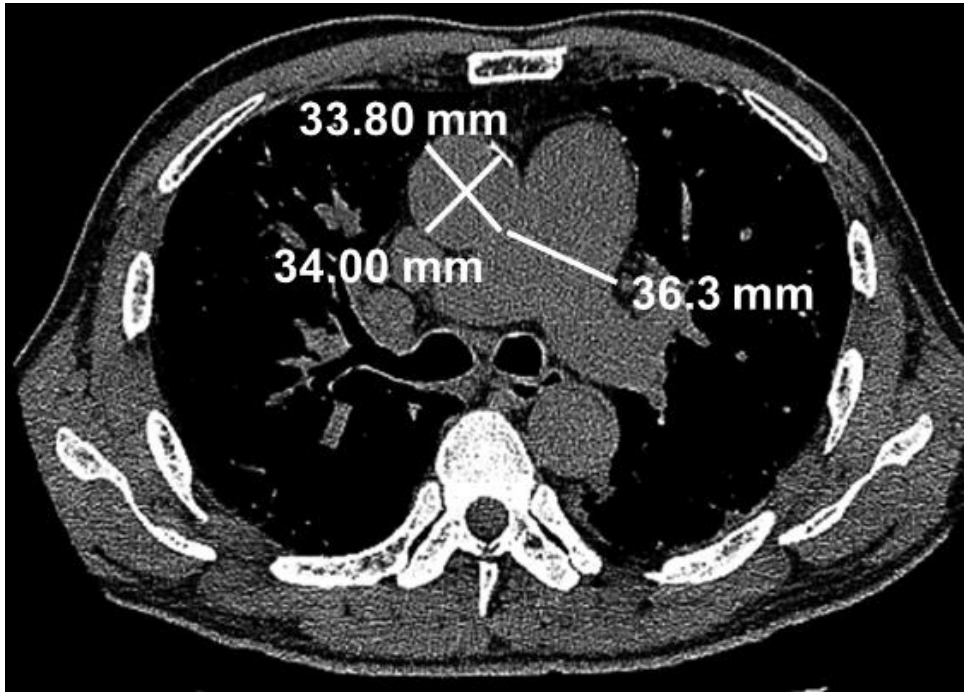
Test	Finding
PFTs	• D_{LCO} < 30% or worsening D_{LCO} in the setting of preserved lung volumes
6MWT	• Marked or worsening exertional desaturation • Severely reduced or worsening 6MWT distance • Impaired (decreased) heart rate recovery after exercise (< 13)
CT scanning	• Increased PA:A ratio (> 0.9) • RV:LV ratio > 1
Echocardiography	• RVSP elevation > 45 • RV dilation • Reduced TAPSE • RVOT diameter > 3.4 cm • Reduced RV fractional area change • Reduced RV ejection fraction on 3-D echocardiography
Laboratory testing	• Elevated BNP

Chest 2020; 158: 1651-1664

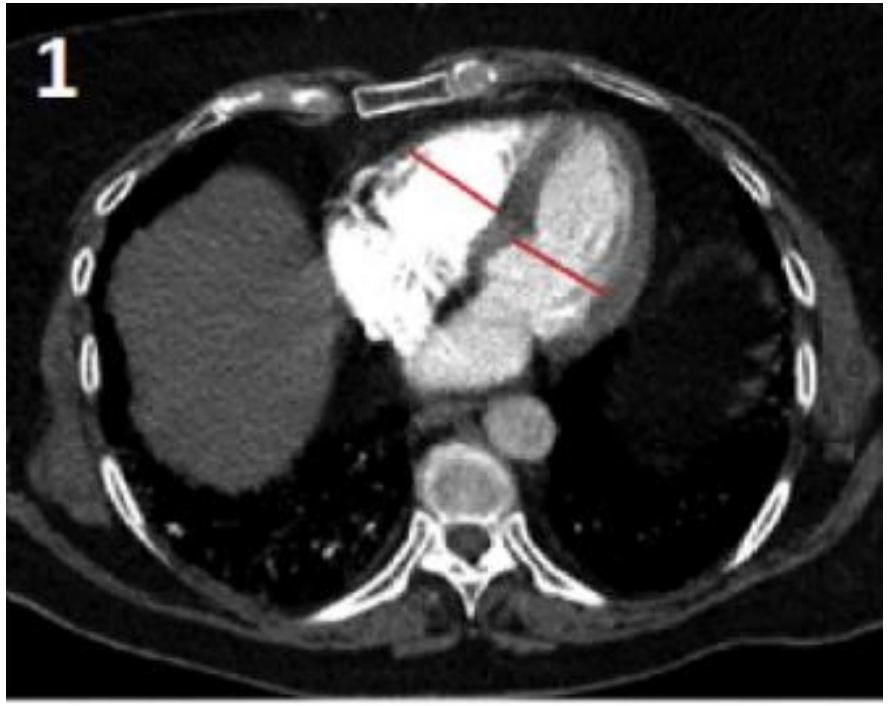
SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Early recognition of patients at risk of PH



Pulmonary artery : Aorta> 0.9



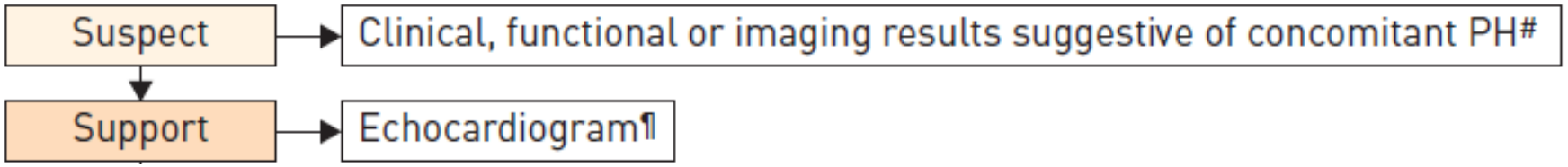
RV : LV > 1.0

Respirology. 2017;22(7):1393-1399
Chest. 2020;157(1):89-98

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Evaluation of PH

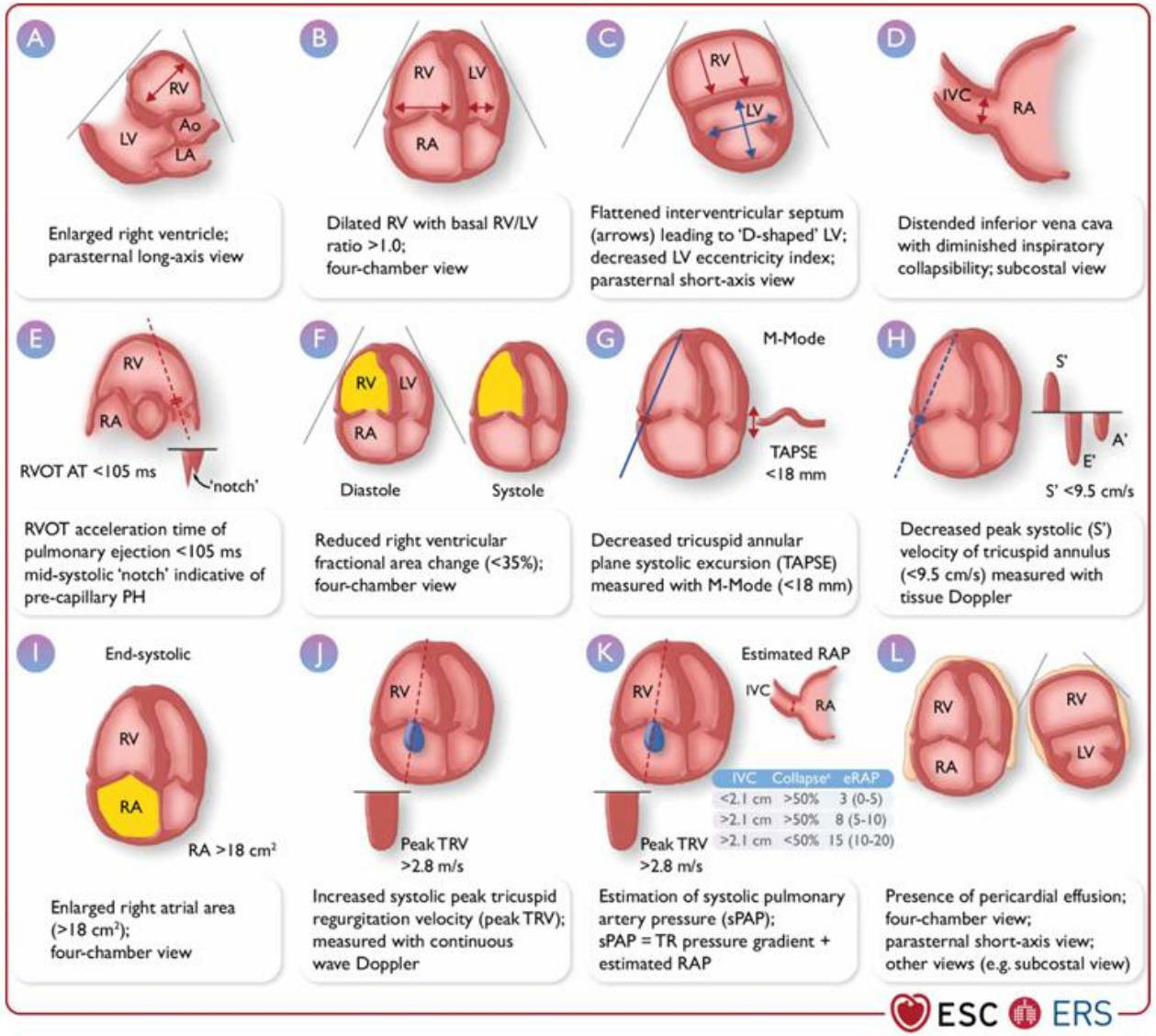


Eur Respir J 2019; 53: 1801914

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Echocardiography

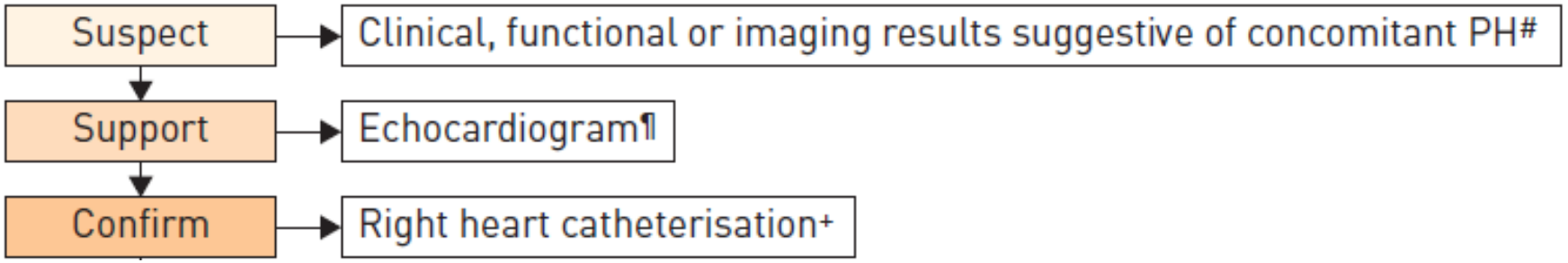


2022 ESC/ERS Guidelines

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Evaluation of PH



Eur Respir J 2019; 53: 1801914

Hemodynamic definitions: 6th WSPH*

* World symposium on pulmonary hypertension

- mPAP >20mmHg
  - Cardiac output ↑
  - L-R shunt
  - Pulmonary arterial wedge pressure ↑
  - Left heart disease
  - Hyperviscosity

+ ***Pulmonary vascular resistance (PVR) ≥ 3 Wood Unit (WU)***
  - $PVR = \frac{(mPAP - PAWP)}{cardiac\ output}$

Hemodynamic profile of PH

Definitions	Characteristics	Clinical groups[#]
Pre-capillary PH	mPAP >20 mmHg PAWP ⩽15 mmHg PVR ⩾3 WU	1, 3, 4 and 5
Isolated post-capillary PH (IpcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR <3 WU	2 and 5
Combined pre- and post-capillary PH (CpcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR ⩾3 WU	2 and 5

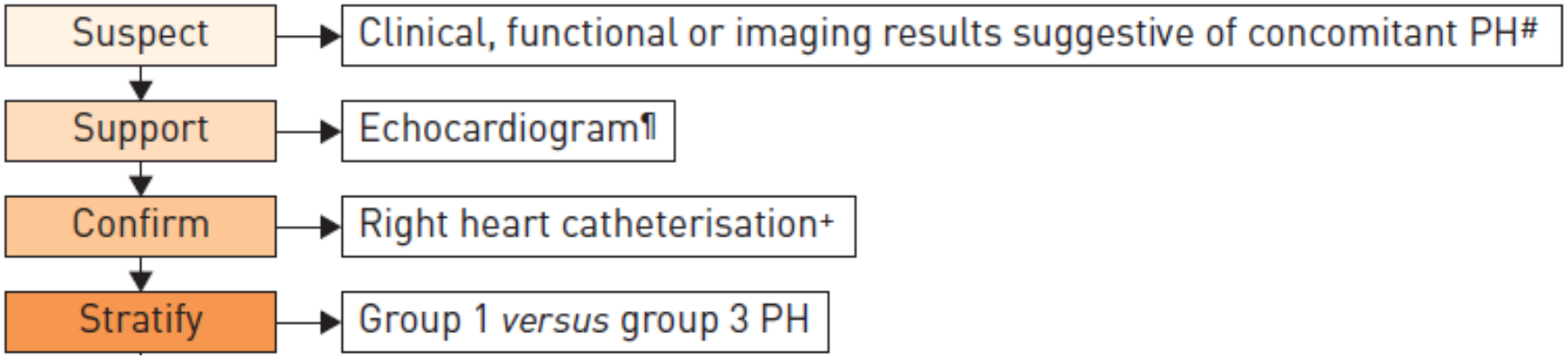
➔ No clear guidance on how discriminate between groups

Eur Respir J 2019; 53: 1801913

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Evaluation of PH



Eur Respir J 2019; 53: 1801914

Diagnosis of ILD-PH

- Right heart catheterization
  - mPAP >20 mmHg
  - Pulmonary artery occlusion pressure ≤15 mmHg
  - Pulmonary vascular resistance ≥3 WU

+ Underlying lung diseases

- **Under stable conditions! Not during acute exacerbation**

Group 1 versus group 3 pulmonary hypertension

Criteria favouring group 1 (PAH)	Testing	Criteria favouring group 3 (PH due to lung disease)
Extent of lung disease		
Normal or mildly impaired: • FEV_1 >60% pred (COPD) • FVC >70% pred (IPF) • Low diffusion capacity in relation to obstructive/restrictive changes	Pulmonary function testing	Moderate to very severely impaired: • FEV_1 <60% pred (COPD) • FVC <70% pred (IPF) • Diffusion capacity "corresponds" to obstructive/restrictive changes
Absence of or only modest airway or parenchymal abnormalities	High-resolution CT scan¶	Characteristic airway and/or parenchymal abnormalities
Haemodynamic profile		
Moderate-to-severe PH	Right heart catheterisation Echocardiogram	Mild-to-moderate PH
Ancillary testing		
Present	Further PAH risk factors (*e.g.* HIV, connective tissue disease, *BMPR2* mutations, *etc.*)	Absent
Features of exhausted circulatory reserve: • Preserved breathing reserve • Reduced oxygen pulse • Low $CO/\dot{V}O_2$ slope • Mixed venous oxygen saturation at lower limit • No change or decrease in P_{aCO_2} during exercise	Cardiopulmonary exercise test+ (P_{aCO_2} particularly relevant in COPD)	Features of exhausted ventilatory reserve: • Reduced breathing reserve • Normal oxygen pulse • Normal $CO/\dot{V}O_2$ slope • Mixed venous oxygen saturation above lower limit • Increase in P_{aCO_2} during exercise
Predominant haemodynamic profile		Predominant obstructive/restrictive profile

Eur Respir J 2019; 53: 1801913

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Severity assessment

Severe PH	non-severe PH
PVR >5 WU	PVR ≤5 WU
<10% in advanced ILD	Common in advanced COPD

2022 ESC/ERS guideline

Pulmonary hypertension associated with lung disease and/or hypoxia – Recommendation Table 23				
R	Echocardiography is recommended for the non-invasive diagnostic assessment of suspected PH in patients with lung disease	I	If PH is suspected in patients with lung disease, it is recommended that echocardiography[d] be performed and the results interpreted in conjunction with ABG, PFTs including DLCO, and CT imaging	I
R	Optimal treatment of the underlying lung disease, including long-term O_2 therapy in patients with chronic hypoxaemia, is recommended in patients with PH due to lung diseases	I	In patients with lung disease and suspected PH, it is recommended to optimize treatment of the underlying lung disease and, where indicated, hypoxaemia, sleep-disordered breathing, and/or alveolar hypoventilation	I
R	Referral to an expert centre is recommended in patients with echocardiographic signs of severe PH and/or severe right ventricular dysfunction	I	In patients with lung disease and suspected severe PH, or where there is uncertainty regarding the treatment of PH, referral to a PH centre is recommended[e]	I
N			In patients with lung disease and severe PH, an individualized approach to treatment is recommended	I
N			It is recommended to refer eligible patients with lung disease and PH for LTx evaluation	I

2022 ESC/ERS Guidelines

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

2022 ESC/ERS guideline

Pulmonary hypertension associated with lung disease and/or hypoxia – Recommendation Table 23				
R	RHC is not recommended for suspected PH in patients with lung disease, unless therapeutic consequences are to be expected (e.g. LTx, alternative diagnoses such as PAH or CTEPH, and potential enrolment in a clinical trial)	III	In patients with lung disease and suspected PH, RHC is recommended if the results are expected to aid management decisions	I

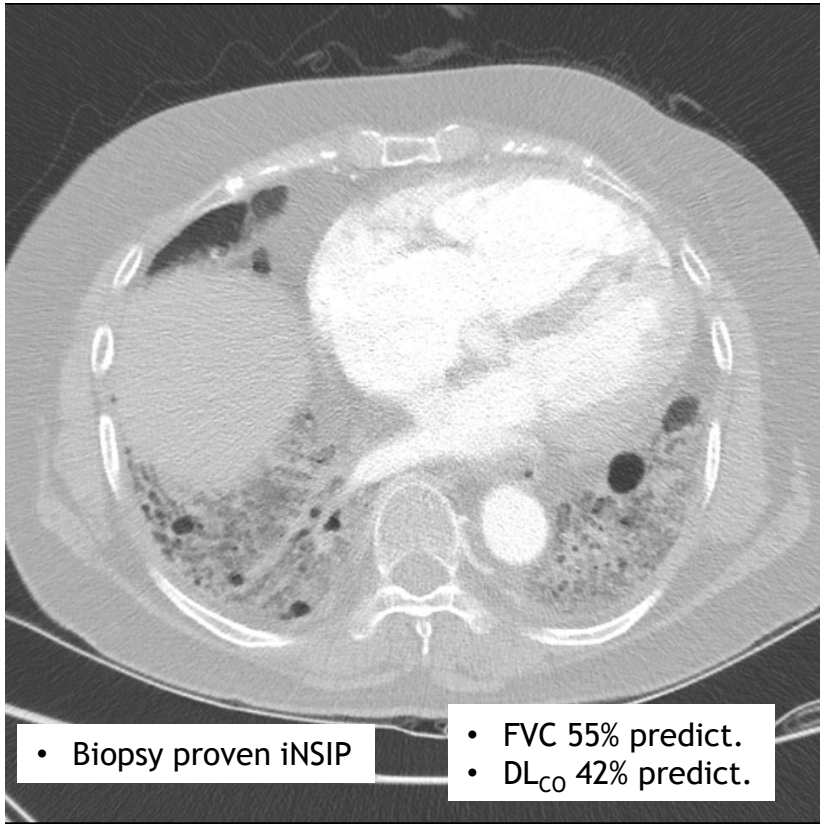
- Indication for RHC
  - Assessment for surgical treatment (e.g. lung transplantation)
  - Suspected PAH or CTEPH
  - Consideration of therapeutic interventions

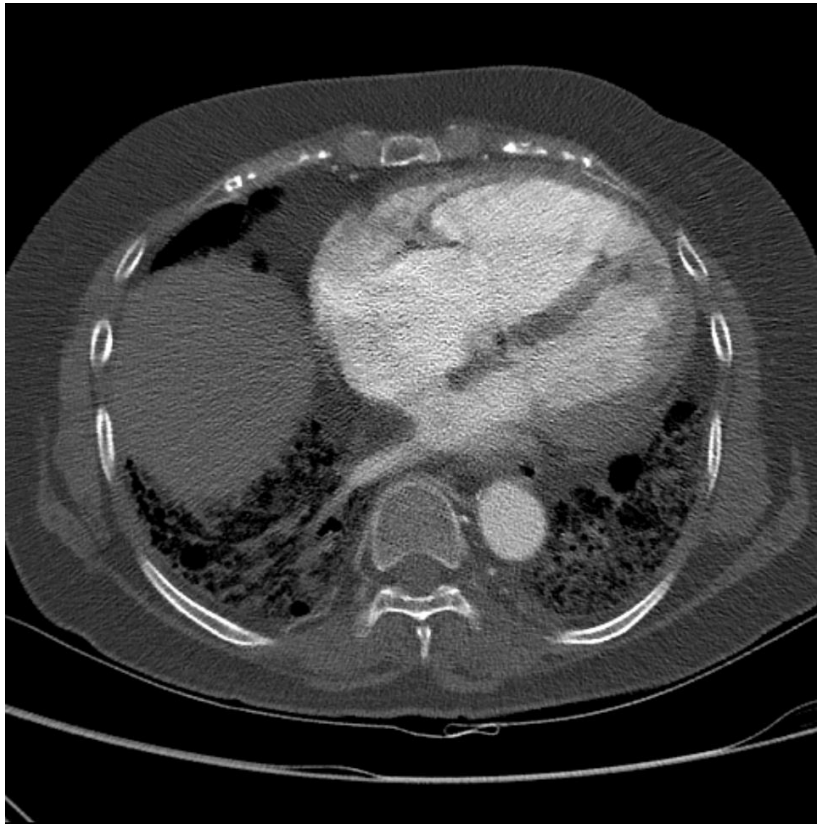
2022 ESC/ERS Guidelines

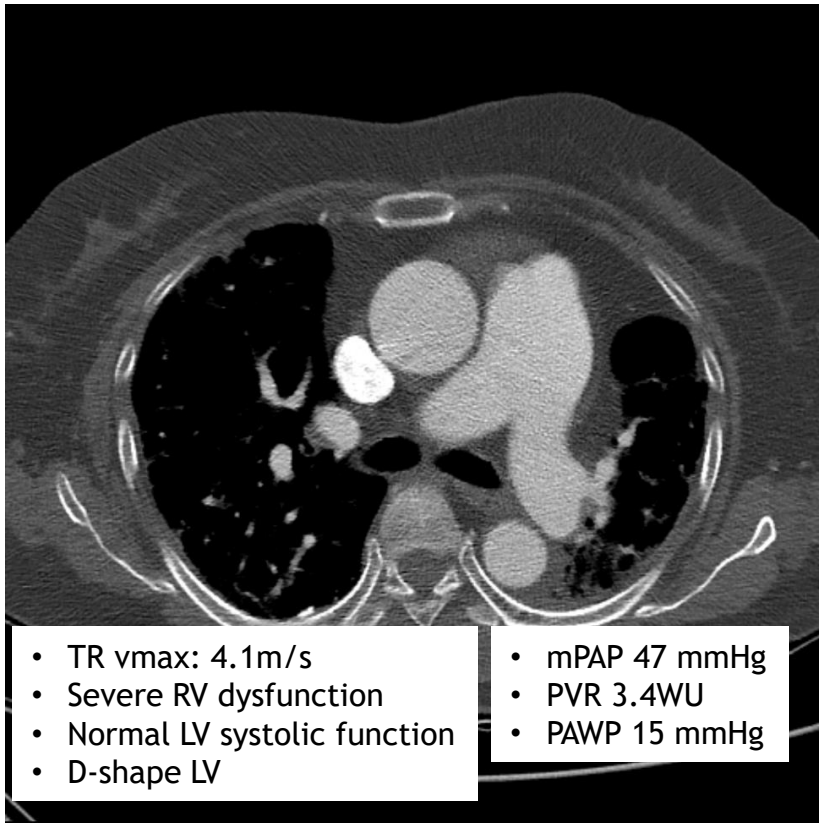
SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Case (60/F)


• Biopsy proven iNSIP
• FVC 55% predict.
• DL_{CO} 42% predict.



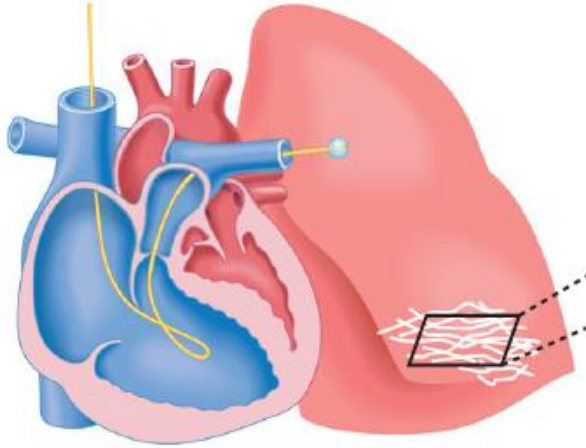

• TR vmax: 4.1m/s
• Severe RV dysfunction
• Normal LV systolic function
• D-shape LV
• mPAP 47 mmHg
• PVR 3.4WU
• PAWP 15 mmHg

Pulmonary vasculopathy and lung fibrosis

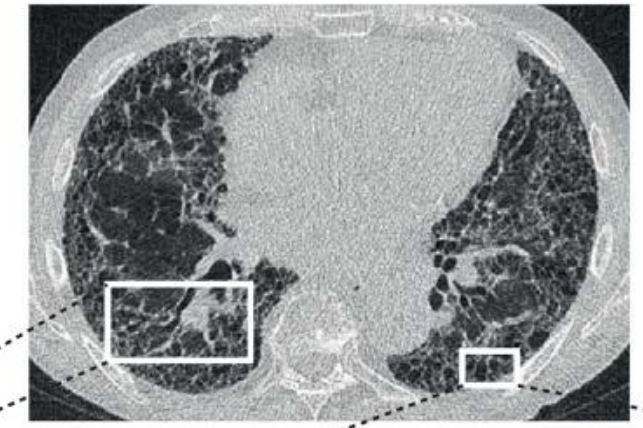
PH due to interstitial lung disease

RV dilatation and maladaptation due to elevated pulmonary vascular resistance and pressure defined by right heart catheter measurement

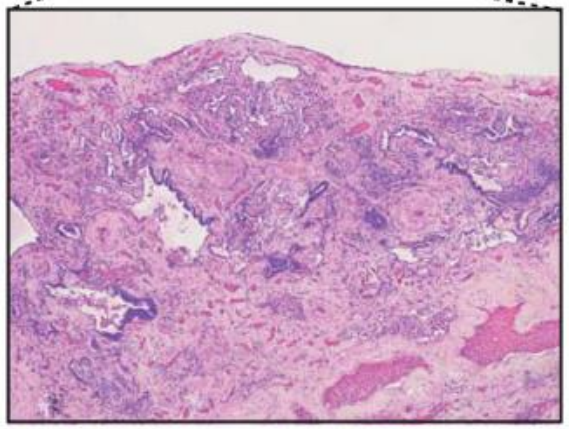
Pulmonary artery catheter

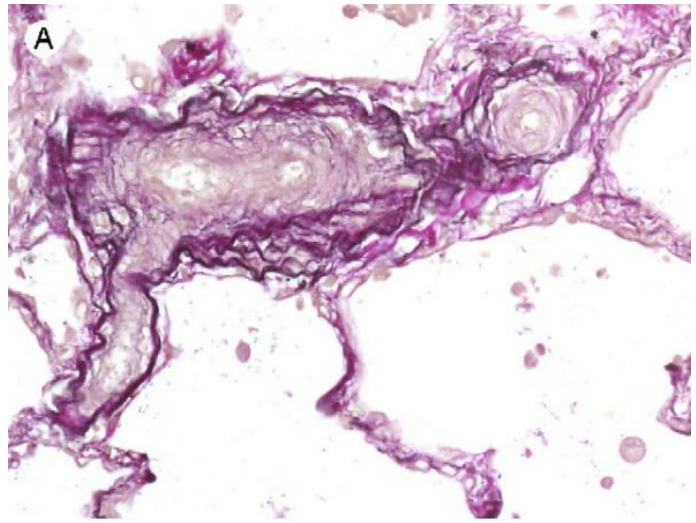


Fibrotic lung disease on HRCT



Characteristic histopathological finding of both lung parenchymal fibrosis and vascular remodeling



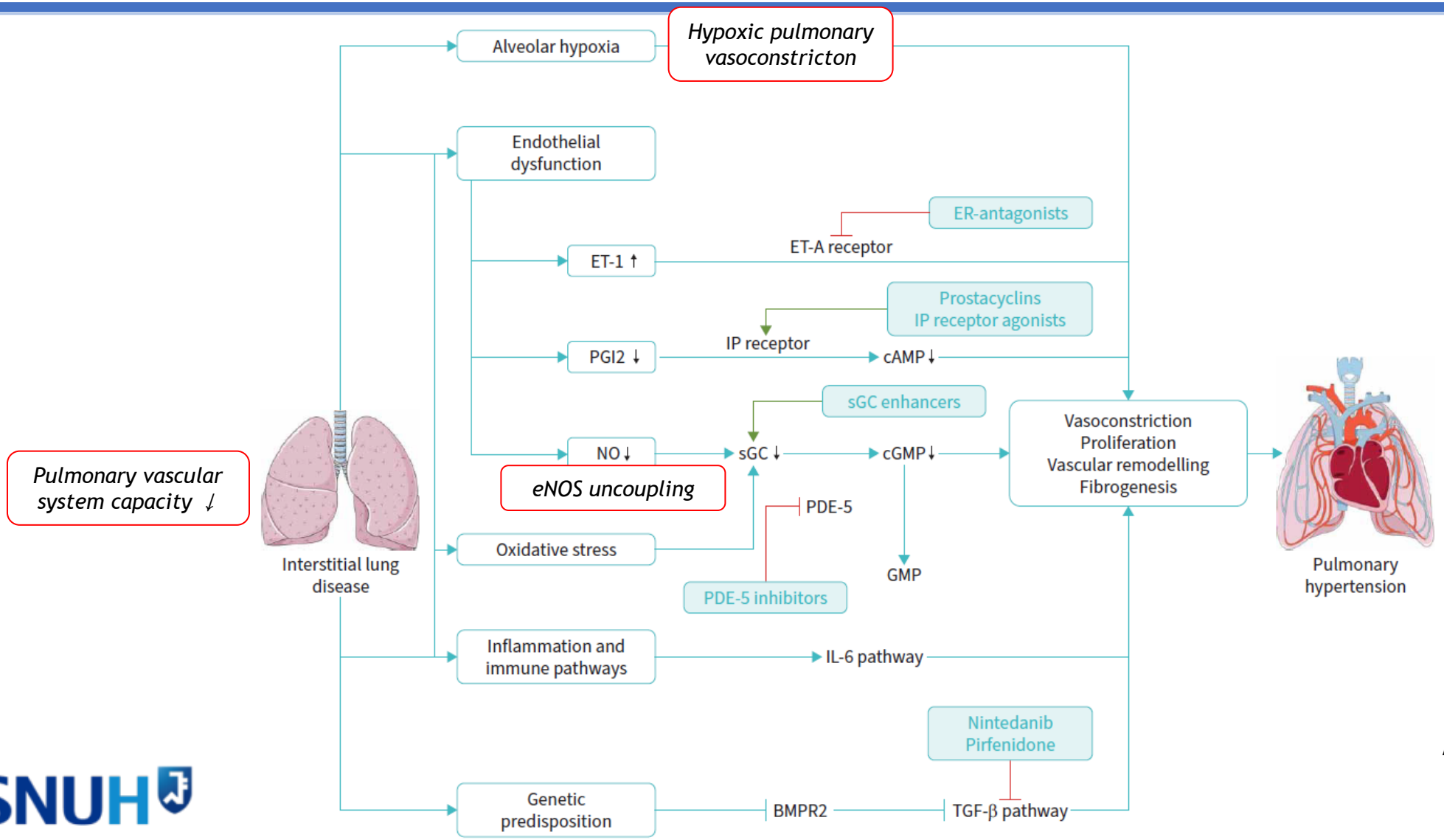


Pulmonary Circulation. 2022;12:e12127
Human Pathology (2007) 38, 60 – 65

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Pathophysiology, shared mechanism



ERJ Open Res 2022; 8: 00272-2022

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Treatment

- Group 3 PH
  - Treat the underlying lung diseases
  - Long-term oxygen therapy
  - Pulmonary rehabilitation
  - Associated comorbidities
    - Thromboembolic disease
    - Sleep disorder
  - **Pulmonary vasodilators ?**

Treatment

- **Against**
  - V/Q mismatch
  - Pulmonary edema

- **For**
  - Supplementary O_2
  - PVR ↓ & C.O ↑ → oxygen delivery ↑

Inhaled treprostinil may be considered in patients with PH associated with ILD[734]			IIb	B
The use of ambrisentan is not recommended in patients with PH associated with IPF[740]			III	B
The use of riociguat is not recommended in patients with PH associated with IIP[181]			III	B
The use of PAH medication is not recommended in patients with lung disease and non-severe PH[e]			III	C
PDE5is may be considered in patients with severe PH associated with ILD (individual decision-making in PH centres)	Very low	Conditional	IIb	C
The use of PDE5is in patients with ILD and non-severe PH is not recommended	Very low	Conditional	III	C

2022 ESC/ERS Guidelines

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i

- STEP-IPF

- IPF with
- DL_{CO}<35%
- 6-min walking distance ≥50m
- Resting SpO_2 ≥92%

sildenafil 20mg tid

Period #1 - 12 wks
Period #2 - 12 wks

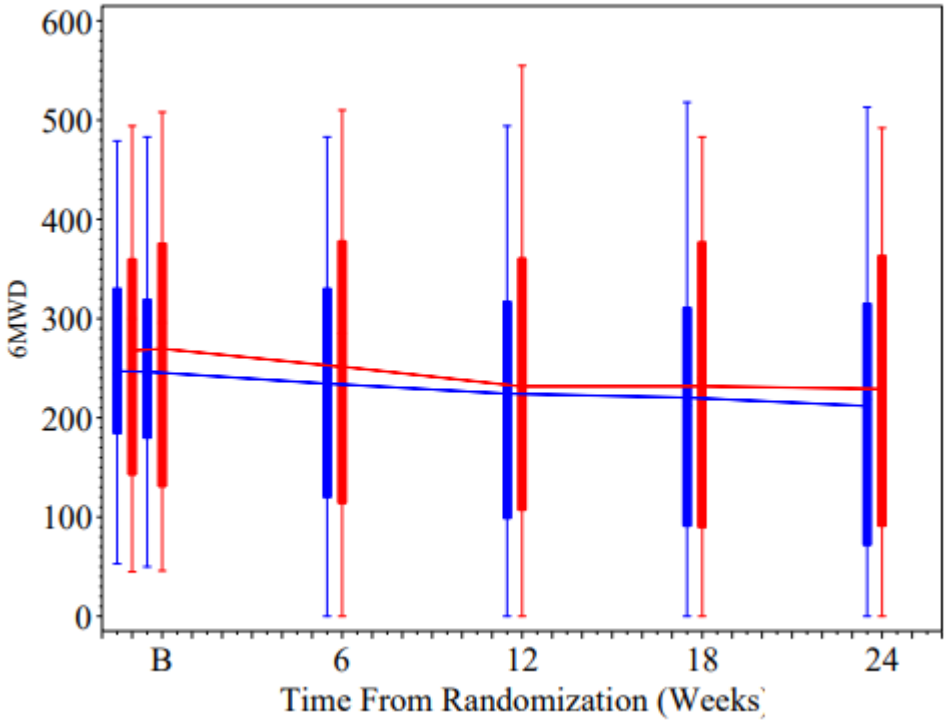
- Primary outcome
  - Improvement of >20% in 6mwt
- Secondary outcomes
  - Change in 6mwd
  - Degree of dyspnea
  - Quality of life

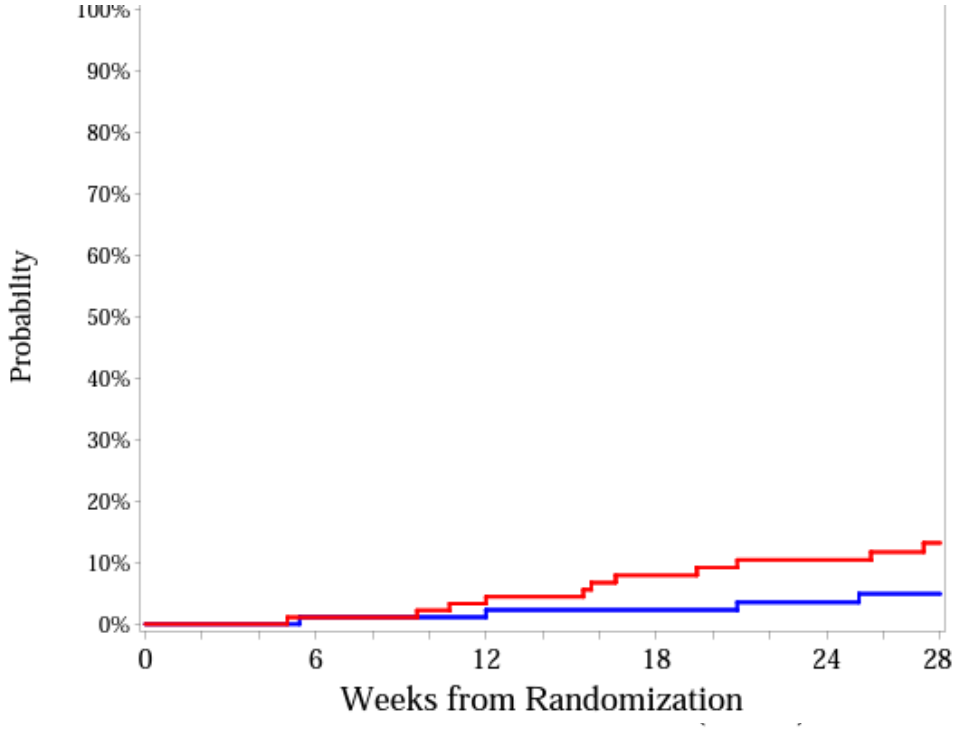
N Engl J Med 2010;363:620-8

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i





N Engl J Med 2010;363:620-8

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i + antifibrotics

- INSTAGE

- IPF with DL_{CO} ≤ *35%*

nintedanib
150mg bid
+- sildenafil
20mg tid

24 wks

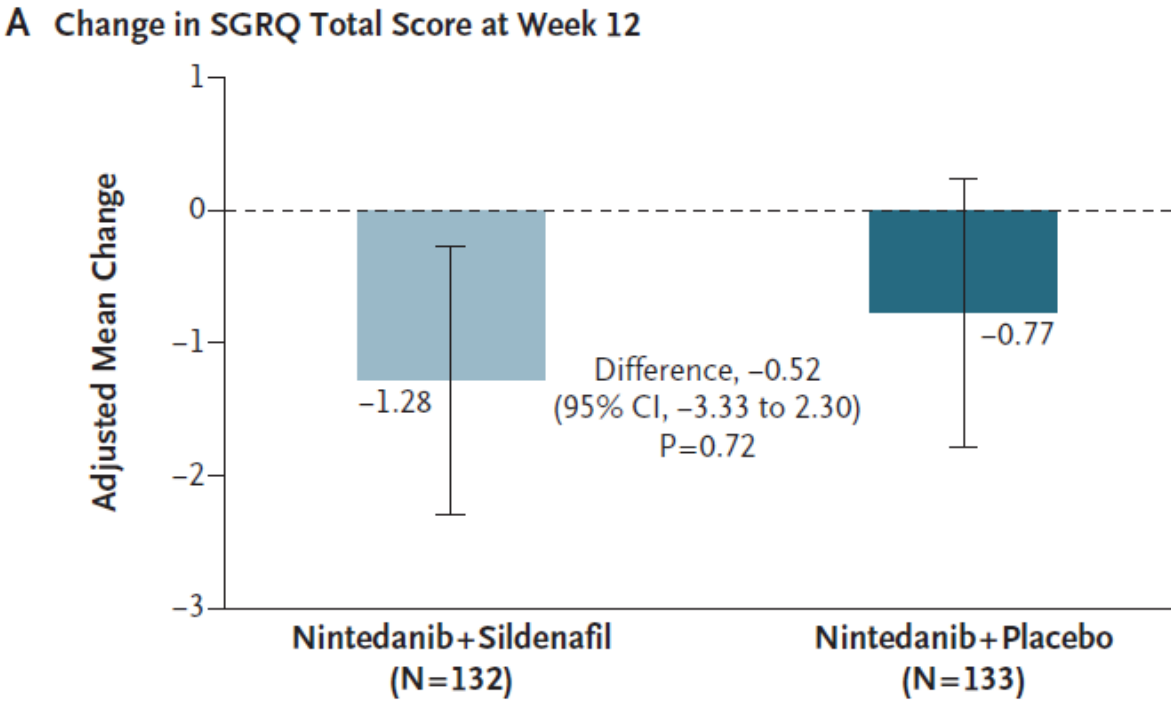
- Primary outcome
  - SGRQ total score at 12 wk
- Secondary outcomes
  - SGRQ at 24 wk
  - UCSD-SOBQ
  - Serious adverse event

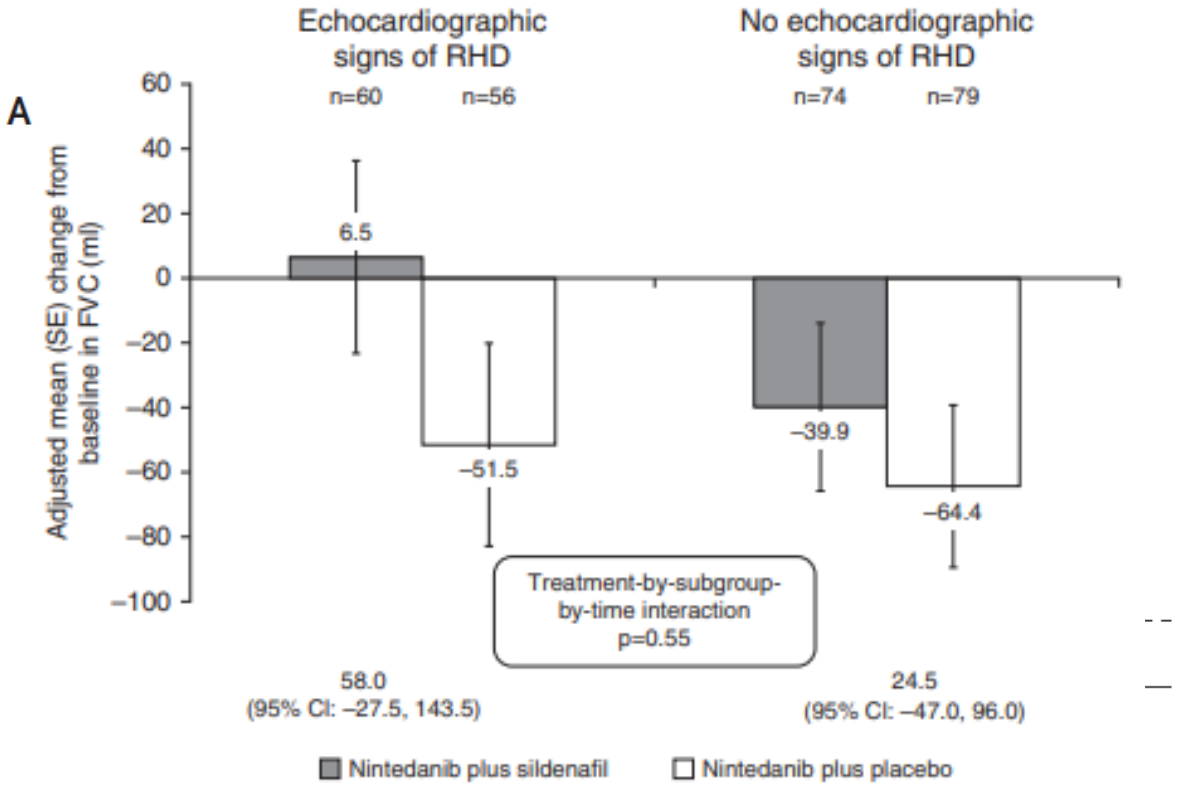
N Engl J Med 2018;379:1722-31

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i + antifibrotics





+ absolute decline of FVC >5% or death : HR 0.56 (0.38 – 0.82)

N Engl J Med 2018;379:1722-31
AJRCCM 2019;15;200(12):1505-1512

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i + antifibrotics

- IPF with DL_{CO} ≤ *40% and at risk PH*

  ** mPAP ≥ 20mmHg and pcwp ≤ 15mmHg or high probability of PH on echoCG*

pirfenidone
801mg tid
+- sildenafil
20mg tid

52 wks

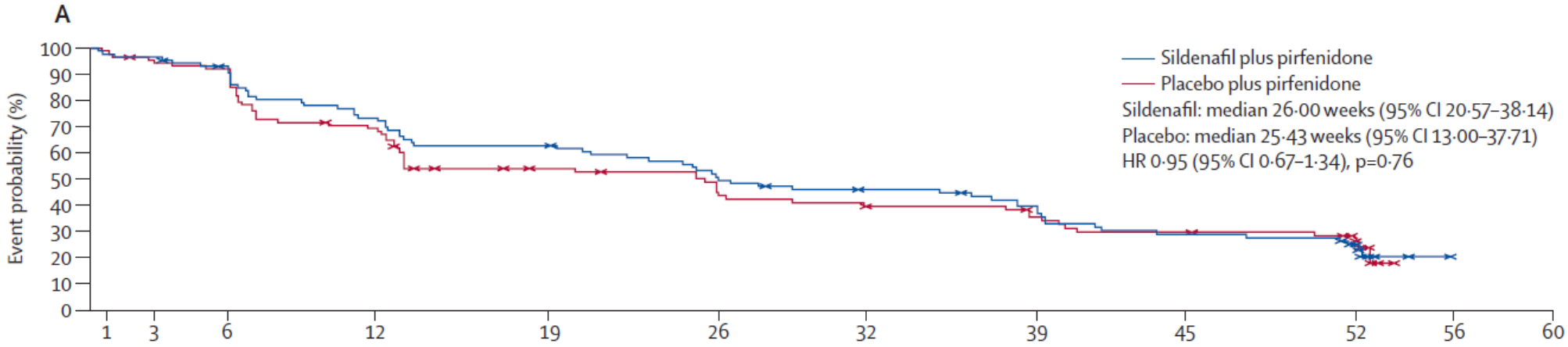
- Primary outcome
  - Disease progression
    - Decline in 6mwt
    + respiratory-related adm.
    + all-cause mortality
- Secondary outcomes
  - Individual components
  - Echocardiography parameter
  - PFT
  - SGRQ, UCSD-SOBQ

Lancet 2021;9(4):e38

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - PDE5i + antifibrotics



Number at risk (number censored)												
Sildenafil plus pirfenidone	86 (0)	85 (0)	78 (2)	63 (2)	54 (2)	41 (4)	36 (6)	28 (7)	22 (7)	12 (14)	0 (24)	..
Placebo plus pirfenidone	88 (0)	83 (1)	81 (1)	60 (2)	42 (7)	33 (8)	29 (9)	25 (10)	21 (10)	10 (19)	0 (27)	..

Lancet 2021;9(4):e38

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trial - ERA

- ARTEMIS-IPF

- IPF with minimal honeycombing

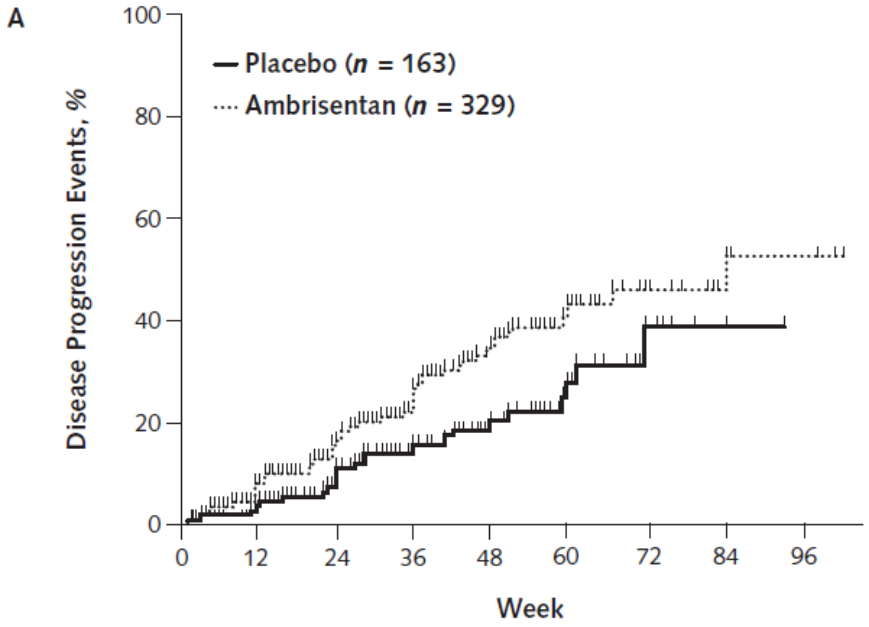
Ambrisentan
10mg qd

16 wks

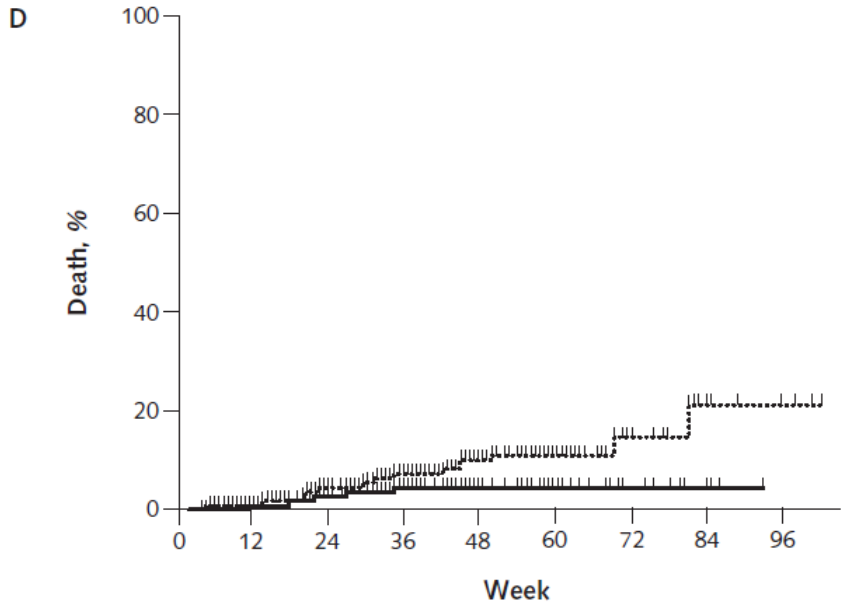
- Primary outcome
  - IPF progression
    - All-cause death
    - Respiratory-related adm
    - Lung function decline
- Secondary outcomes
  - Change in FVC, DL_{CO}, 6mwt

Ann Intern Med. 2013;158:641-649

Clinical trial - ERA



Patients, *n*								
Placebo	143	110	76	47	27	8	4	0
Ambrisentan	271	204	140	81	42	15	8	3



Patients, *n*								
Placebo	145	115	85	56	31	11	5	0
Ambrisentan	278	228	168	110	58	23	10	4

Ann Intern Med. 2013;158:641-649

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trial - ERA

- BPHIT

- IIP with RHC confirmed PH

** mPAP ≥ 25mmHg and pcwp ≤ 15mmHg*

Bosentan 125mg bid

16 wks

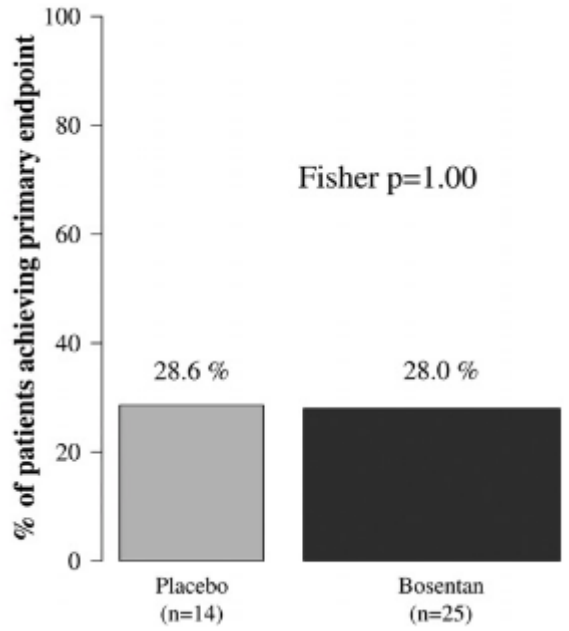
- Primary outcome
  - Decrease in PVRi ≥20%
- Secondary outcomes
  - mPAP, RA pressure, absol. PVRi
  - 6mwt
  - Quality of life
  - Lung functions
  - O_2 saturation, BNP

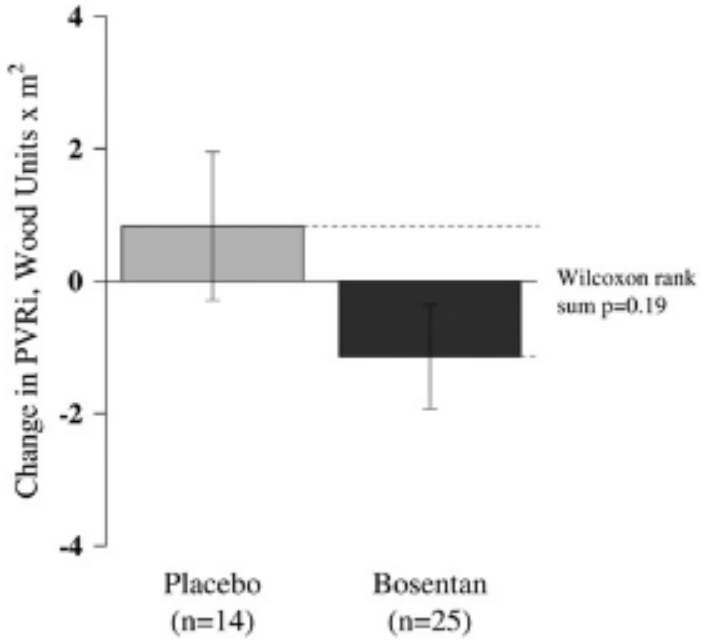
AJRCCM. 2014 Jul 15;190(2):208-17

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trial - ERA





- $PVRi = \frac{(mPAP - LApr)}{cardiac\ index}$

AJRCCM. 2014 Jul 15;190(2):208-17

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trials - guanylate cyclase stimulator

- RISE-IIP

- PH-IIP confirmed by RHC
- FVC ≥45%
- 6-min walking distance ≥150m
- sBP ≥95mmHg

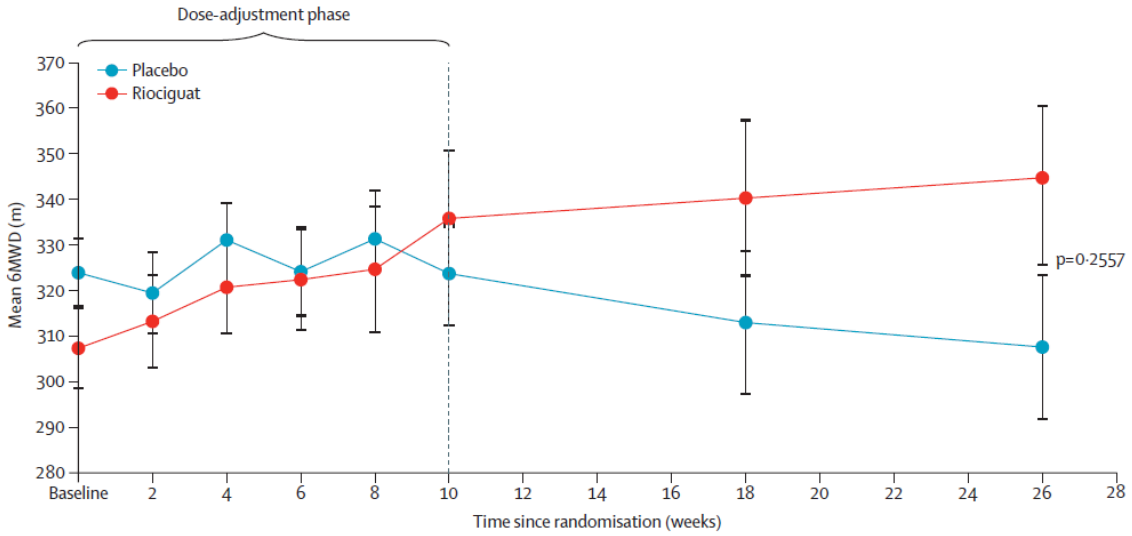
riociguat 0.5-2.5 mg tid

Main study- 26 wks
Open-label extension

- Primary outcome
  - Mean change in 6mwd
- Secondary outcomes
  - Clinical worsening
    - All-cause mortality
    - Hospital admission
  - >15% decrease in 6mwd

Lancet Respir Med 2019;7: 780-90

Clinical trials - guanylate cyclase stimulator



Number of patients															
Placebo	74	73	66	60	53	50	..	..	..	40	..	..	..	38	..
Riociguat	73	69	64	57	48	43	..	..	..	34	..	..	..	31	..
Mean (SD) absolute 6MWD, m															
Placebo	324 (66)	320 (77)	331 (68)	324 (77)	332 (78)	324 (81)	..	..	..	313 (100)	..	..	..	308 (98)	..
Riociguat	307 (80)	313 (87)	321 (81)	323 (86)	325 (97)	336 (99)	..	..	..	340 (101)	..	..	..	345 (107)	..

	Main phase		Long-term extension phase*	
	Riociguat up to 2·5 mg (n=73)	Placebo (n=74)	Riociguat up to 2·5 mg (n=32)	Former placebo (n=38)
Any AE	65 (89%)	64 (86%)	29 (91%)	34 (89%)
Study drug-related AEs	29 (40%)	28 (38%)	12 (38%)	18 (47%)
AEs leading to study drug discontinuation	11 (15%)	3 (4%)	1 (3%)	4 (11%)
Any SAE	27 (37%)	17 (23%)	12 (38%)	21 (55%)
Study drug-related SAEs	5 (7%)	4 (5%)	3 (9%)	5 (13%)
SAEs leading to study drug discontinuation	10 (14%)	1 (1%)	1 (3%)	2 (5%)
Deaths	8 (11%)	3 (4%)	1 (3%)	8 (21%)

Data are n (%). AE=adverse event. SAE=serious adverse event. *Both groups received riociguat up to 2·5 mg three times daily. †A riociguat and immediately started the safety follow-up phase. The length of the safety follow-up ranged from 30 to 120 days.

Lancet Respir Med 2019;7: 780–90

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Clinical trial - summary

Ambrisentan

- Disease progression ↑
- Respiratory hospitalization ↑

Bosentan

- Hemodynamics →
- Functional capacity / sx →

Riociguat

- Serious adverse events ↑
- Death ↑
- 6mwt →

Sildenafil

- 6mwt →
- Quality of life ↑
- PaO_2 ↑
- DL_{CO} ↑

Sildenafil + nintedanib

- Functional capacity / sx →
- Death and/or decline in FVC<5% ↓

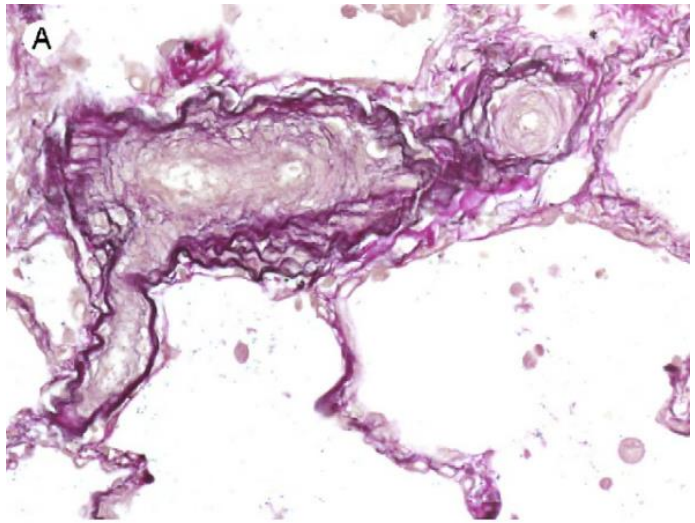
~~*Endothelin receptor antagonists*~~ ~~*Soluble guanylate stimulator*~~ *Phosphodiesterase 5 inhibitor*

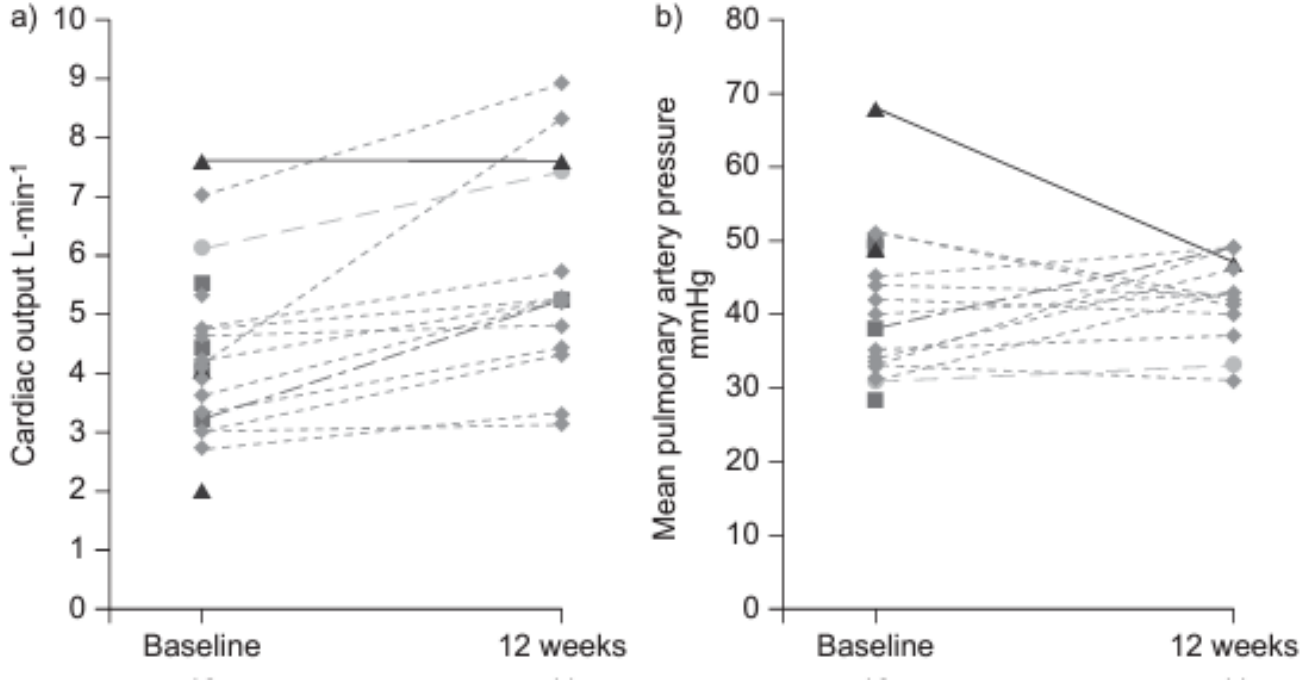
→Unlikely to be harmful, may be beneficial

Worsening of V-Q mismatching ?

Parameter	Mean change from baseline to week 26 (SD)			
	Riociguat (n=73)	n	Placebo (n=74)	n
PCO_2, mm Hg	0·1 (7·0)	33	0·4 (3·9)	38
PaO_2, mm Hg	–0·5 (21·0)	33	–10·4 (24·9)	38
SaO_2, %	1·1 (10·2)	33	–4·0 (6·0)	37
SpO_2, %*	–5·7 (6·9)	29	–5·7 (7·1)	34
FVC, % predicted	–1·3 (9·5)	33	–2·1 (6·0)	37
FEV_1, % predicted	–1·8 (8·7)	33	–2·6 (6·3)	37

Pulmonary venous fibrosis ?





Human Pathology (2007) 38, 60 – 65
Eur Respir J 2013; 41: 853-860

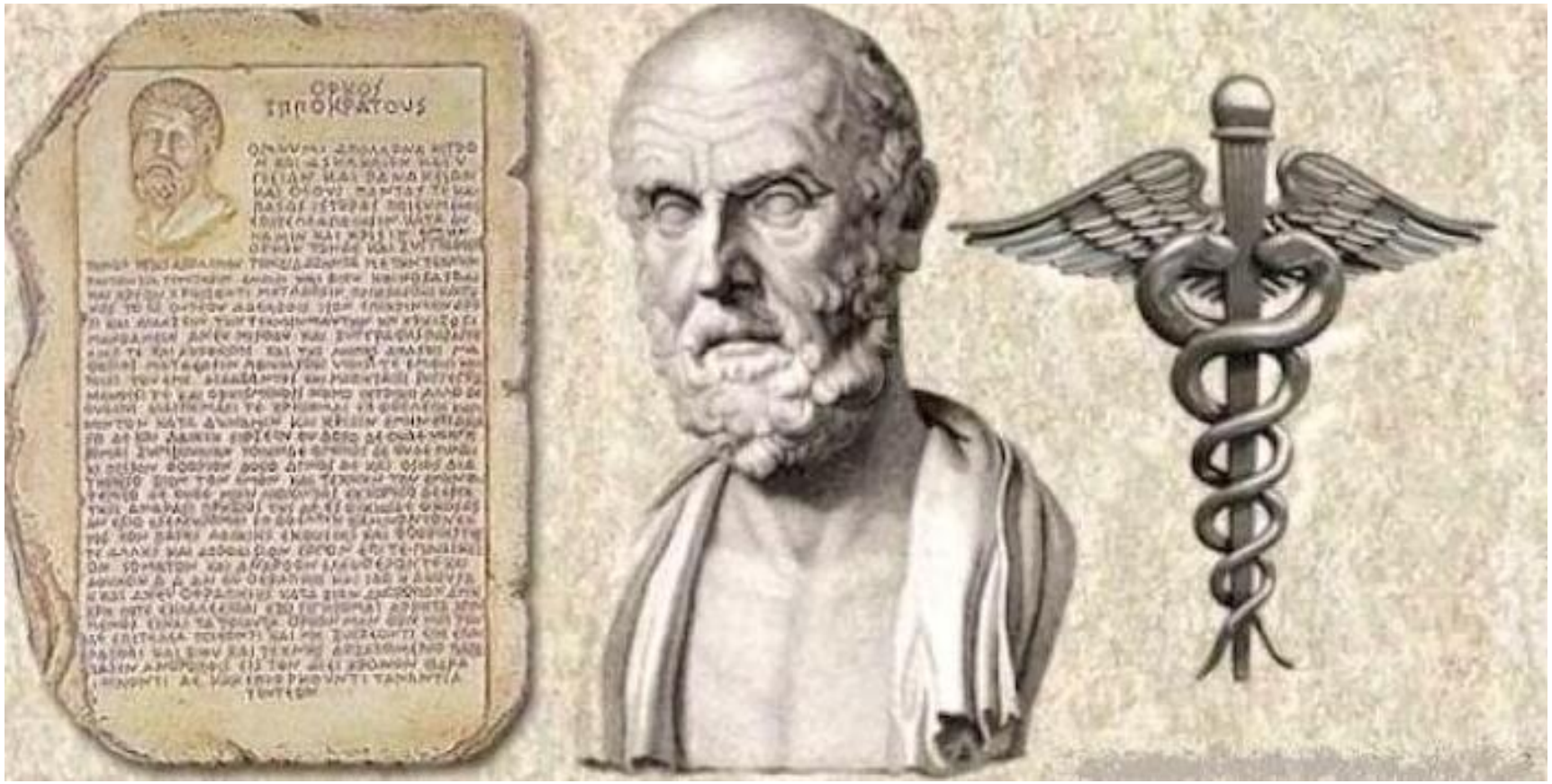
SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

The optimal endpoint ?

- Hemodynamic parameter
- Functional / emotional
- Survival – all-cause, PH-related
- Composite outcomes

Do no harm



Is effective treatment an impossible dream ?

- INCREASE study

- ILDs confirmed by RHC
- FVC <70%
- 6-min walking distance ≥100m

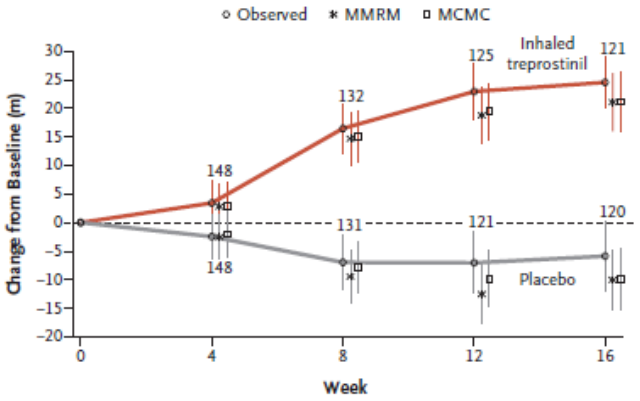
Inhaled treprostinil
9 times(6ug/breath)
q 6 hrs

16 wks

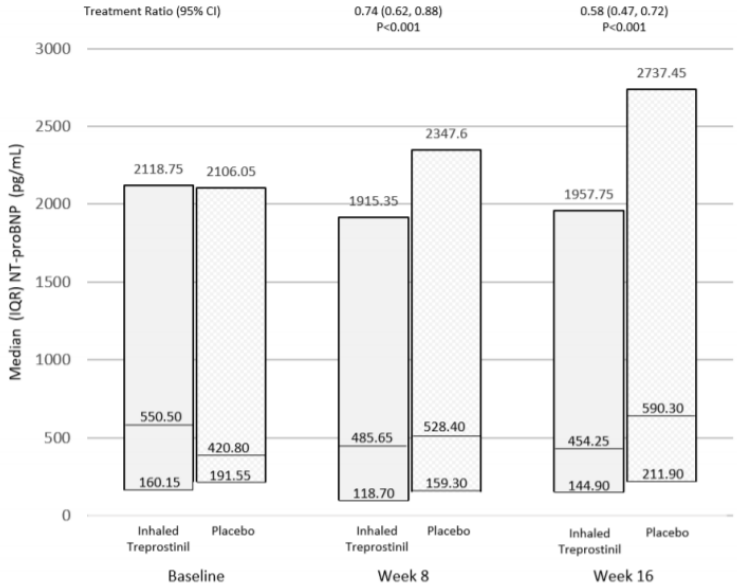
- Primary outcome
  - Change in 6mwd
- Secondary outcomes
  - Clinical worsening
    - All-cause mortality
    - Hospital admission
    - >15% decrease in 6mwd
  - Change in NT-proBNP

N Engl J Med 2021;384:325-34

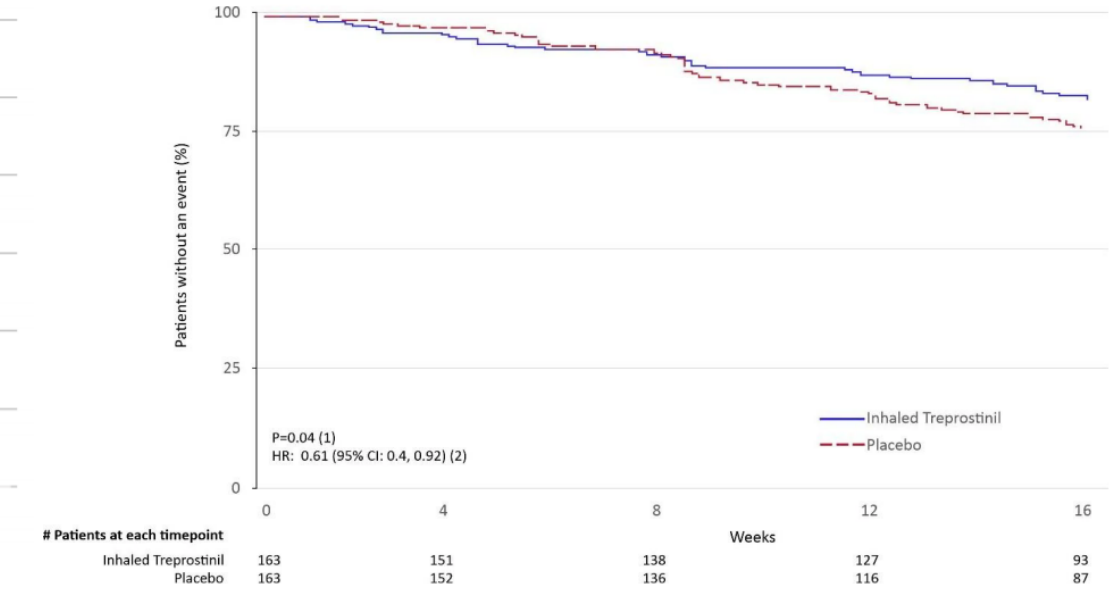
Prevention of deterioration



Improvements in exercise capacity



Reductions in NT-proBNP



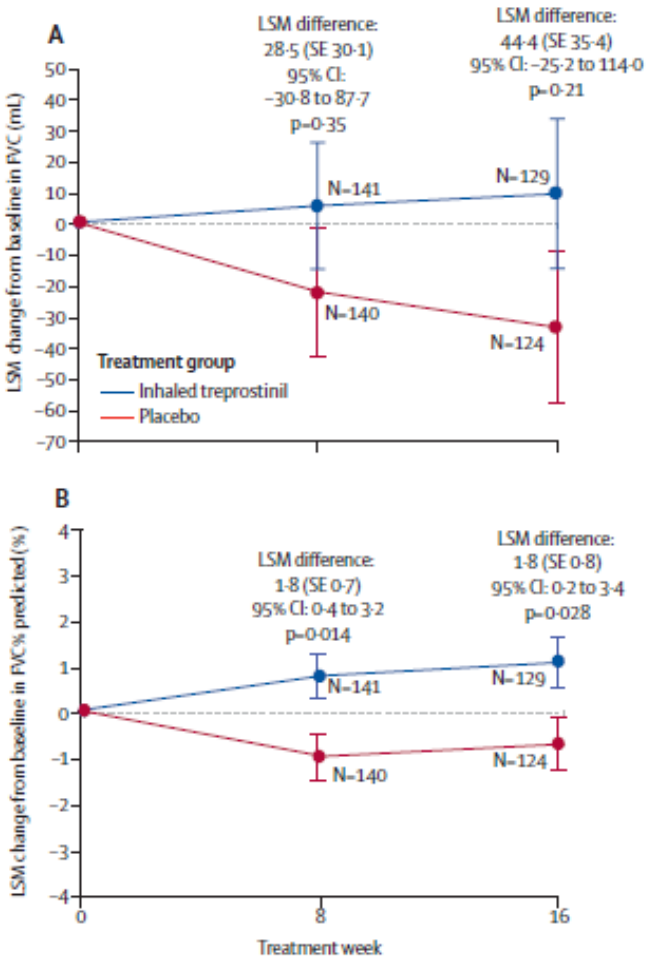
Lower risk of clinical worsening

N Engl J Med 2021;384:325-34

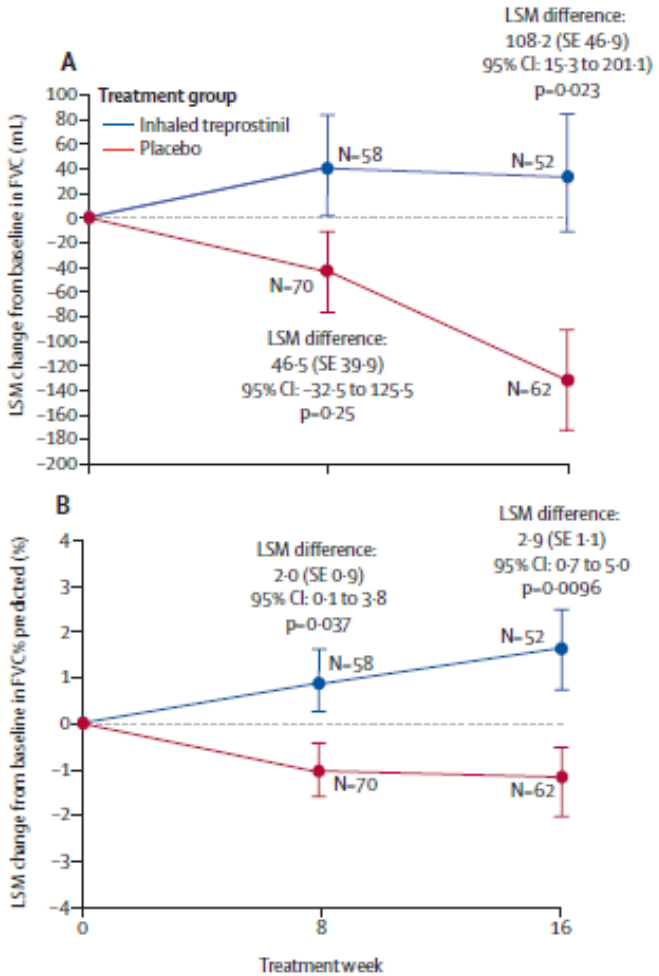
SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

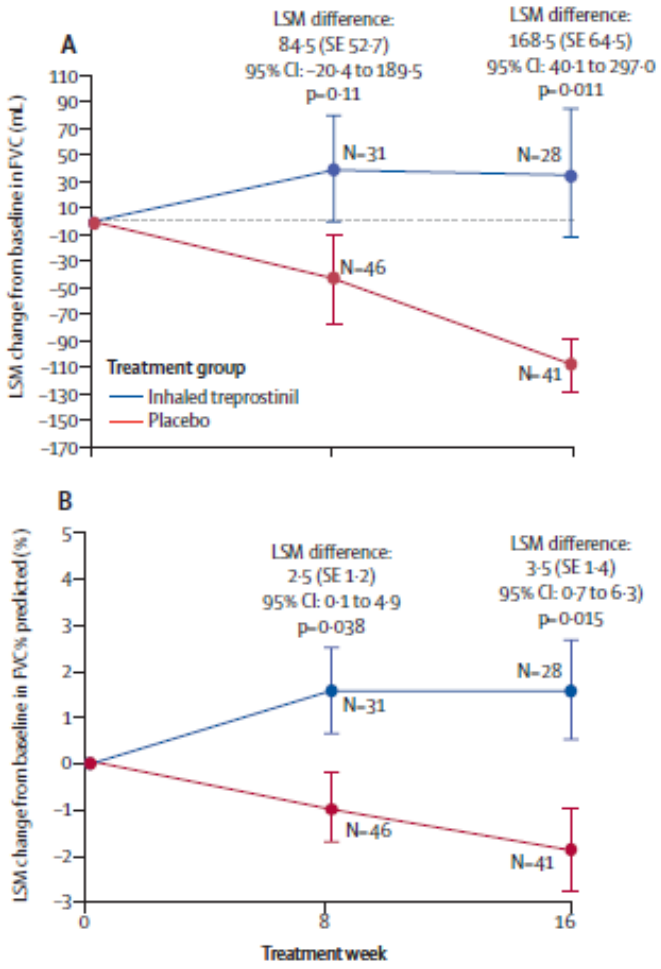
Prevention of deterioration



Overall population



Subgroup - IIP



Subgroup - IPF

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Greater treatment effect in higher PVR & BNP

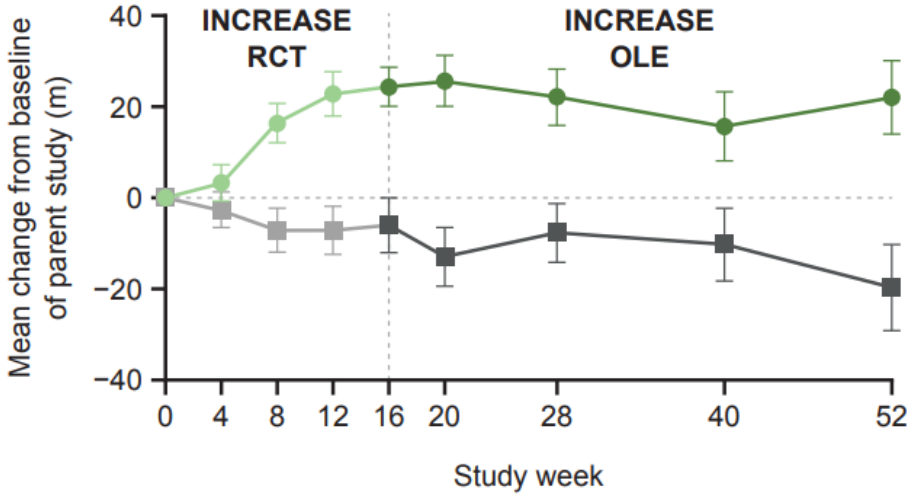
	Inhaled treprostinil (n)	Placebo (n)	Placebo-corrected difference in week-16 FVC, mL	p value
Pulmonary vascular resistance, Wood units				
<5·275	64	75	–1·6 (47·9; –95·9 to 92·8)	0·97
≥5·275	65	49	112·5 (52·6; 9·0 to 215·9)	0·033
NT-proBNP, pg/mL				
<503·85	62	75	19·9 (53·7; –86·3 to 126·1)	0·71
≥503·85	63	47	94·4 (47·4; 0·7 to 188·2)	0·048

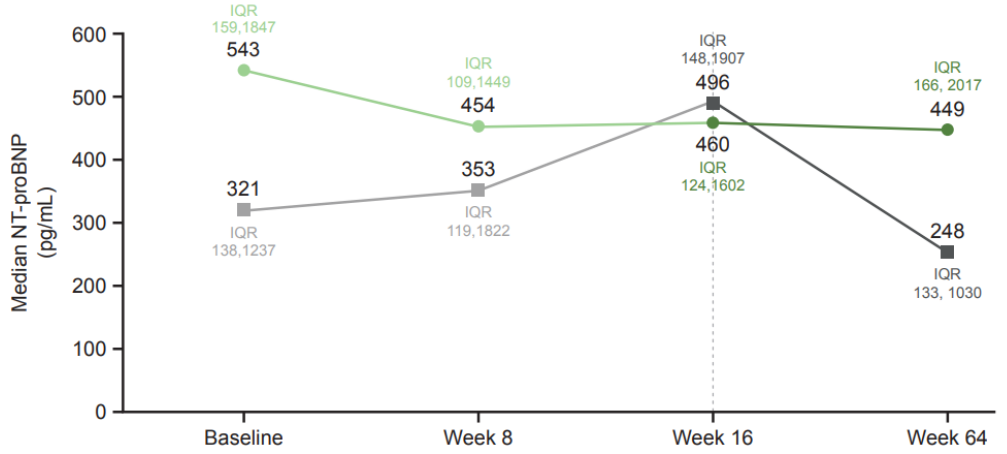
Lancet respire med 2021; 9(11):1266-1274

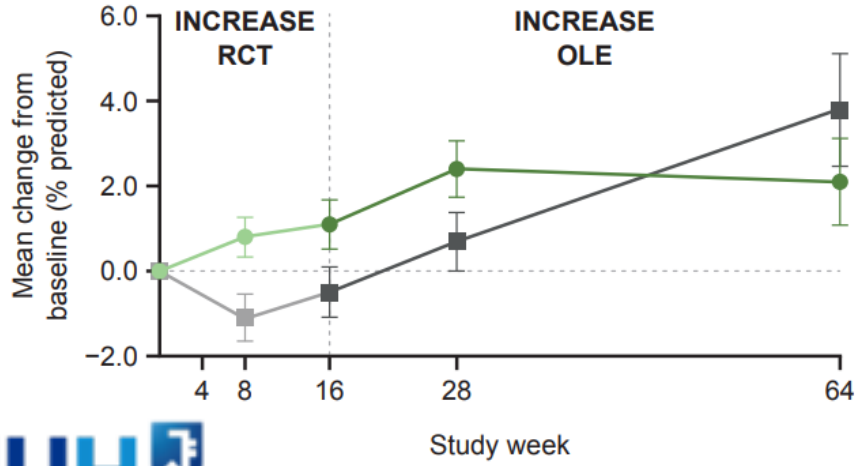
SNUH

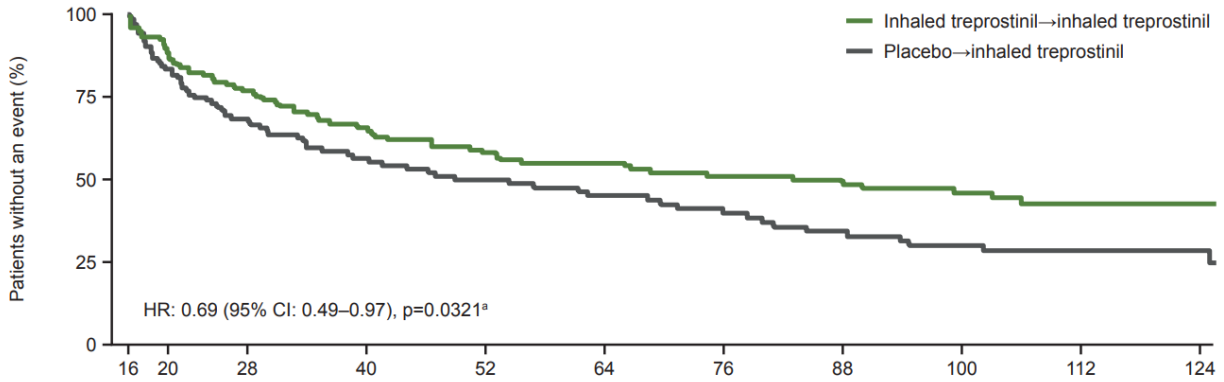
대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Open label extension study









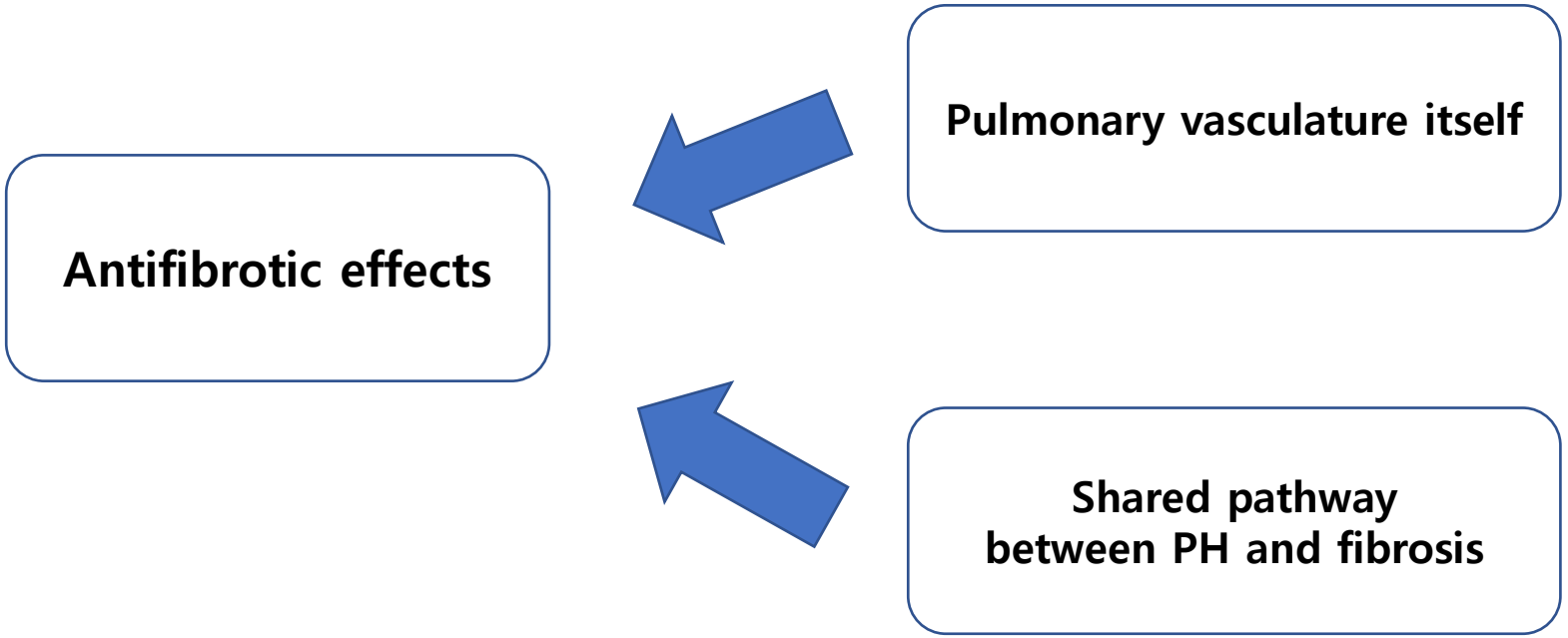
ERJ 2023 early view

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Inhaled treprostinil

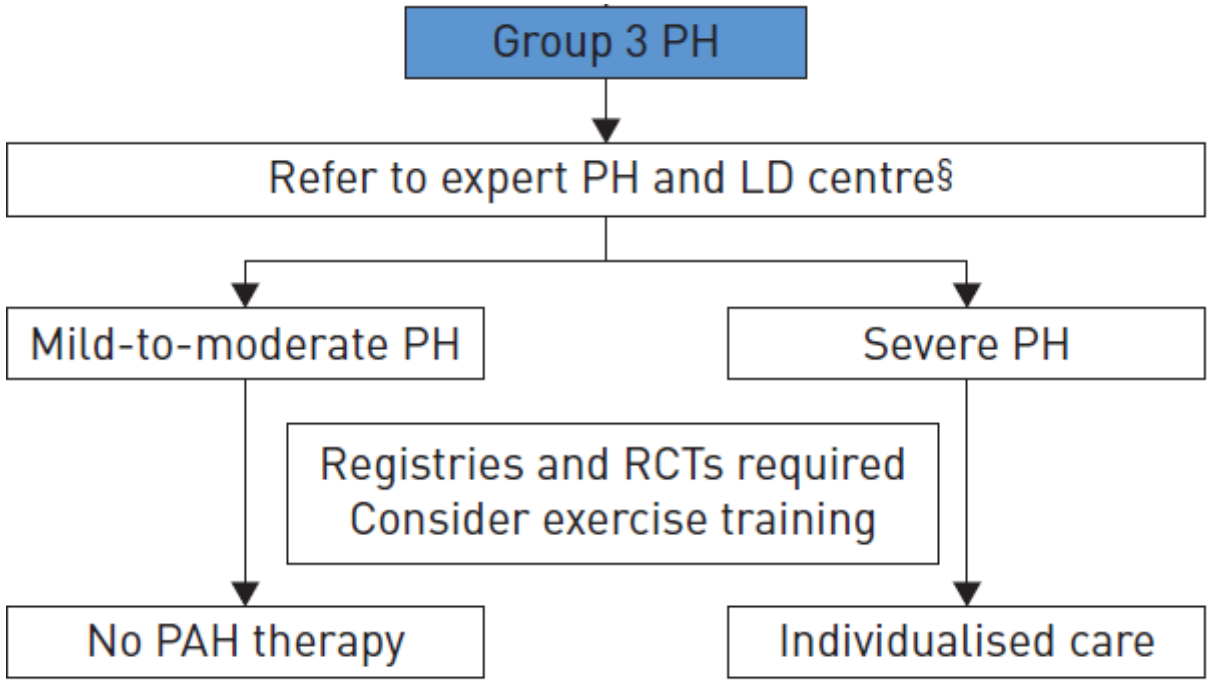
- Greater deposition of drug at the site of disease
  - Improvement of V-Q matching
- Fewer systemic side-effects



: amelioration of FVC decline by inhaled treprostinil

: greater treatment effect in higher PVR and NP-proBNP

Treatment strategy



+ inhaled treprostinil

Eur Respir J 2019; 53: 1801914

SNUH

대한결핵 및 호흡기학회
The Korean Academy of Tuberculosis and Respiratory Diseases

Summary

- Incompletely understood, under-recognised clinical entity
- Associated with significant mortality and morbidity
- Diagnostic dilemma
  - mPAP >20mmHg, PAWP ≤15mmHg, PVR ≥3WU + significant lung diseases
    - PAH with concomitant lung disease vs. PH due to lung disease

  → physiological testing, CT, and clinical context
- An area of great unmet medical need
  - Feasible option in severe PH, PDE5i (sildenafil)
  - The first therapeutic option, prostacyclin analogue (treprostinil)

Thank you for your attention

Email: bskwon82@snubh.org