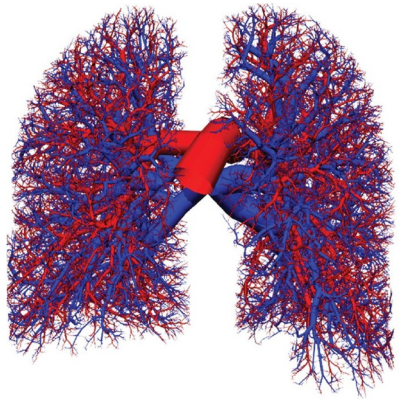

Pulmonary Vascular Disease Program

Brigham and Women's Hospital

Harvard Medical School

Assessment and Treatment of Pulmonary Hypertension

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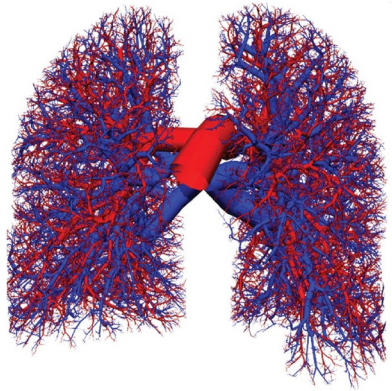
Harvard Medical School

BRIGHAM AND WOMEN'S HOSPITAL

PVDOMICS

PHA CCC Center of Comprehensive Care

HARVARD MEDICAL SCHOOL



Pulmonary Vascular Disease Program

Brigham and Women's Hospital

Harvard Medical School

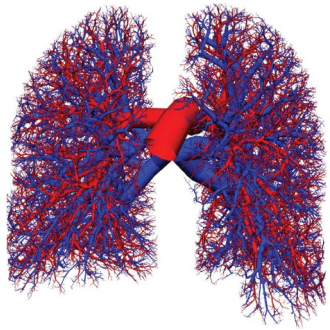
- Disclosures
- Clinical Trial Steering Committees
  - Delivery Trial – United Therapeutics and Medtronic - PI
  - INCREASE Trial – United Therapeutics - PI
  - PERFECT Trial – United Therapeutics - PI
  - Sotatercept Trial – Acceleron
  - ASPIRE Trial – Aria CV - PI

BWH BRIGHAM AND WOMEN'S HOSPITAL

PVDOMICS

PHA CCC Center of Comprehensive Care

HARVARD MEDICAL SCHOOL



Pulmonary Vascular Disease Program

Brigham and Women's Hospital

Harvard Medical School

- Learning Objectives
  - Updates on Pulmonary Hypertension for 2019.
  - Selection of appropriate combinations of PAH therapy based on empirical data
  - What is at the cutting edge now?

Hemodynamic Definitions of PH

	5th WSPH[1]	6th WSPH[2]
PH	mPAP ≥25 mm Hg at rest during RHC	mPAP >20 mm Hg
Pre-capillary PH	mPAP ≥25 mm Hg PAWP ≤15 mm Hg PVR >3 WU	mPAP >20 mm Hg PAWP ≤15 mm Hg PVR ≥3 WU

mPAP: mean pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; PVR: pulmonary vascular resistance; RHC: right heart catheterization; WU: Wood Units. **Pre-capillary PH is included in clinical groups 1, 3, 4 and 5.[2]**

1. Hoeper MM, et al. J *Am Coll Cardiol.* 2013;62:D42-D50.
2. Simonneau G, et al. *Eur Respir J*. 2019 Jan 24;53(1). pii: 1801913.

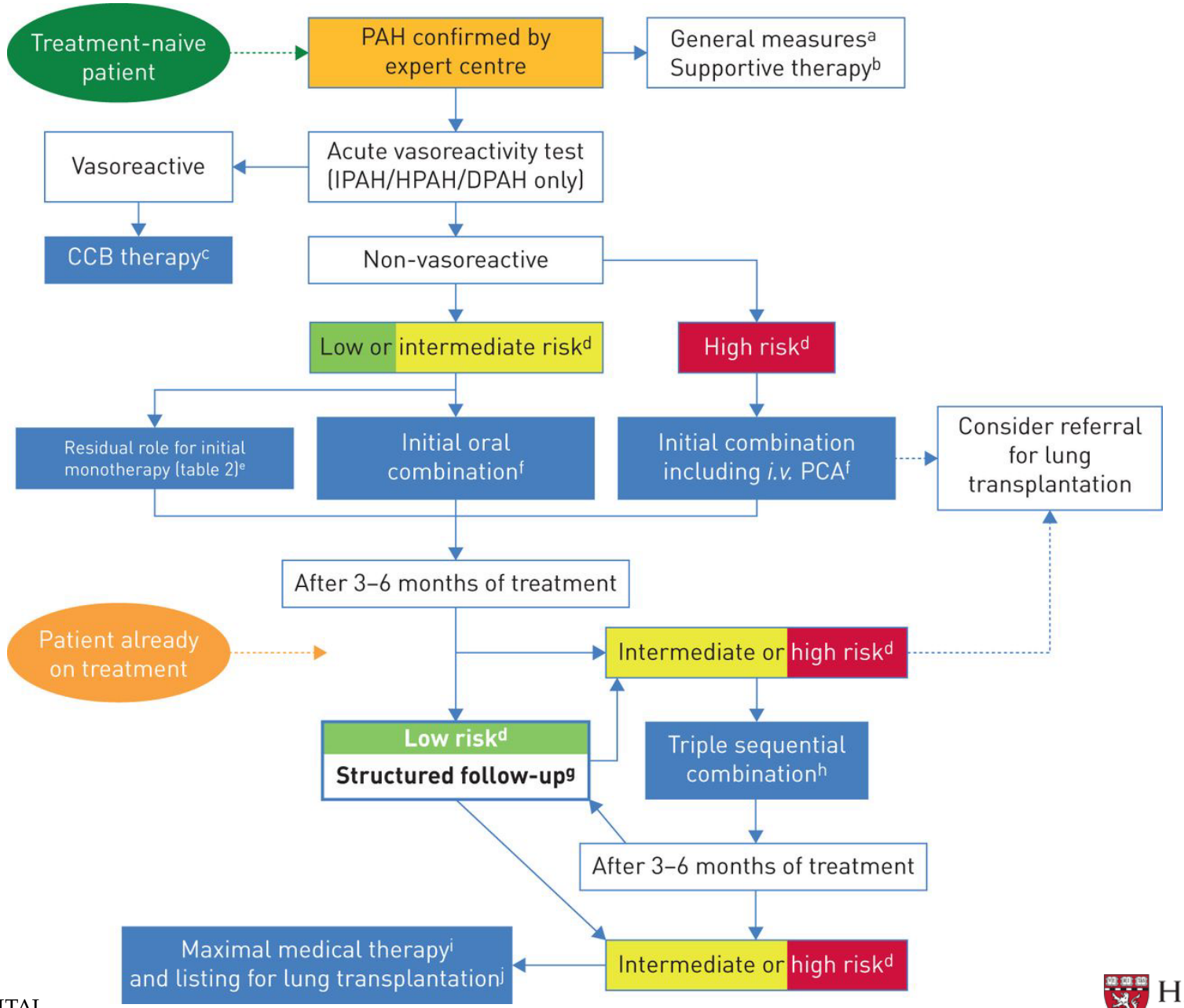
Hemodynamic Definitions of PH

Definitions	Characteristics	Clinical Groups[a]
Isolated post-capillary PH (IpcPH)	mPAP >20 mm Hg PAWP >15 mm Hg PVR <3 WU	2 and 5
Combined pre- and post-capillary PH (CpcPH)	mPAP >20 mm Hg PAWP >15 mm Hg PVR ⩾3 WU	2 and 5

[a]Group 1: PAH; group 2: PH due to left heart disease; group 3: PH due to lung diseases and/or hypoxia; group 4: PH due to pulmonary artery obstructions; group 5: PH with unclear and/or multifactorial mechanisms.

Simonneau G, et al. *Eur Respir J*. 2019 Jan 24;53(1)

Recommended Treatment Algorithm



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European Respiratory Journal Jan 2019, 53 (1) 1801889

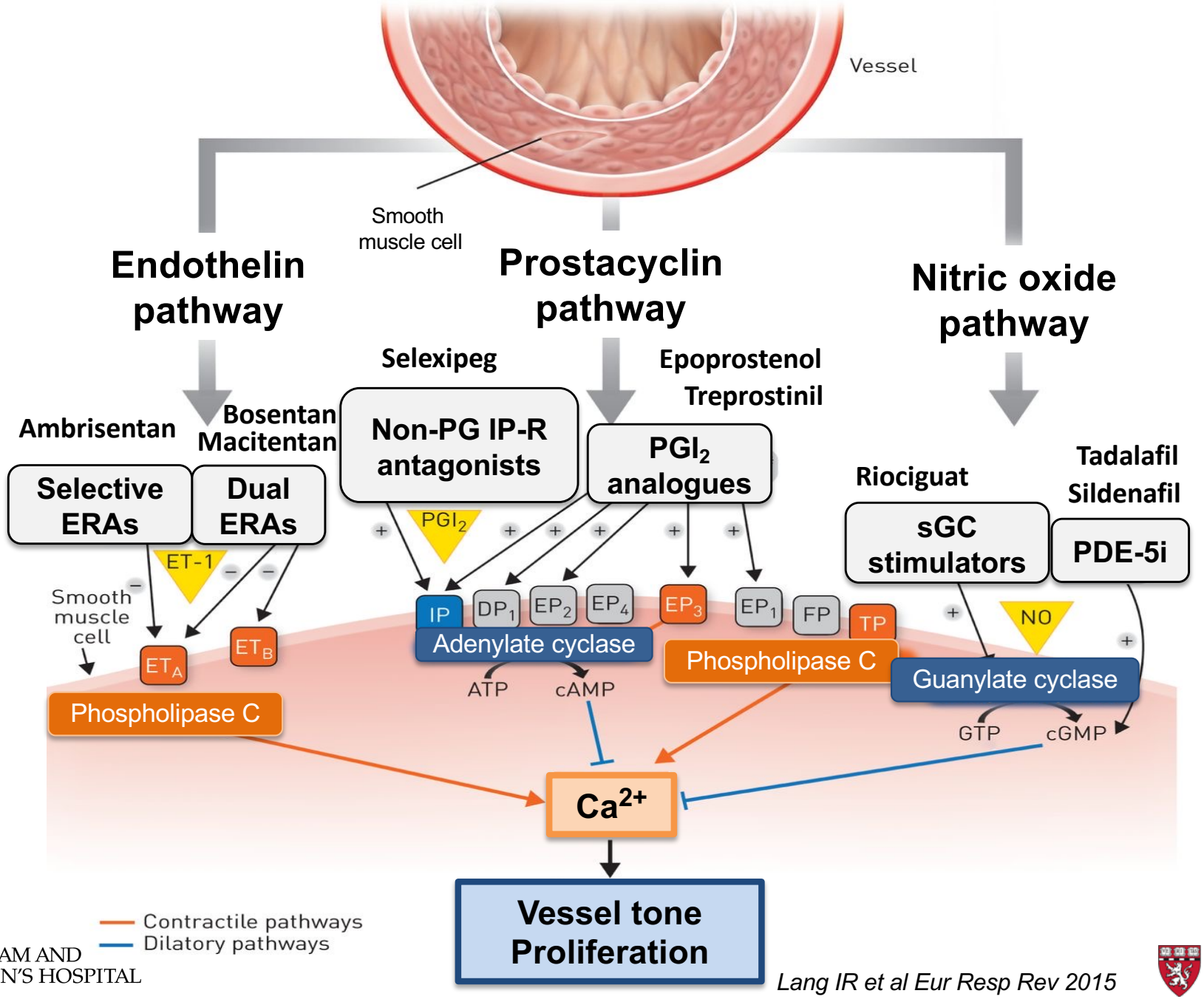
Treatment Algorithm

General Measures	Supportive Therapy
• Avoid pregnancy • Influenza and pneumococcal immunization • Psychological counseling • Supervised exercise training • Supplemented oxygen • Regional anesthesia preferred over general anesthesia	• Diuretics • Long-term oxygen therapy • Anticoagulant therapy • Iron deficiency correction • Use of ACEi, AT1-antagonists, β-blockers, ivabradine only if specifically indicated • Treatment of arrhythmias

Note: **Oral anticoagulant therapy is not recommended in associated forms of PAH, while in IPAH, HPAH and DT-PAH the data on efficacy is more conflicting**. The decision about anticoagulation has to be made on a case-by-case basis after an individual risk–benefit analysis.

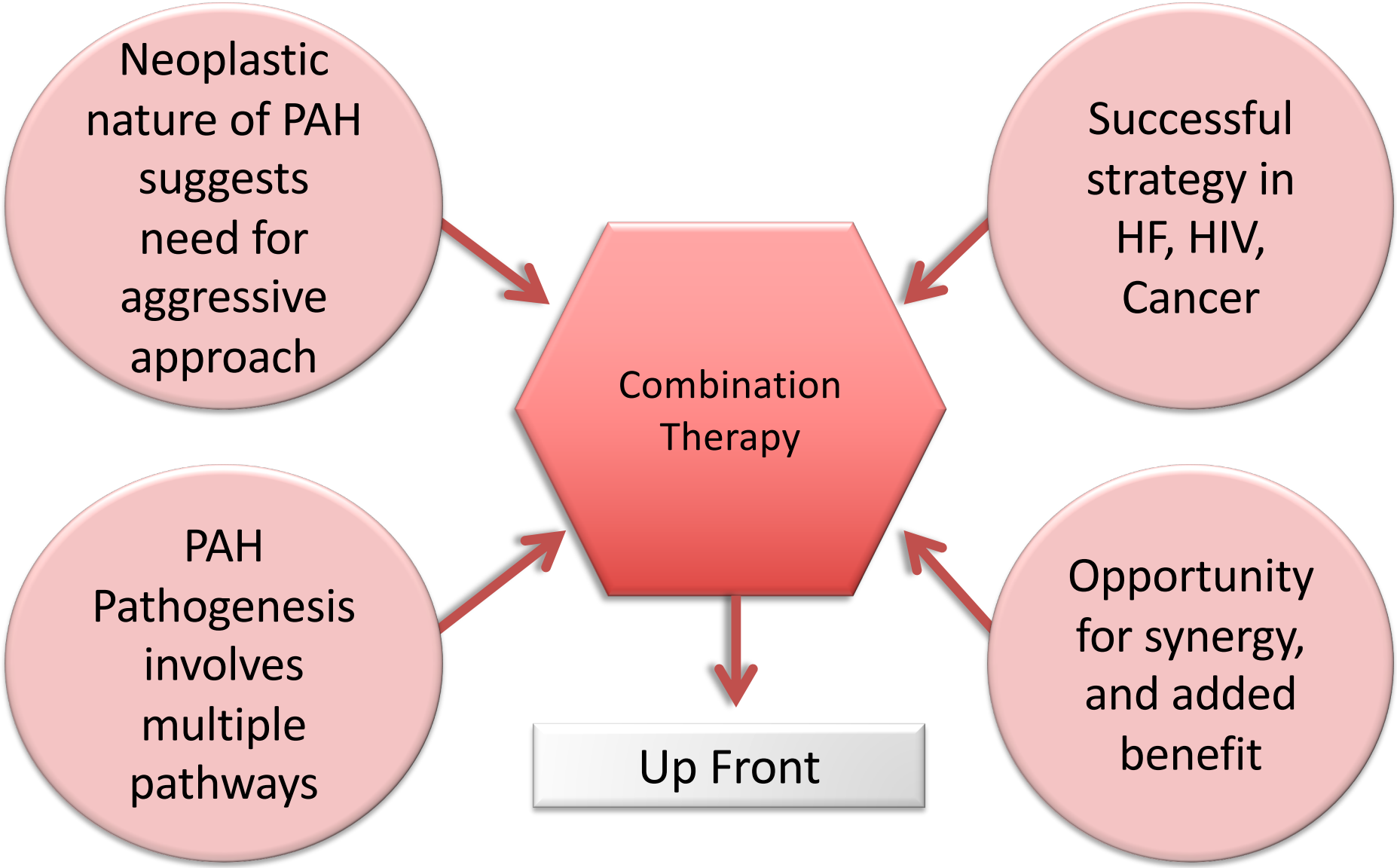
Galié N, et al. *Eur Respir J*. 2016;37:67–119.

Current Therapeutic Targets in PAH

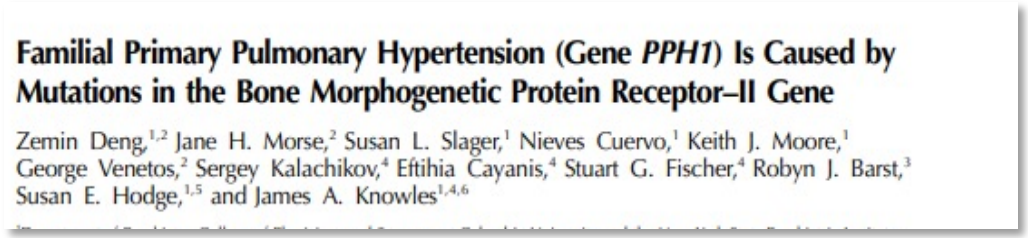


Lang IR et al Eur Resp Rev 2015

Rational for Combination Therapy



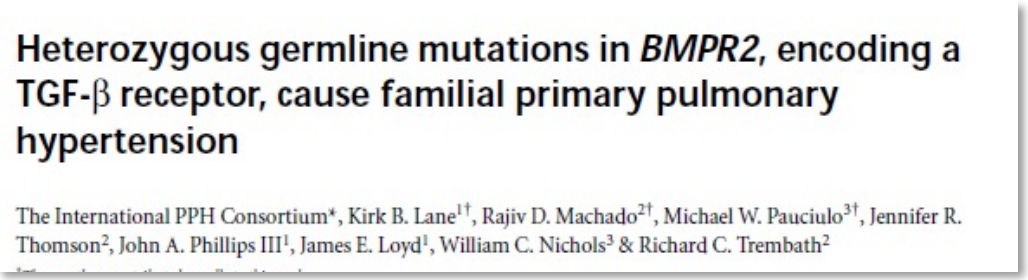
Identifying the Role of *BMPR2* in Pulmonary Hypertension



Familial Primary Pulmonary Hypertension (Gene *PPH1*) Is Caused by Mutations in the Bone Morphogenetic Protein Receptor–II Gene

Zemin Deng,[1,2] Jane H. Morse,[2] Susan L. Slager,[1] Nieves Cuervo,[1] Keith J. Moore,[1] George Venetos,[2] Sergey Kalachikov,[4] Eftihia Cayanis,[4] Stuart G. Fischer,[4] Robyn J. Barst,[3] Susan E. Hodge,[1,5] and James A. Knowles[1,4,6]

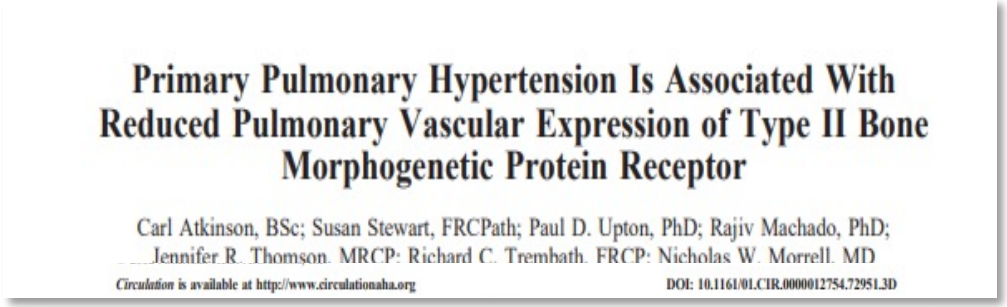
- The BMP signaling pathway is defective in patients with familial primary pulmonary hypertension[1]



Heterozygous germline mutations in *BMPR2*, encoding a TGF-β receptor, cause familial primary pulmonary hypertension

The International PPH Consortium*, Kirk B. Lane[1†], Rajiv D. Machado[2†], Michael W. Pauciulo[3†], Jennifer R. Thomson[2], John A. Phillips III[1], James E. Loyd[1], William C. Nichols[3] & Richard C. Trembath[2]

- Familial primary PH is caused by mutations in *BMPR2*
- The TGF-β superfamily and Smad signaling are important for the maintenance of blood vessel integrity[2]



Primary Pulmonary Hypertension Is Associated With Reduced Pulmonary Vascular Expression of Type II Bone Morphogenetic Protein Receptor

Carl Atkinson, BSc; Susan Stewart, FRCPath; Paul D. Upton, PhD; Rajiv Machado, PhD; Jennifer R. Thomson, MRCP; Richard C. Trembath, FRCP; Nicholas W. Morrell, MD

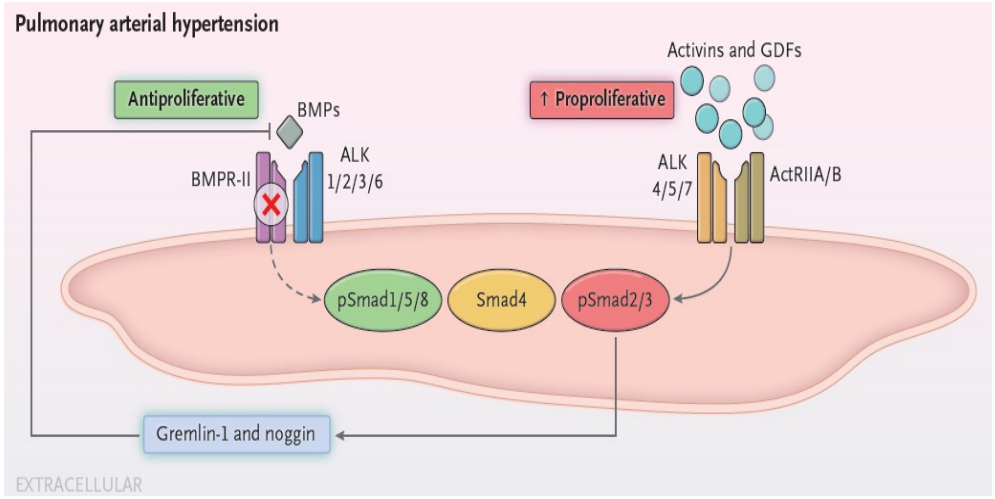
Circulation is available at http://www.circulationaha.org DOI: 10.1161/01.CIR.0000012754.72951.3D

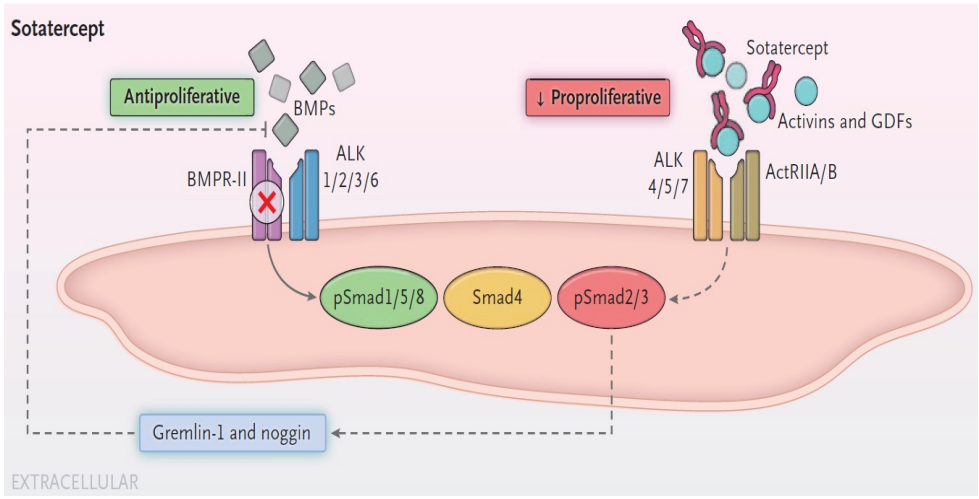
- Additional evidence of the role of BMP signaling pathway in PH, demonstrating reduced BMPR-II expression in primary pulmonary hypertension[3]

Deng Z *et al*. Am J Hum Genet 2000;67:737–44; 2. International PPH Consortium. Nat Genet 2000;26:81–4; 3. Atkinson C *et al*. Circulaion 2002;105:1672–78 ion 2002;105:1672–78.

Pulmonary arterial hypertension and sotatercept

- Pulmonary arterial hypertension (PAH) is characterized by pulmonary vascular remodeling, resulting in increased pulmonary artery pressure and progressive right ventricular dysfunction[1]





- Sotatercept is a first-in-class selective ligand trap proposed to rebalance pro- (ActRIIA-mediated) and anti- (BMPR-II-mediated) proliferative signaling, thereby having the potential to reverse the characteristic vascular remodeling that underlies PAH pathology[2–4]

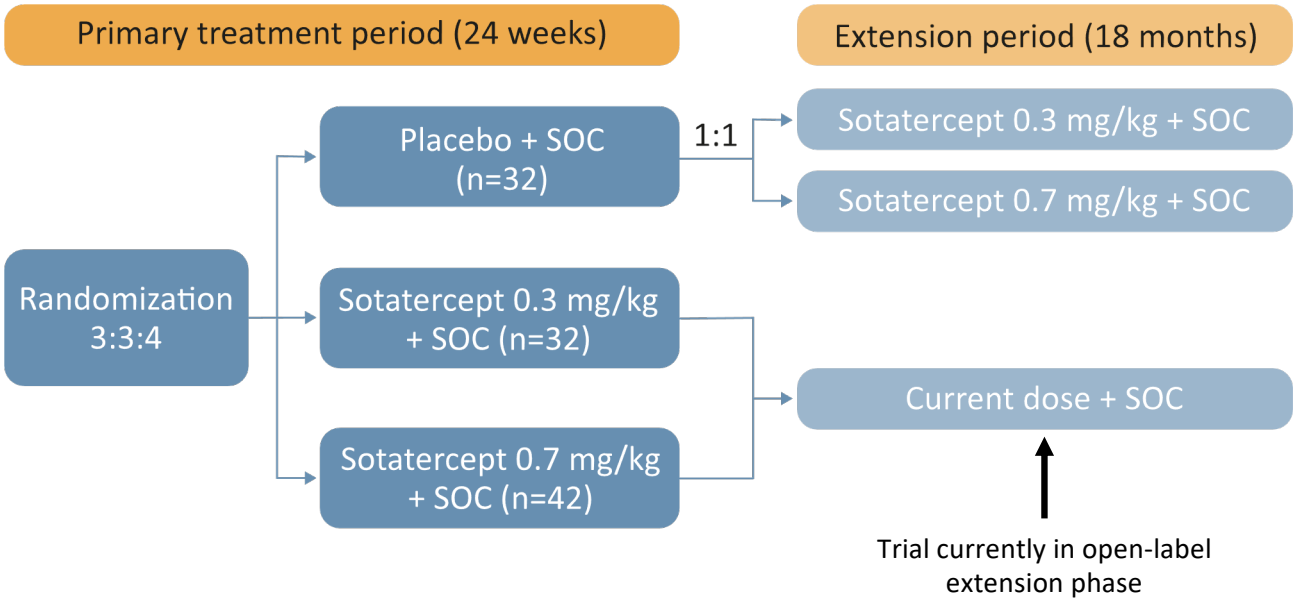
S Lai YC *et al. Circ Res*. 2014; 115: 115–30; 2. Humbert M, *et al. N Engl J Med*. 2021; 384: 1204–15; 3. Cappellini MD, *et al. Haematologica.* 2019; 104: 477–84; 4. Yung L-M, *et al. Sci Transl Med.* 2020; 12: eaaz5660.

PULSAR Study Design

- A phase 2 randomized, double-blind, placebo-controlled study to compare the efficacy and safety of sotatercept versus placebo when added to standard of care (SOC) for the treatment of PAH in 106 patients

Inclusion Criteria

- WHO Group 1 PAH
- WHO Functional Class II or III
- Baseline right heart catheterization with PVR ≥5 Wood units
- Baseline 6-minute walk distance 150–550 m
- Stable treatment with SOC therapies including mono, double, and triple therapies:
  - An endothelin-receptor antagonist, a phosphodiesterase 5 inhibitor, a soluble guanylate cyclase stimulator, and/or a prostacyclin (including IV)



N Engl J Med. 2021 Apr 1;384(13):1204-1215

PULSAR Study: Endpoints

- Endpoints measured as change from baseline to 24 weeks versus placebo

Primary endpoint:
- Change in pulmonary vascular resistance

Key secondary endpoint:
- Change in 6-minute walk distance

Additional endpoints and analyses included:
- Change in NT-proBNP
- Change in WHO functional class
- Change in hemodynamics
- Proportion achieving multi-component improvement (WHO FC, NT-proBNP, 6MWD)
- Time to clinical worsening*

N Engl J Med. 2021 Apr 1;384(13):1204-1215

PULSAR Study: Baseline Characteristics (1)

	Placebo n=32	Sotatercept 0.3 mg/kg n=32	Sotatercept 0.7 mg/kg n=42	Total N=106
Female, n (%)	26 (81)	29 (91)	37 (88)	92 (87)
Age, mean (range), years	46 (21–71)	48.5 (23–80)	48.5 (19–77)	48 (19–80)
Time since diagnosis, mean (range), years	7.2 (0.3–22)	7.6 (0.7–26)	6.2 (0.8–24)	7.4 (0.3–26)
PAH classification, n (%)				
Idiopathic	19 (59)	13 (41)	29 (69)	61 (58)
Heritable	7 (22)	5 (16)	5 (12)	17 (16)
Associated with connective-tissue disease	3 (9)	9 (28)	6 (14)	18 (17)
Drug or toxin-induced	1 (3)	4 (13)	2 (5)	7 (7)
Associated with corrected congenital shunts	2 (6)	1 (3)	0 (0)	3 (3)

N Engl J Med. 2021 Apr 1;384(13):1204-1215

PULSAR Study: Baseline Characteristics (2)

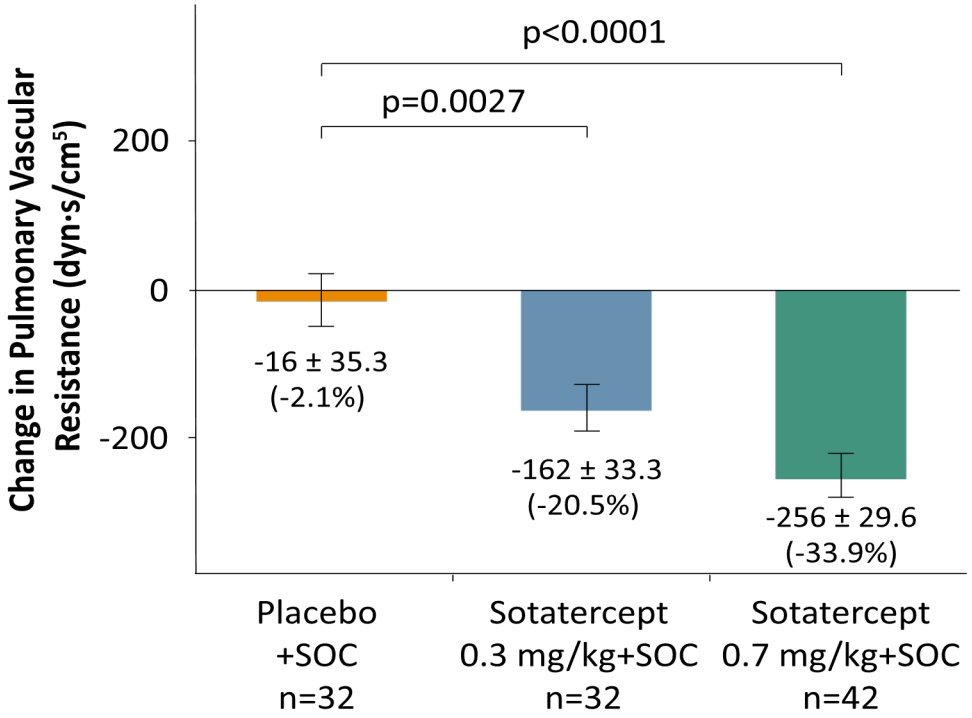
	Placebo n=32	Sotatercept 0.3 mg/kg n=32	Sotatercept 0.7 mg/kg n=42	Total N=106
WHO functional class, n (%)				
II	17 (53)	15 (47)	24 (57)	56 (53)
III	15 (47)	17 (53)	18 (43)	50 (47)
Standard-of-care PAH therapy, n (%)				
Parenteral prostacyclin	10 (31)	11 (34)	18 (43)	39 (37)
Monotherapy	3 (9)	3 (9)	4 (10)	10 (9)
Double therapy	12 (38)	11 (34)	14 (33)	37 (35)
Triple therapy	17 (53)	18 (56)	24 (57)	59 (56)
Pulmonary vascular resistance, dyn· s/cm^5	797 ± 57.0	789 ± 50.8	756 ± 63.5	779 ± 33.9
6-minute walk distance, m	409 ± 11.3	386 ± 15.7	398 ± 14.1	398 ± 8.1
NT-proBNP, pg/mL	870 ± 214.5	999 ± 227.6	871 ± 248.2	908 ± 135.4

Mean ± SE unless otherwise noted

N Engl J Med. 2021 Apr 1;384(13):1204-1215

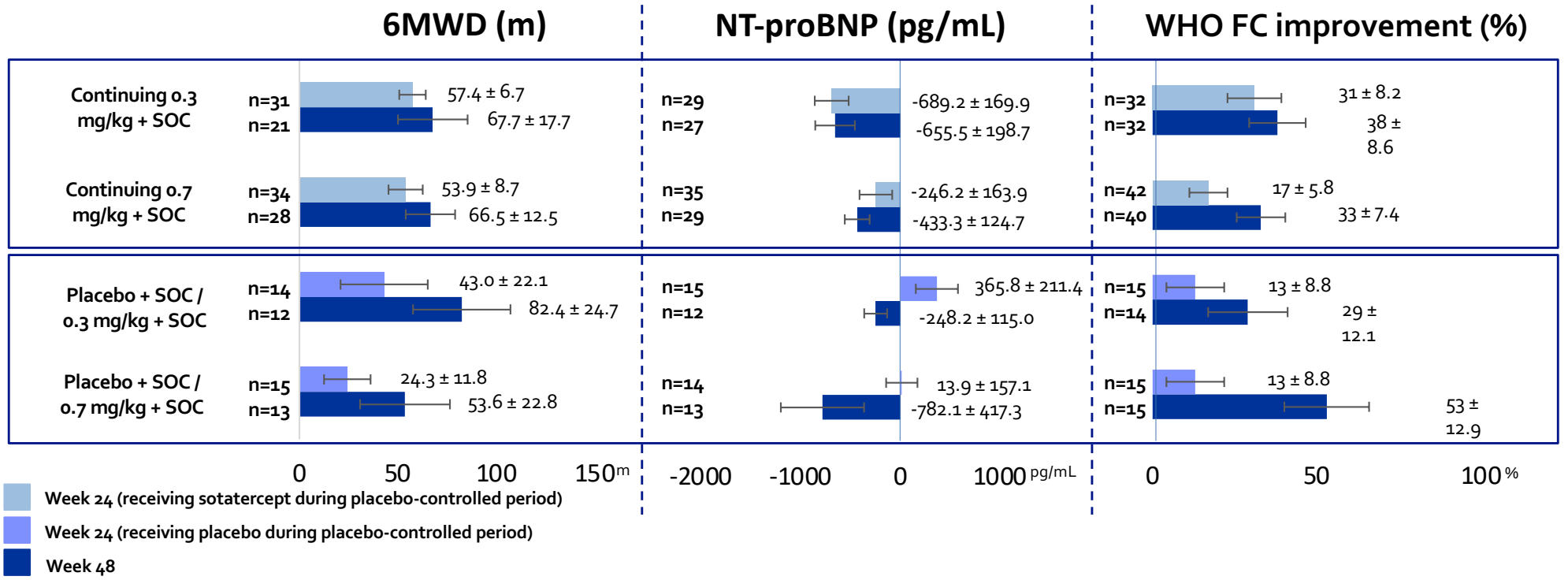
PULSAR Study: Primary Endpoint – *Pulmonary Vascular Resistance* (1)

- Change from baseline to end of placebo-controlled treatment period (week 24) in PVR



Mean ± SE

PULSAR: Change from baseline at week 24 and change from baseline at week 48



Data presented as mean ± SE change from baseline for 6MWD and NT-proBNP; percentage of patients ± SE who improved by ≥1 WHO FC; not all data for in-person assessments (6MWD, NT-proBNP) were available due to COVID-19 delays and missing visits.
Per the statistical methods for calculating WHO FC, missing data for reasons other than COVID-19 are recorded as non-responders and therefore the overall n is different for WHO FC.
6MWD: 6-minute walk distance; FC: functional class; NT-proBNP: N-terminal pro-brain natriuretic peptide; SE: standard error; SOC: standard of care; WHO: World Health Organization.

PULSAR: Overall safety experience including open-label extension

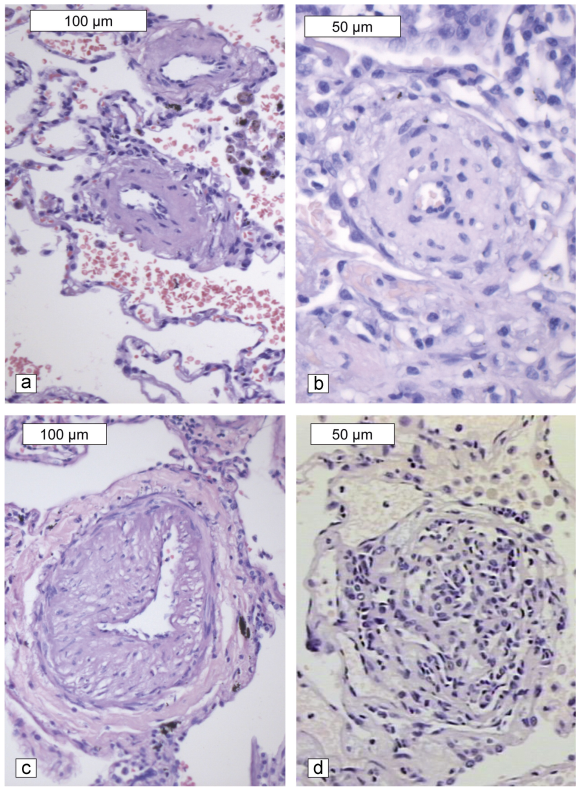
- As of the interim data cut, 103/106 (97%) patients reported treatment-emergent adverse events (TEAEs)
- Serious TEAEs occurred in 30/106 (28%) patients
- Overall, 9/106 (9%) patients had TEAEs that led to study discontinuation; 2/106 (2%) died (cardiac arrest, brain abscess) and deaths were not considered related to study drug by the investigators
- The safety profile of sotatercept was consistent with the placebo-controlled treatment period

TEAEs during the OLE period only, n (%)	Continuing 0.3 mg/kg + SOC (n=31)	Continuing 0.7 mg/kg + SOC (n=36)	Placebo + SOC / 0.3 mg/kg + SOC (n=15)	Placebo + SOC / 0.7 mg/kg + SOC (n=15)
TEAEs	29 (94)	33 (92)	13 (87)	15 (100)
TEAEs of special interest*	1 (3)	2 (6)	5 (33)	0 (0)
Serious TEAEs	8 (26)	4 (11)	4 (27)	2 (13)
Serious related TEAEs	1 (3)	0 (0)	1 (7)	0 (0)
TEAEs leading to treatment discontinuation	1 (3)	0 (0)	0 (0)	0 (0)
TEAEs leading to study discontinuation	1 (3)	1 (3)	0 (0)	0 (0)
TEAEs leading to death	0 (0)	1 (3)	0 (0)	0 (0)

Interim extension analysis data cut-off date: 14 September 2020.
*TEAEs of special interest defined as any adverse event of leukopenia, neutropenia, or thrombocytopenia.
OLE: open-label extension; SOC: standard of care; TEAE: treatment-emergent adverse event.

Group 3 PH - Statement of the Problem

- WHO Group-3PH is frequently encountered and adversely affects patients' quality of life and survival.
- Pulmonary vascular remodeling is a component of advanced lung disease and probably reflects the inflammatory nature of the disease

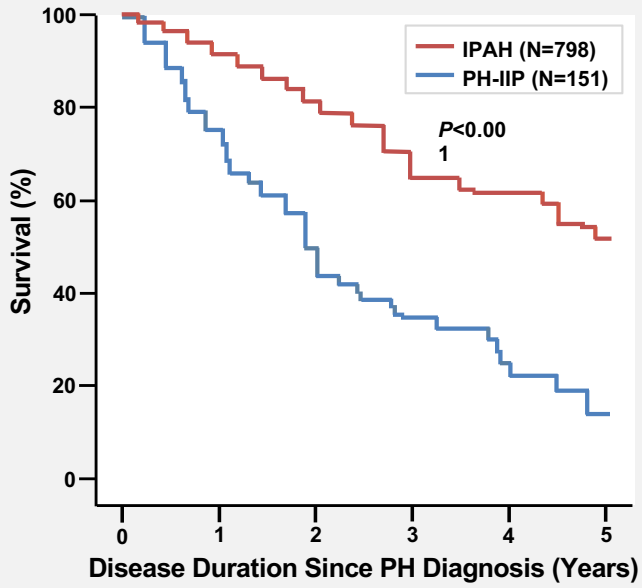


The Journal of Heart and Lung Transplantation 2013; 32:347-354

Pulmonary Hypertension due to Interstitial Lung Disease (PH-ILD)

- Interstitial lung disease (ILD) encompasses a heterogeneous group of parenchymal lung diseases.
- PH-ILD is associated with poor prognosis, worsened functional status, decreased quality of life, increased need for supplemental oxygen, and markedly reduced survival.[1,2]

Kaplan-Meier Survival Estimates in Patients with PH Associated with Chronic Fibrosing Idiopathic Interstitial Pneumonias and Idiopathic PAH – Data from the COMPERA Registry[3]



IIP: idiopathic interstitial pneumonias; ILD: interstitial lung disease; IPAH: idiopathic pulmonary arterial hypertension; PH: pulmonary hypertension.

1. Nathan SD. Int J Clin Pract. 2008;62(Suppl 160):21-28. 2. Nathan SD, Hassoun PM. Clin Chest Med. 2013;34(4):695-705. 3. Hoeper MM, Behr J, Held M, et al. PLOS ONE. 2015; 10(12): e0141911.

INCREASE – Study Design and Inclusion Criteria

Phase 3, multicenter, randomized (1:1), double-blind, placebo-controlled, 16-week, parallel-group (inhaled treprostinil / placebo) study (NCT02630316)

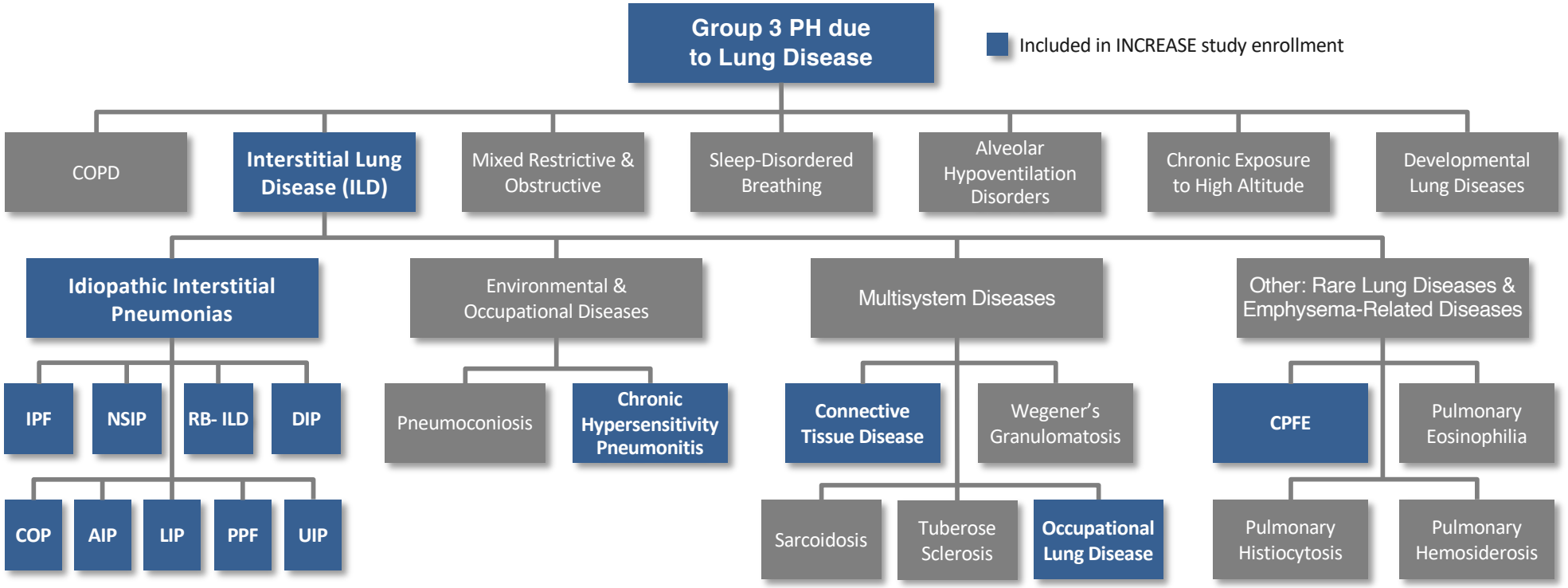
Key Inclusion Criteria

- Confirmed diagnosis of Group 3 PH based on CT within 6 months prior to randomization and demonstrated evidence of diffuse parenchymal lung disease. Subjects had any form of ILD or CPFE
- Right heart catheterization within 1 year prior to randomization with the following documented parameters:
  - **PVR >3 WU and**
  - **PCWP ≤15 mmHg and**
  - **mPAP ≥25 mmHg**
- Baseline 6MWD ≥100 m
- Subjects on a chronic medication for underlying lung disease (i.e., pirfenidone, nintedanib, etc.) were on a stable and optimized dose for ≥30 days prior to randomization
- Subjects with Group 3 connective tissue disease had a Baseline forced vital capacity <70%

Key Exclusion Criteria

- Diagnosis of PAH or PH for reasons other than Group 3 PH-ILD
- Use of any PAH-approved therapy, within 60 days of randomization (or during the study)
- Evidence of clinically significant left-sided heart disease as defined by:
  - **PCWP >15 mmHg**
  - **Left ventricular ejection fraction <40%**
- Receiving >10 L/min of oxygen supplementation by any mode of delivery at rest at Baseline
- Initiation of pulmonary rehabilitation within 12 weeks prior to randomization
- Acute pulmonary embolism within 90 days of randomization

INCREASE Eligible Study Population



AIP: Acute interstitial pneumonitis; COP: Cryptogenic organizing pneumonia; CPFE: Combined pulmonary fibrosis and emphysema; DIP: Desquamative interstitial pneumonia; IPF: Idiopathic Pulmonary Fibrosis; LIP: Lymphoid Interstitial pneumonia; NSIP: Nonspecific interstitial pneumonia; PPF: Pleuroparenchymal fibroelastosis; RB-ILD: Respiratory bronchiolitis-associated interstitial lung disease; UIP: Unclassifiable interstitial pneumonia.

1. Simonneau G, et al. J Am Coll Cardiol. 2013;62(25):D34-41. 2. Bourke SJ. Postgrad Med J. 2006;82:494-499. 3. "Interstitial Lung Disease" www.erswhitebook.com – accessed December 2015.

Study Assessments

Primary Endpoint

- Change in 6MWD measured at peak exposure from Baseline to Week 16
  - 6-minute walk test (6MWT) performed at peak plasma treprostinil exposure
    - Between 10 to 60 minutes after most recent dose of study drug

Secondary Endpoints

- Change in NT-proBNP from Baseline to Week 16
- Time to clinical worsening - time of randomization until study discontinuation
  - Hospitalization due to a cardiopulmonary indication,
  - Decrease in 6MWD >15% from Baseline directly related to disease under study at 2 consecutive visits and at least 24 hours apart,
  - Death (all causes),
  - Or lung transplantation
- Change in Peak 6MWD at Week 12
- Change in Trough 6MWD at Week 15
  - ≥4 hours after the most recent study drug dose and ≥24 hours prior to Week 16 6MWT

6MWD: six-minute walk distance; 6MWT: six-minute walk test; NT-proBNP: N-terminal pro-brain natriuretic peptide.

N Engl J Med. 2021 384:325-334

Study Assessments

Exploratory Endpoints

- Change in Quality of Life (SGRQ)
- Change in peak distance saturation product (DSP)
- Change in peak 6MWD from Baseline to Weeks 4 and 8
- Optional evaluation of change in biomarkers and whole genome sequence at Baseline

Additional Safety Endpoints

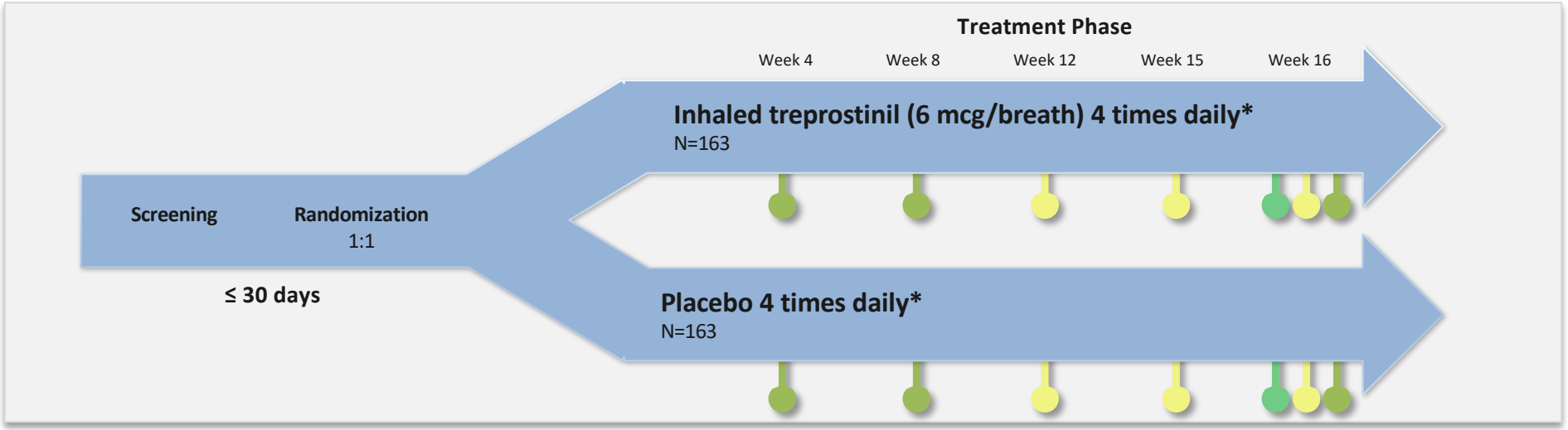
- Adverse events (AEs)
- Supplemental Oxygenation Requirements
- Pulse oximetry
- Changes in pulmonary function tests (PFTs)
- Clinical laboratory parameters
- Vital signs
- Electrocardiograms (ECG)
- Exacerbations of underlying lung disease
  - Defined as an acute, clinically significant, respiratory deterioration characterized by evidence of new widespread alveolar abnormality

SGRQ: St. George's Respiratory Questionnaire.

N Engl J Med. 2021 384:325-334

INCREASE – Study Procedures

Timeline of Study Endpoint Assessments



* All subjects initiated study drug at a dose of 3 breaths (18 mcg) 4 times daily (during waking hours). Dose escalations (additional 1 breath 4 times daily) could occur up to every 3 days, with a target dose of 9 breaths (54 mcg) 4 times daily and a maximum dose of 12 breaths (72 mcg) 4 times daily, as clinically tolerated.

- Primary endpoint measure - 6MWD at peak exposure from Baseline to Week 16
- Secondary endpoint measures - Change in peak 6MWD Baseline to Week 12; Change in plasma concentration NT-proBNP Baseline to Week 16; Change in trough 6MWD from Baseline to Week 15.
- Exploratory endpoint measures

6MWD: six-minute walk distance; NT-proBNP: N-terminal pro-brain natriuretic peptide.

N Engl J Med. 2021 384:325-334

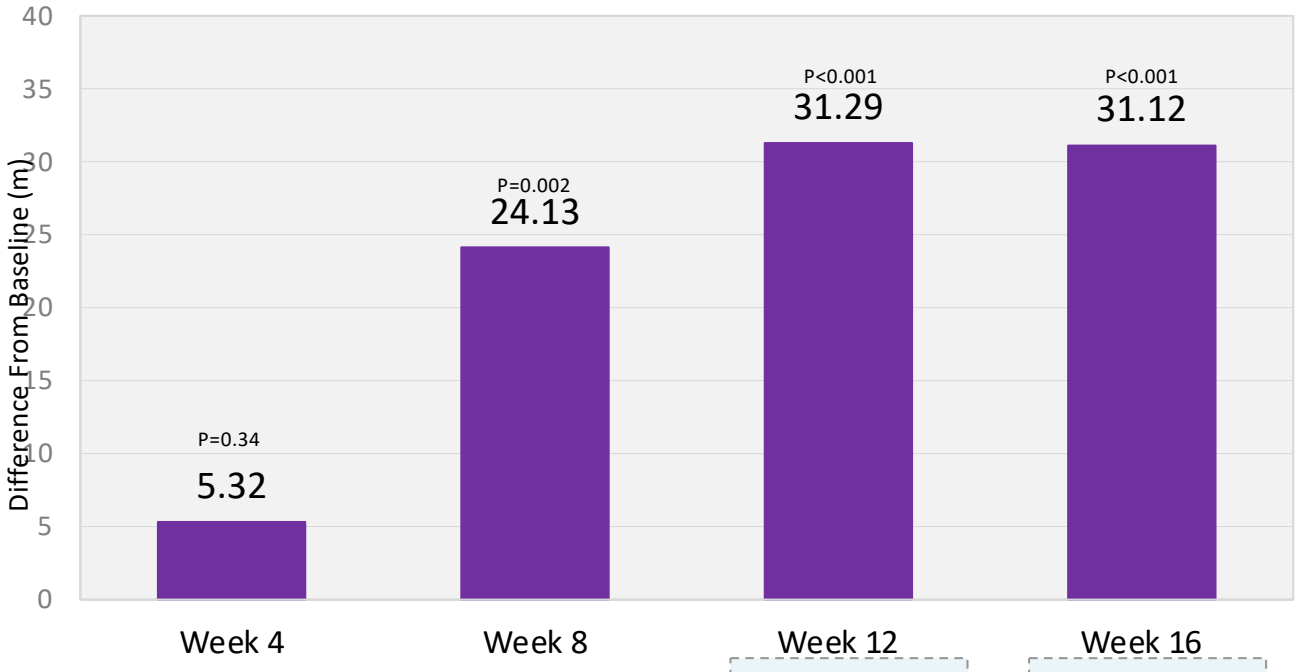
Baseline Characteristics

- A total of 326 patients were enrolled in the study.
- The most common PH-ILD etiologies included:
  - Idiopathic interstitial pneumonia (45%)
  - Idiopathic pulmonary fibrosis (28%)
- 14% of patients were on single background therapy with pirfenidone and 9% on nintedanib
- The median dose of inhaled treprostinil achieved at Week 8 and Week 16 were 10 and 12 breaths per session, respectively.

6MWD Results Through Week 16

At Week 16, inhaled treprostinil patients had a placebo-corrected difference from Baseline in peak 6MWD of 31.12 meters

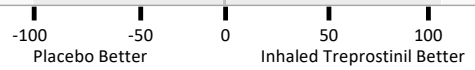
(95% CI: 16.85, 45.39; P<0.001).



Mixed Model Repeated Measurement treatment effect is provided.
6MWD, 6-Minute Walk Distance; m, meter.

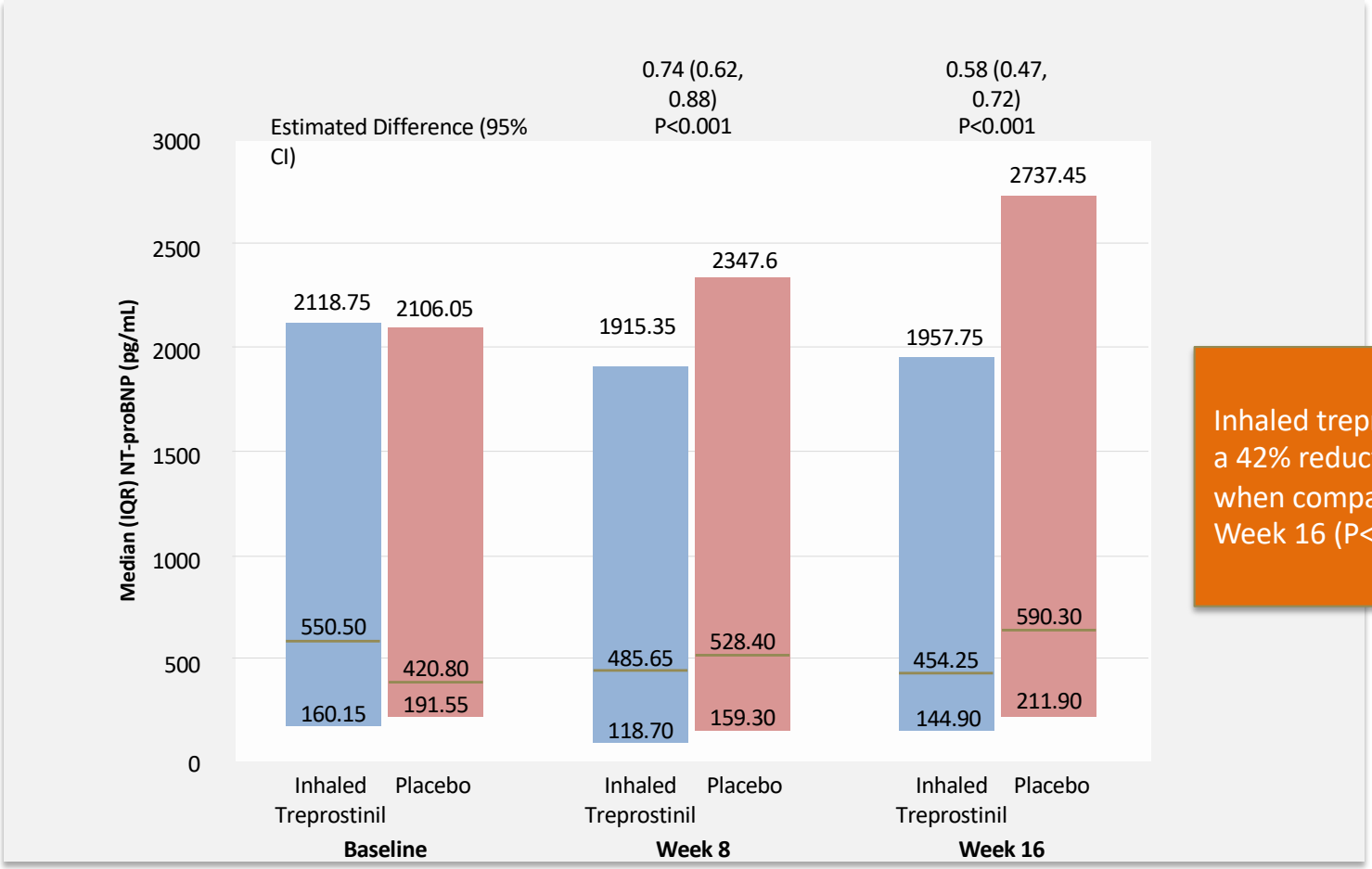
Subgroup Analyses of Peak 6MWD at Week 16

Subgroup	Inhaled Treprostinil # Patients	Placebo # Patients	Hodges-Lehmann Estimate (95% CI)
All Patients	163	163	21.0 (7.0, 37.0)
Age Group			
<65 years	64	48	11.0 (-11.0,46.0)
65 to 80 years	83	100	27.0 (7.0, 46.0)
≥ 80 years	16	15	19.5 (-38.0, 74.0)
Sex			
Male	78	95	8.0 (-12.0, 30.0)
Female	85	68	34.0 (12.0, 57.0)
Baseline 6MWD Category			
≤ 350 meters	136	133	24.0 (6.0, 41.0)
> 350 meters	27	30	16.0 (-16.0, 47.0)
PH-ILD Etiology			
Idiopathic Interstitial Pneumonia	65	81	32.0 (12.0, 55.0)
Combined Pulmonary Fibrosis and Emphysema	42	40	2.0 (-28.0, 32.0)
Connective Tissue Disease	40	32	39.0 (3.0, 78.0)
Other	16	10	0.0 (-89.0, 54.0)
Baseline PVR Category			
< 4 Wood units	32	34	-3.0 (-26.0, 26.0)
≥ 4 Wood units	131	129	28.0 (11.0, 46.0)
Study Drug Dose at Week 16			
4-6 breaths	6	2	-16.5 (-62.0, 29.0)
7-9 breaths	37	24	18.0 (-8.0, 43.0)
10-12 breaths	78	94	30.0 (14.0, 48.0)



6MWD, 6-minute walk distance; CI, confidence interval; H-L, Hodges-Lehmann; ILD, interstitial lung disease; LOCF, last observation carried forward; PH, pulmonary hypertension; PVR, pulmonary vascular resistance

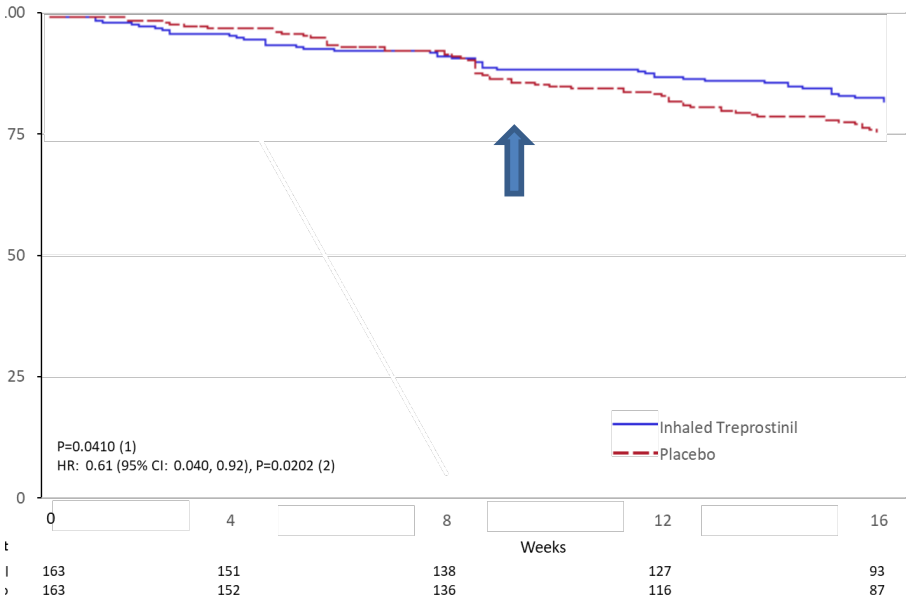
NT-proBNP Results by Study Visit



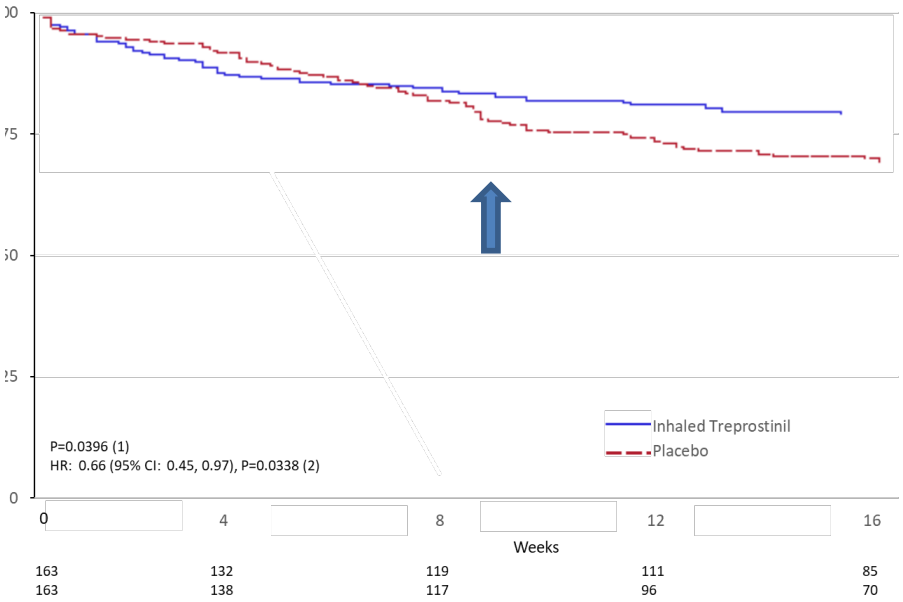
Inhaled treprostinil resulted in a 42% reduction in NT-proBNP when compared to placebo at Week 16 (P<0.001)

CI, confidence interval; LS Mean, least squares mean; NT-proBNP, N-terminal pro-brain natriuretic peptide.
LS Mean, p-values, estimated difference, and associated 95% CIs were from the mixed model repeated measurement with the change from baseline in log-transformed NT-proBNP as the dependent variable; treatment, week, treatment by week interaction as the fixed effects; and log-transformed baseline NT-proBNP as the covariate. An unstructured variance/covariance structure shared across treatment groups was used to model the within-subject errors.

Time to Exacerbation of Underlying Lung Disease



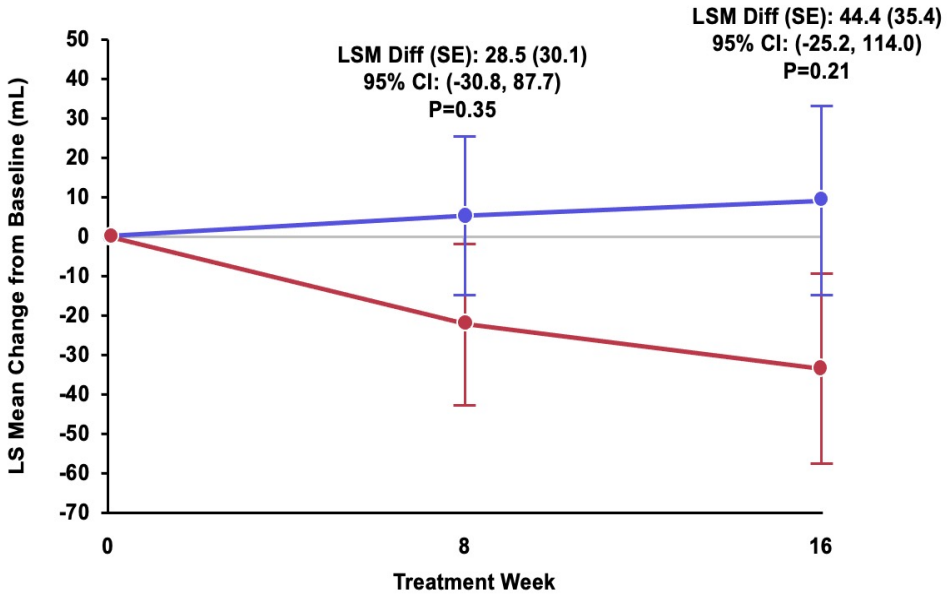
Time to Clinical Worsening Events



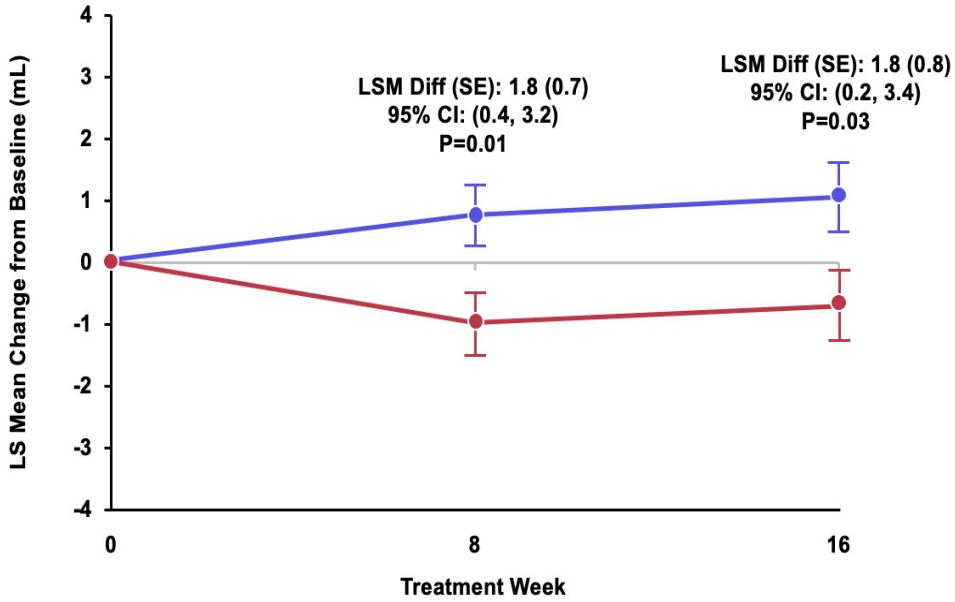
Exacerbation: acute, clinically significant, respiratory deterioration characterized by evidence of new widespread alveolar abnormality
TTCW: death, need for and/or worsening-related listing for lung and/or heart transplant, need to initiate an approved PAH SOC rescue therapy, PAH-specific hospitalization, or functional deterioration (worsened WHO Functional Class AND 15% decrease in 6MWD)

FVC improved with inhaled treprostinil by 28.47 mL and 44.40 mL at Weeks 8 and 16, respectively, when compared to placebo

LS mean change in FVC (mL) by week for overall ITT population



LS mean change in FVC % predicted by week for overall ITT population



BRIGHAM AND WOMEN'S HOSPITAL

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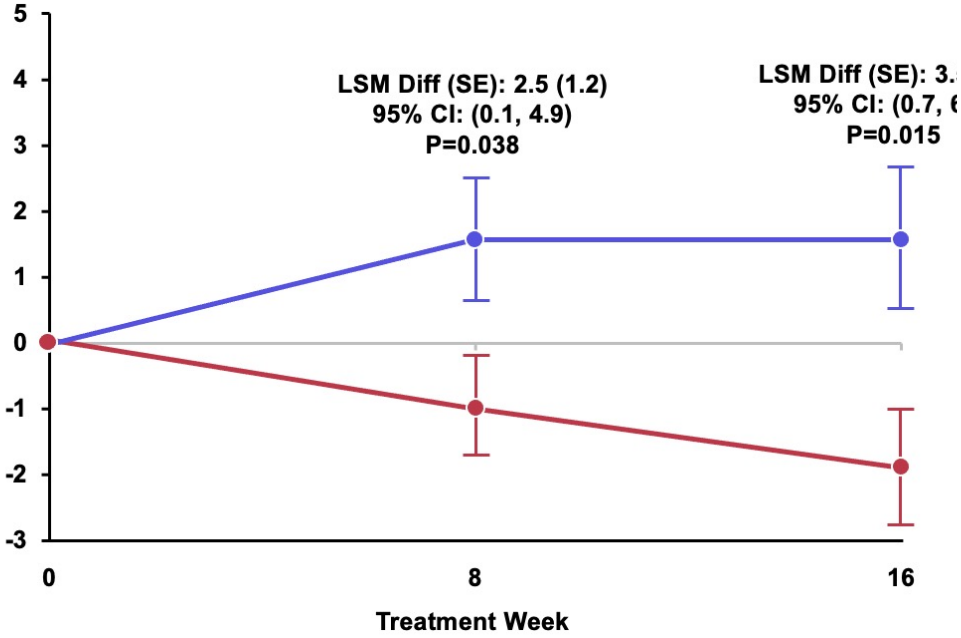
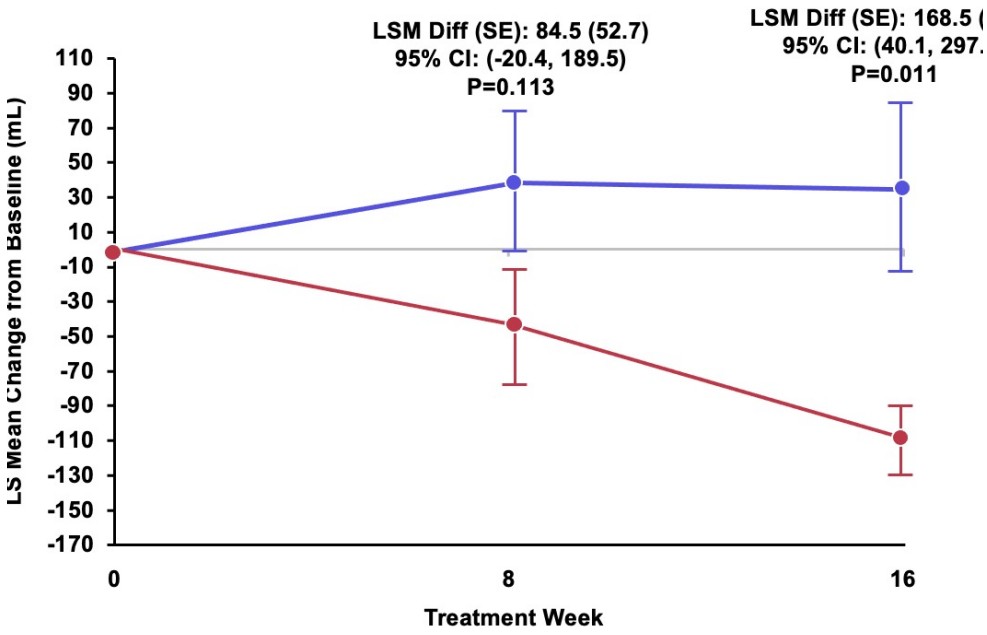
HARVARD MEDICAL SCHOOL

For patients with IPF FVC improvements of 84.52 mL and 168.52 mL (N=92, p=0.0108) at Weeks 8 and 16

LS mean change in FVC (mL) by week for subset of patients with IPF



LS mean change in FVC % predicted by week for subset of patients with IPF



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Conclusions

- Complex pathogenesis
- Improved outcomes, but long way to go
- Clear rational for combination therapy
- Clear benefit to treating patients with interstitial lung disease and pulmonary hypertension
- Room for additional therapeutic targets

You are asked to see a 32-year-old woman with a history of Raynaud's disease. No other past medical history. Family history is notable only for hypertension and type II diabetes. She complains of about 1-2 years of exertional intolerance that has been progressively worse. She now reports being very winded after climbing a flight of stairs. She denies lightheadedness or presyncope. Her physical examination was unrevealing.

Her primary care physician had ordered PFT's that were notable for a borderline DLCO, but otherwise normal. Her chest radiograph was read as no acute disease. An echocardiogram showed a normal left heart, with borderline dilation of the right atrium and an estimated right ventricular systolic pressure (RVSP) of 65 mmHg. What should you do next?

a. Order a pulmonary angiogram
b. Order a right heart catheterization
c. Start her on the combination of Sildenafil 20mg TID and Ambrisentan 10mg QD
d. Order a high-resolution CT scan of the chest

- Correct answer is “b”
- Importantly, the RVSP obtained by echo is an estimate. It can over or underestimate the right ventricular pressure. It also will not differentiate pre from post capillary disease. Only a right heart catheterization will allow for a clear diagnosis of pulmonary hypertension and specifically pulmonary arterial hypertension. Once the diagnosis is made then a test to rule out thromboembolic disease will be important, as well as testing to make sure there is no underlying parenchymal lung disease.