TRIUMPH 1: Long-term Safety and Efficacy of Inhaled Treprostinil Sodium in Patients With Pulmonary Arterial Hypertension (PAH): 2-Year Follow-up

R Benza,[1] L Rubin,[2] V McLaughlin,[3] R Channick,[2] R Voswinckel,[4] V Tapson,[5] I Robbins,[6] H Olschewski,[7] W Seeger[4]

[1]Univ of Alabama, Birmingham, AL; [2]UCSD, La Jolla, CA; [3]Univ of Michigan, Ann Arbor, MI; [4]Univ of Giessen Lung Center, Giessen, Germany; [5]Duke Univ, Durham, NC; [6]Vanderbilt Univ, Nashville, TN; [7]Medical Univ, Graz, Austria

Disclosure of Commercial Interests

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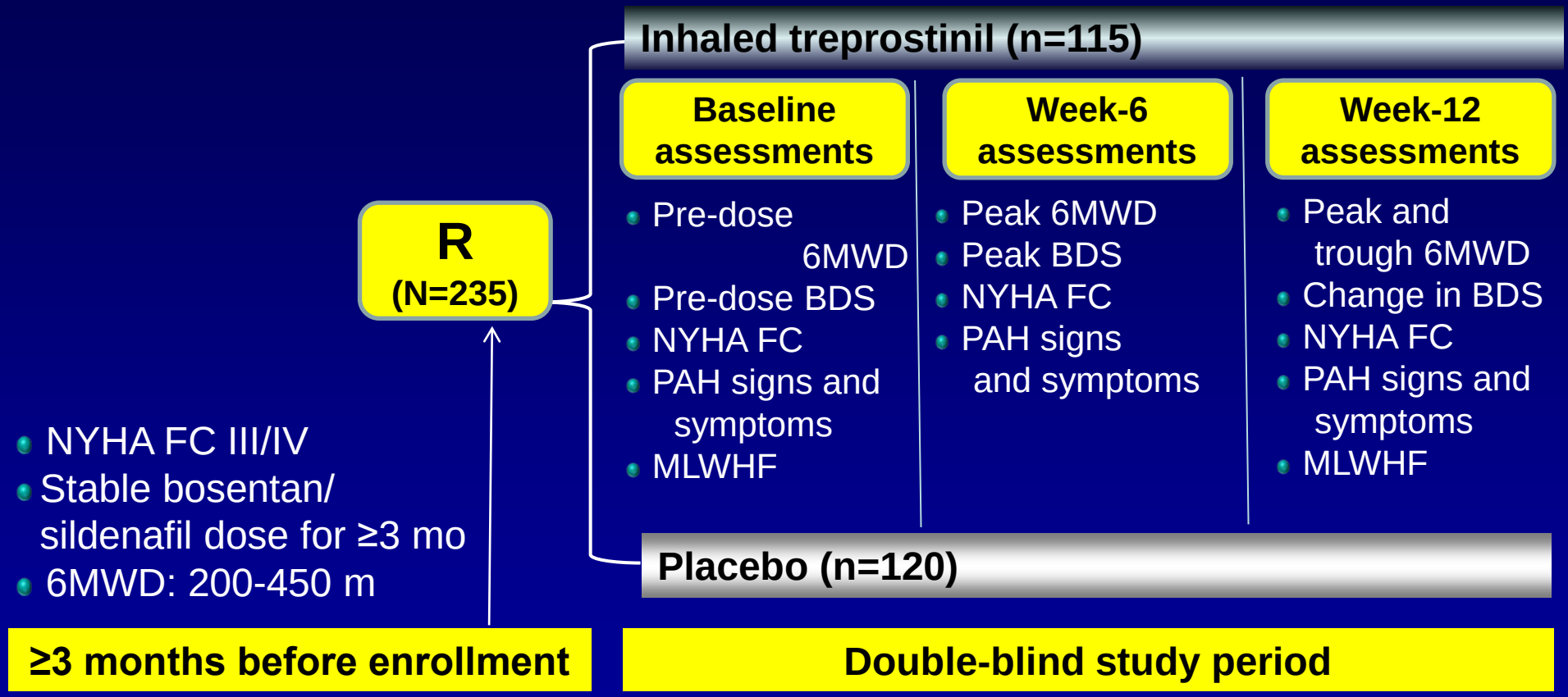
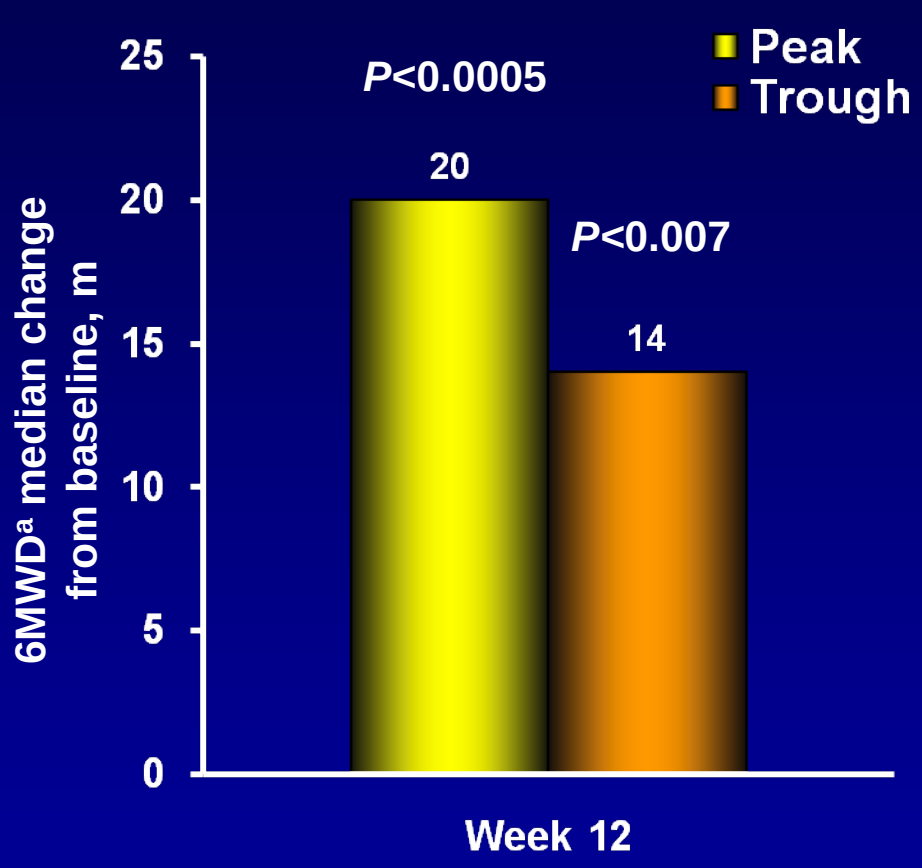
Study Design: Double-blind Phase



BDS, Borg dyspnea score; FC, functional class; MLWHF, Minnesota Living with Heart Failure; 6MWD, 6-minute walk distance; NYHA, New York Heart Association.

Conclusions- Double-blind Phase



- **Addition of inhaled treprostinil significantly improved**
  - Peak and trough 6MWD
  - BNP
  - QOL
- **Inhaled treprostinil was well tolerated**
  - Systemic AE profile was typical of other prostacyclin based therapies
  - Cough and throat irritation were related to inhalation delivery route

AE, adverse event; BNP, B-type natriuretic peptide; QOL, quality of life.

[a] Placebo-adjusted values. Peak defined as measured between 10 and 60 minutes after dose. Trough defined as measured ≥4 hours after dose.

McLaughlin et al., ATS 2008

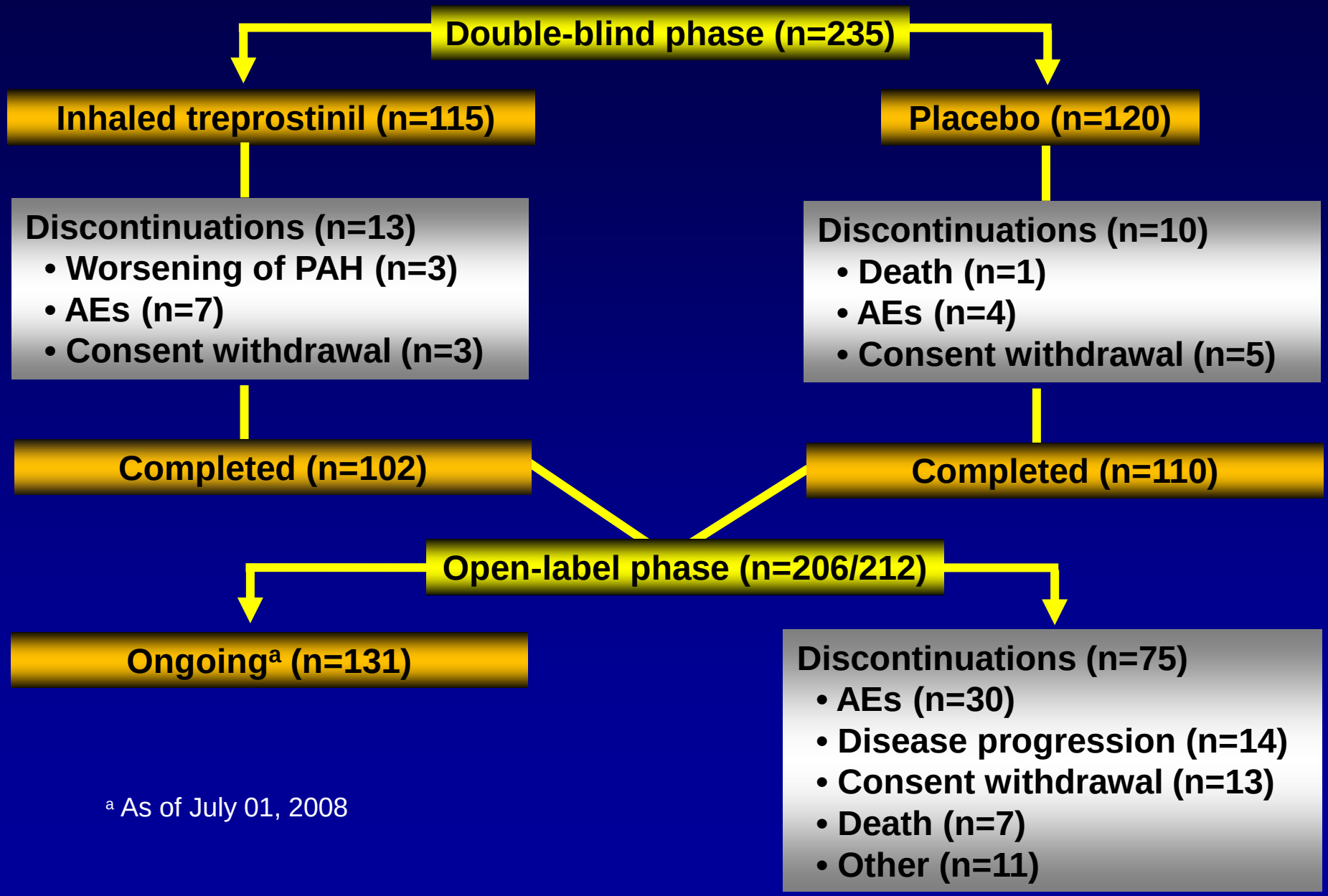
TRIUMPH-1: Open-label Phase

- Primary objective
  - Long-term effects of chronically administered inhaled treprostinil on exercise capacity (6MWD)
- Secondary objectives
  - Safety of inhaled treprostinil
  - BDS
  - Clinical worsening
  - NYHA functional class
  - QOL changes (MLWHF)
- Study visits: every 3 months to assess objectives

Key Points

- Dose: All patients initiated/reinitiated at 3 breaths (18 ug) QID in the open label and then titrated to 12 breaths (72 ug) QID
- Baseline: Refers to time initiated on active treprostinil
- Efficacy results computed for patients remaining on active drug at respective time points

Patient Disposition



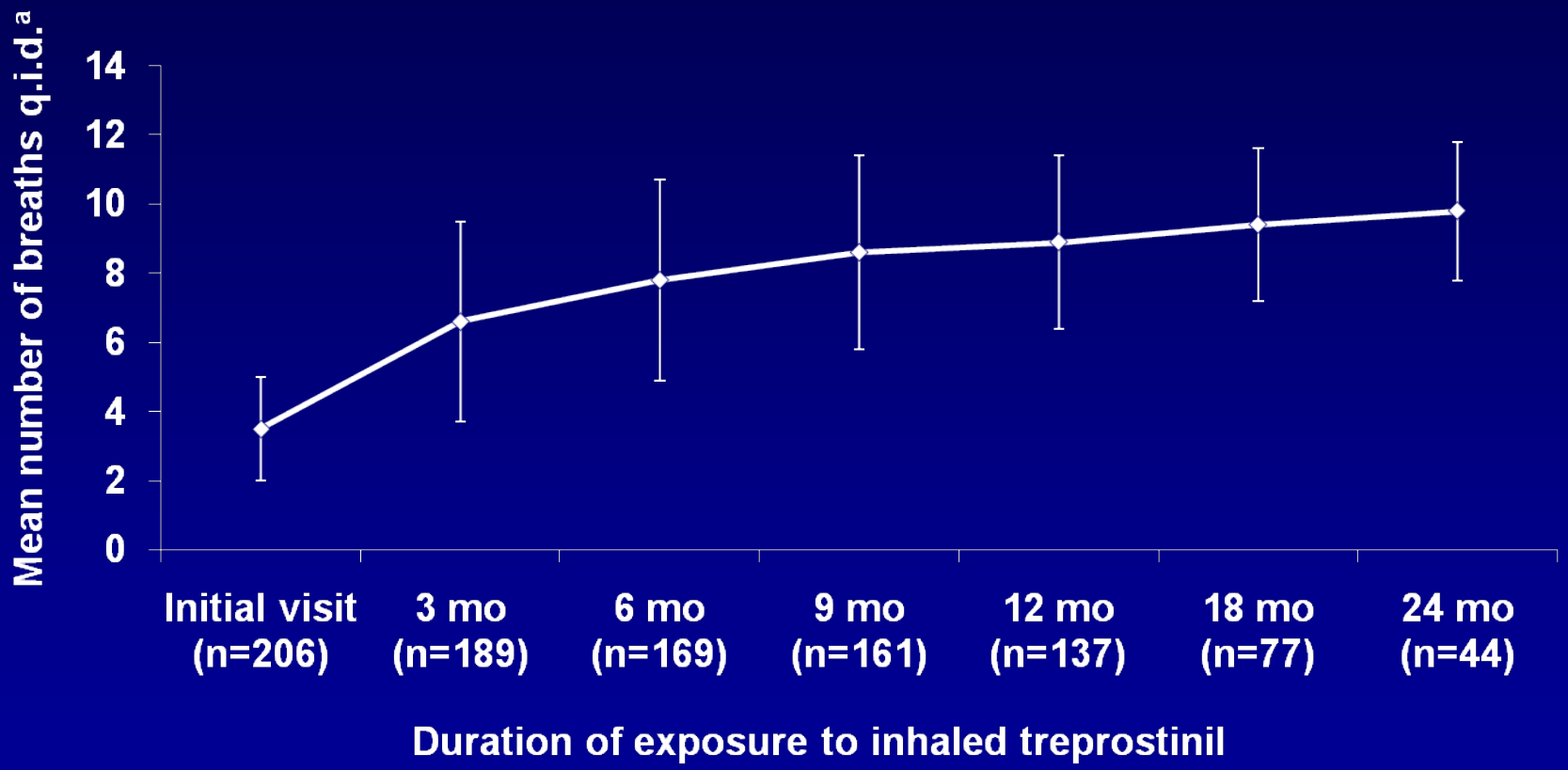
[a] As of July 01, 2008

Baseline Demographics

Characteristic	Inhaled treprostinil (n=206)
Age in years: mean (range)	54 (18-75)
Female:Male, %	81:19
PAH etiology, n (%)	
IPAH	116 (56)
CVD	66 (32)
Other (e.g., HIV, anorexigen)	24 (12)
Background PAH therapy, n (%)	
Bosentan	143 (69)
Sildenafil	63 (31)
Time on background therapy, mean ± SD, wk	90 ± 74
Baseline NYHA class II:III:IV, %	11:86:3
Baseline 6MWD, mean ± SD, m	349 ± 81

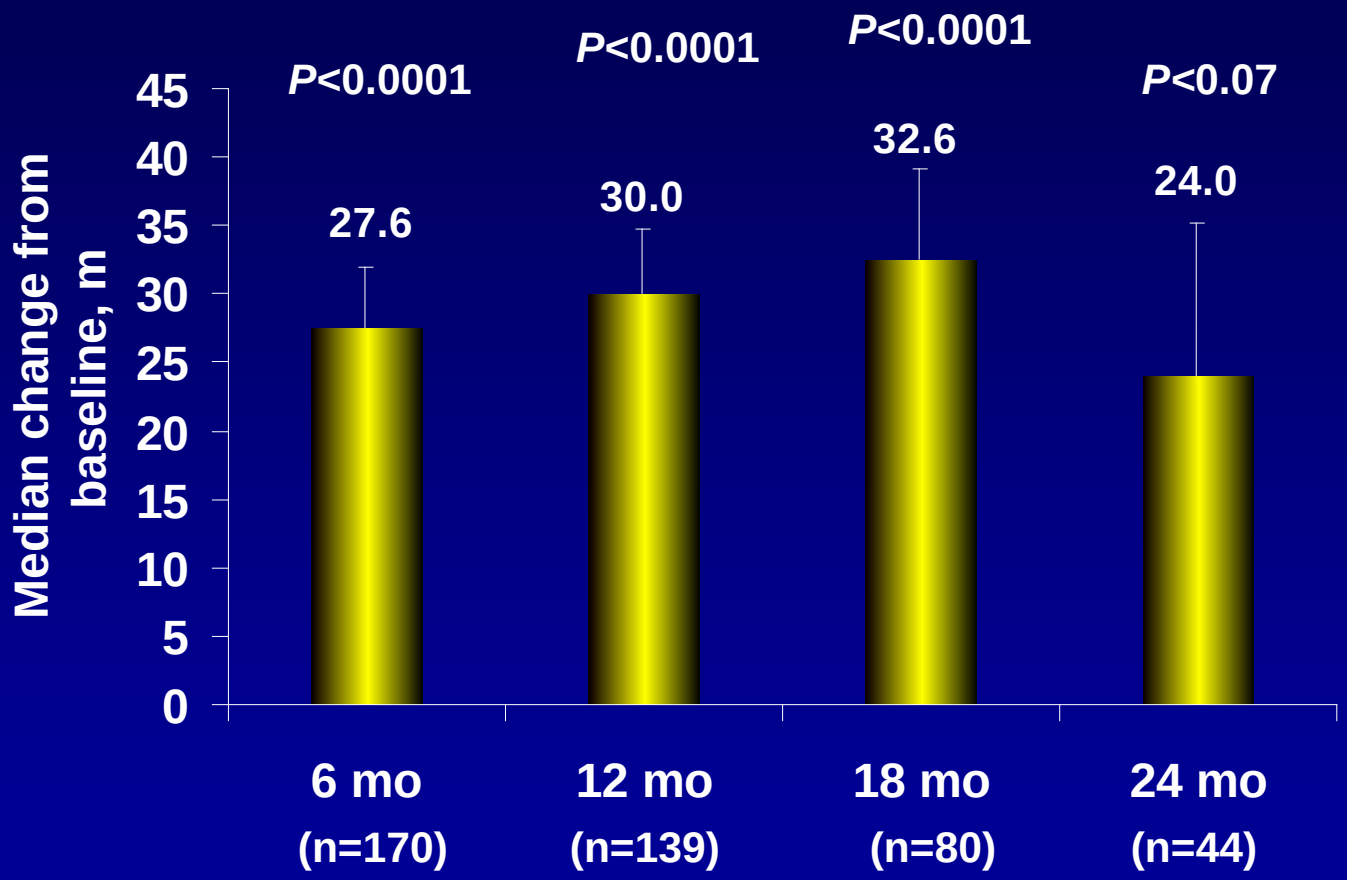
CVD, collagen vascular disease; HIV, human immunodeficiency virus; IPAH, idiopathic PAH; SD, standard deviation.

Achieved Inhaled Treprostinil Dose



[a] Each breath = 6 μg.

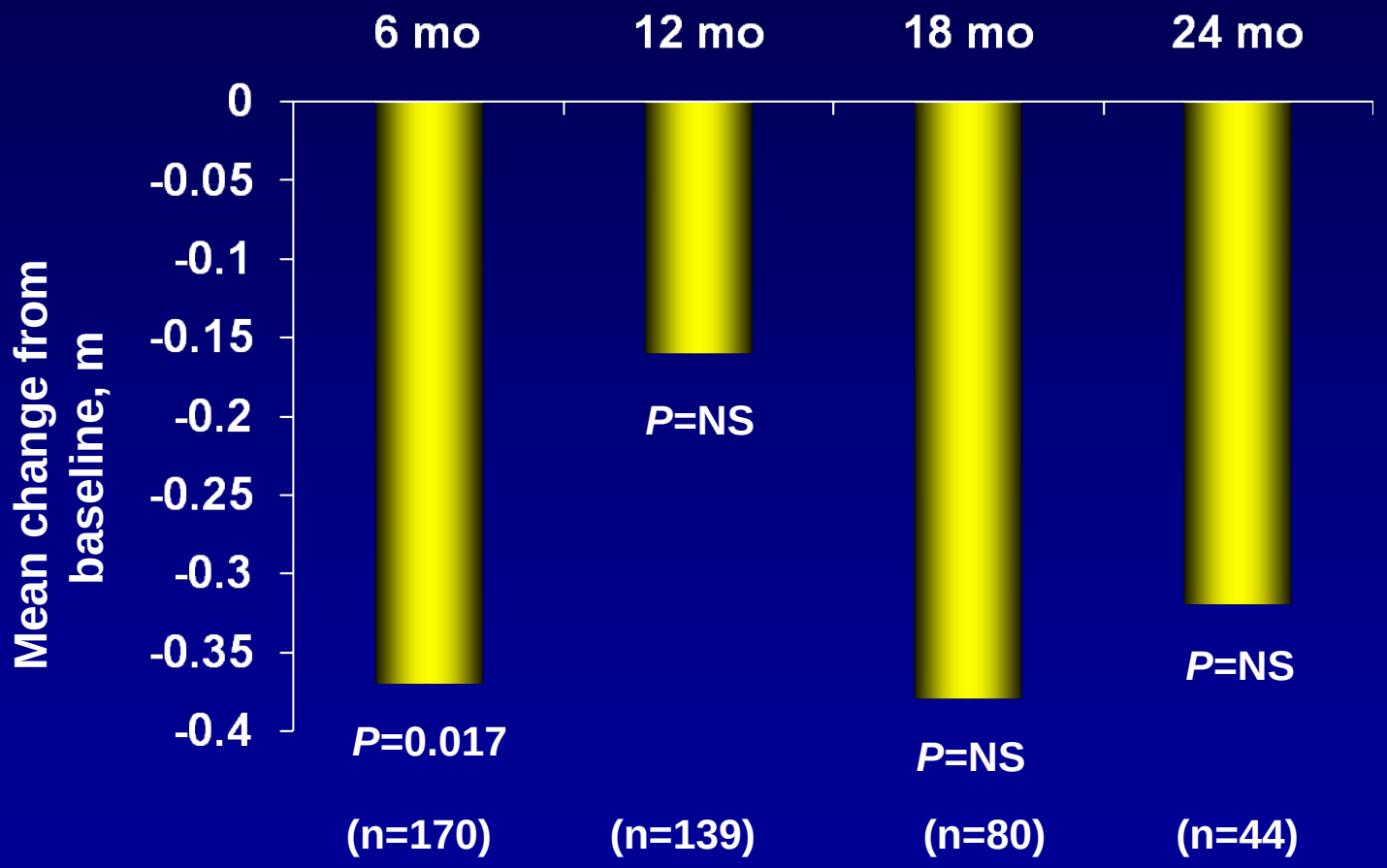
6MWD Median Change From Baseline



Median baseline value, m	**365.2**	**363.0**	**358.5**	**350.5**

NS, not significant. *P* values calculated using Wilcoxon signed rank test.

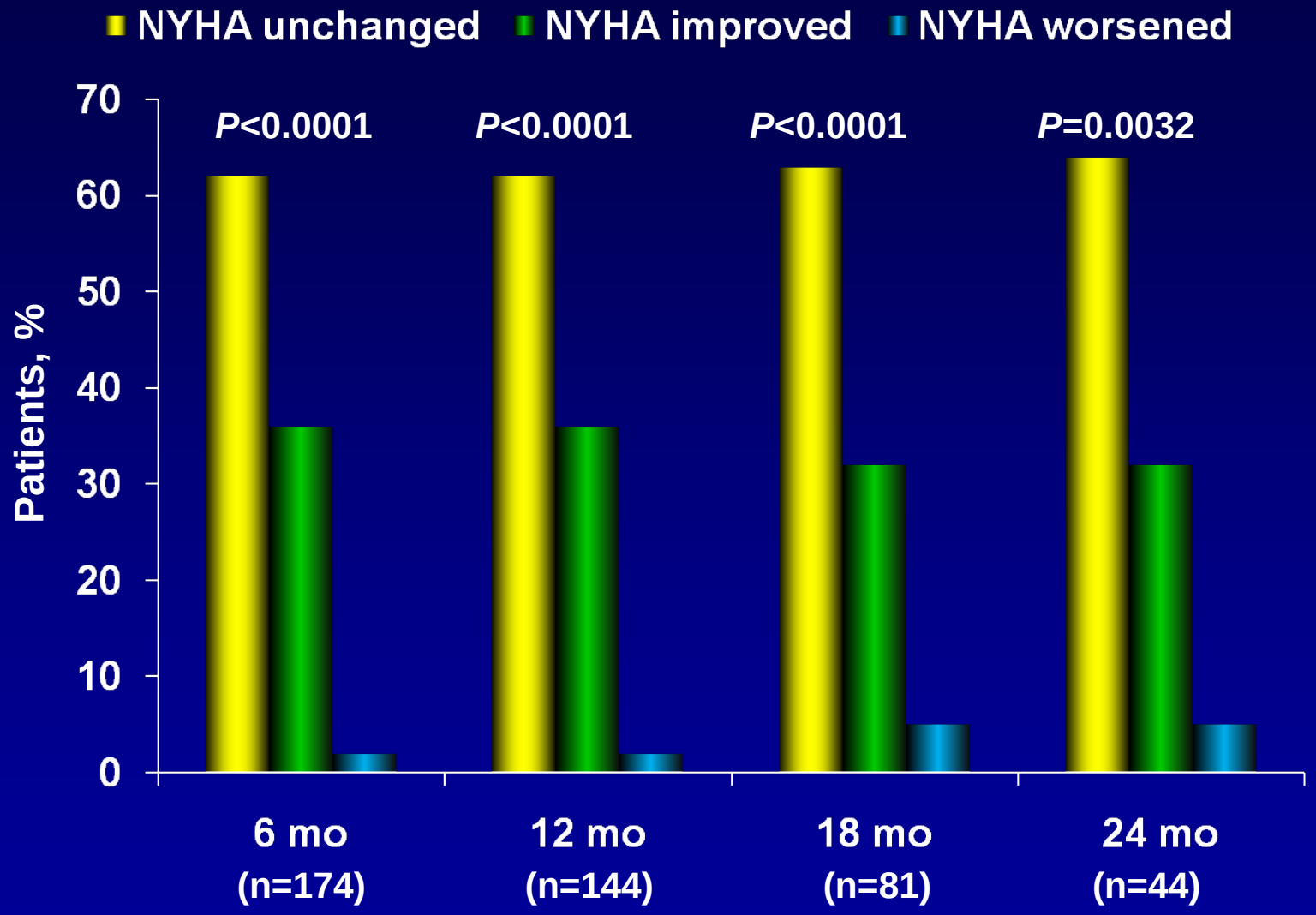
Borg Dyspnea Score Mean Change From Baseline



Mean baseline value	**3.8**	**3.9**	**3.9**	**3.9**

P values calculated using paired *t* test.

NYHA Functional Class Change From Baseline



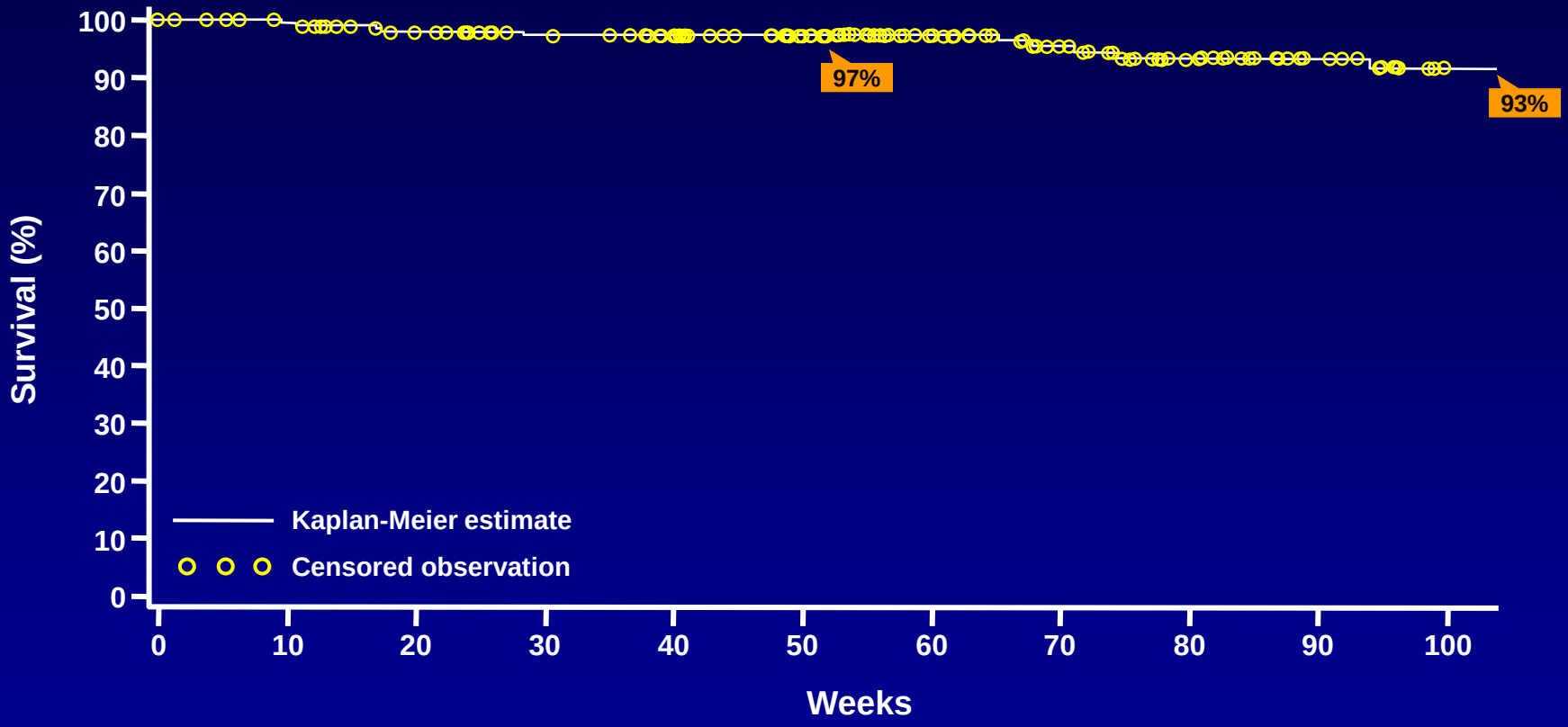
Baseline FC I:II:III:IV, %	6 mo (n=174)	12 mo (n=144)	18 mo (n=81)	24 mo (n=44)
	0:8:90:2	0:9:88:1	0:14:84:2	0:16:82:2

P values calculated using Wilcoxon signed rank test.

Quality of Life
Mean Change From Baseline

		MLWHF global score		
Time point	Patients, n	Baseline, mean	Change from baseline, mean ± SD	*P* value
6 months	163	45.8	-5.6 ± 16	<0.0001
12 months	137	45.2	-6.2 ± 17	<0.0001
18 months	74	42.7	-7.0 ± 17	0.0007
24 months	42	42.5	-4.2 ± 19	NS

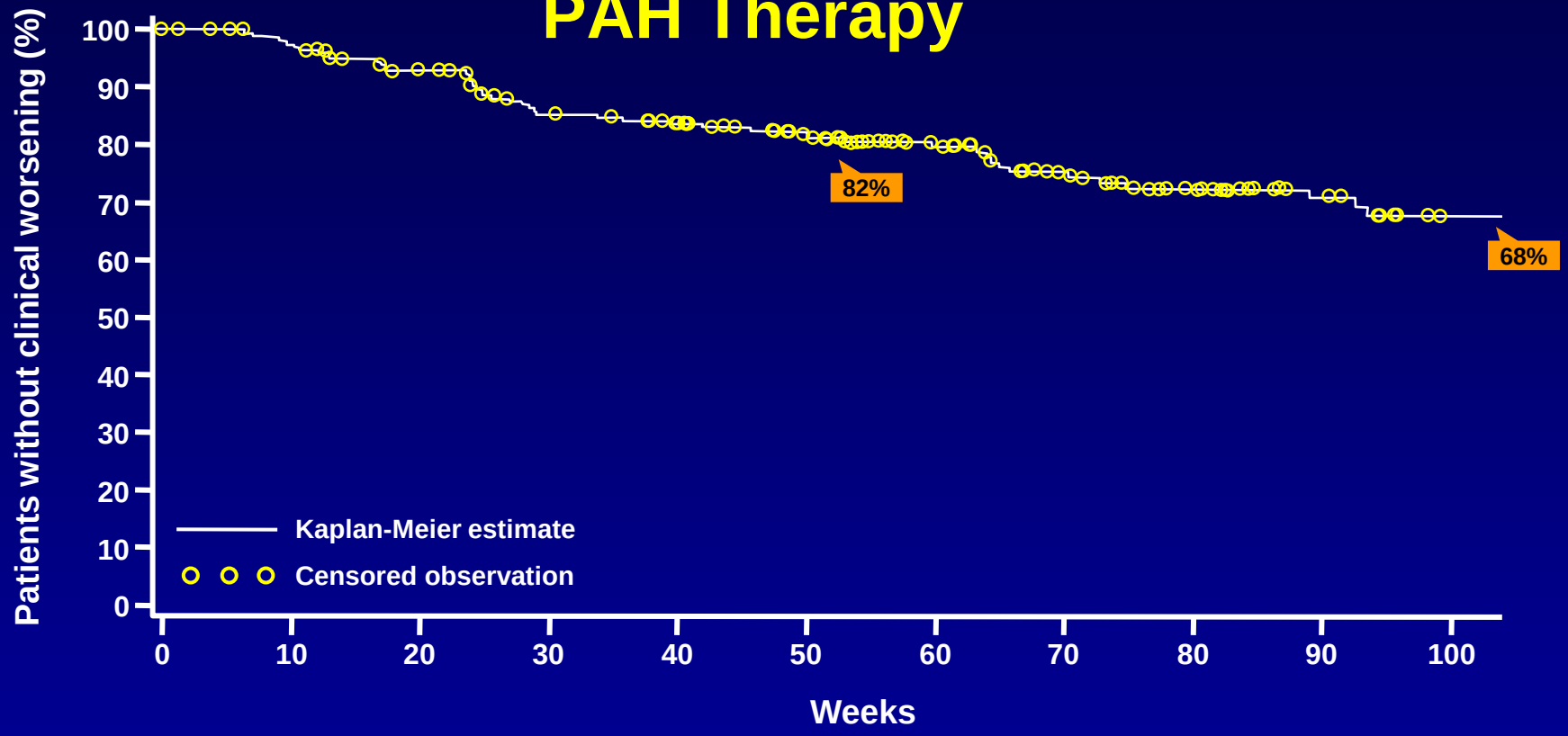
Overall Survival



Weeks	0	13	26	39	52	65	78	91	104
Events (n)	0	2	4	5	5	5	9	9	10[a]
Censored (n)	1	13	31	39	62	97	120	139	152
Patients remaining (n)	205	191	171	162	139	104	77	58	44

[a] Patients who died during open-label study or within 14 days of discontinuation from study.

Kaplan-Meier Analysis of Death, Discontinuation due to Disease Progression or Addition of Approved PAH Therapy



Weeks	0	13	26	39	52	65	78	91	104
Events (n)	0	9	22	29	34	39	44	45	47
Censored (n)	1	11	24	30	53	81	98	115	125
Patients remaining (n)	205	186	160	147	119	86	64	46	34

Summary of Adverse Events

AE[a]	Patients, n (%) (n=206)
Any AE	188 (91)
Cough	71 (34)
Headache	46 (22)
Dyspnea	32 (16)
Nausea	30 (15)
Pulmonary hypertension	26 (13)
Upper respiratory tract infection	23 (11)
Chest pain	20 (10)
Dizziness	20 (10)
Pharyngolaryngeal pain	20 (10)

- No clinically significant changes in clinical chemistry or hematologic parameters

[a] Individual AEs reported in ≥10% of patients, regardless of causality.

Adverse Events Leading to Discontinuation

AE[a]	Patients, n (%) (n=206)
Any AE	33 (16)
Pulmonary hypertension	7 (3)
Cough	6 (3)
Headache	4 (2)
Nausea	2 (<1)
Pneumonia	2 (<1)
Pulmonary embolism	2 (<1)

[a] Individual AE reported in >1 patient.

Summary

- Inhaled treprostinil in combination with oral monotherapy can provide a durable effect on physical functioning and QOL with a favorable safety profile
- Survival rate was 93% at 2 years for patients on combined therapy with inhaled treprostinil
- 68% of patients at 2 years remained clinically stable on combined therapy with inhaled treprostinil without the need for additional PAH therapy
- Over 90% of evaluable subjects maintained or improved their NYHA functional class from BL

TRIUMPH Study Investigators

David Badesch
Univ of Colorado Health Sciences Center

Jose Albert Barbera
Hospital Clinic I Provincial de Barcelona

Raymond Benza
Univ of Alabama at Birmingham

Neville Berkman
Hadassah Ein Kerem Medical Center

Robert Bourge
Univ of Alabama at Birmingham

Richard Channick
UCSD Medical Center

Gerry Coghlan
Royal Free Hospital

Marion Delacroix
Univ Hospital Gasthuisburg

Nazzereno Gaile
Instituto Malattie dell'Apparato Vascolare

Sean Gaine
Mater Misericordiae

Simon Gibbs
Hammersmith Hospital

Reda Girgis
Johns Hopkins Univ

Nicholas Hill
Tufts New England Medical Center

Steven Knoper
Univ of Arizona Health Sciences Center

Mordechai Kramer
Rabin Medical Center

Irene Lang
Medizinische Universtaet Wien

Vallerie McLaughlin
Univ of Michigan

Srinivas Murali
Allegheny Medical Center

Robert Naeije
Univ Libre de Bruxelles

Horst Olchewski
Medical University Graz

Ronald Oudiz
Harbor-UCLA Medical Center

Andrew Peacock
Scottish Pulmonary Vascular Unit

Joanna Pepke-Zaba
Papworth Hospital

Ivan Robbins
Vanderbilt Univ Med Center

Werner Seeger
Univ of Giessen Lung Center

Gerald Simonneau
Hospital Antonnine Beclere

Roxana Sulica
Beth Israel Medical Center

Victor Tapson
Duke University Medical Center

James Tarver
Orlando Health Care

Fernando Torres
UTSW Medical Center Dallas/ St. Paul Univ Hospital

Timothy Williamson
Kansas University Medical Center

Mordechai Yigla
Rambam Medical Center