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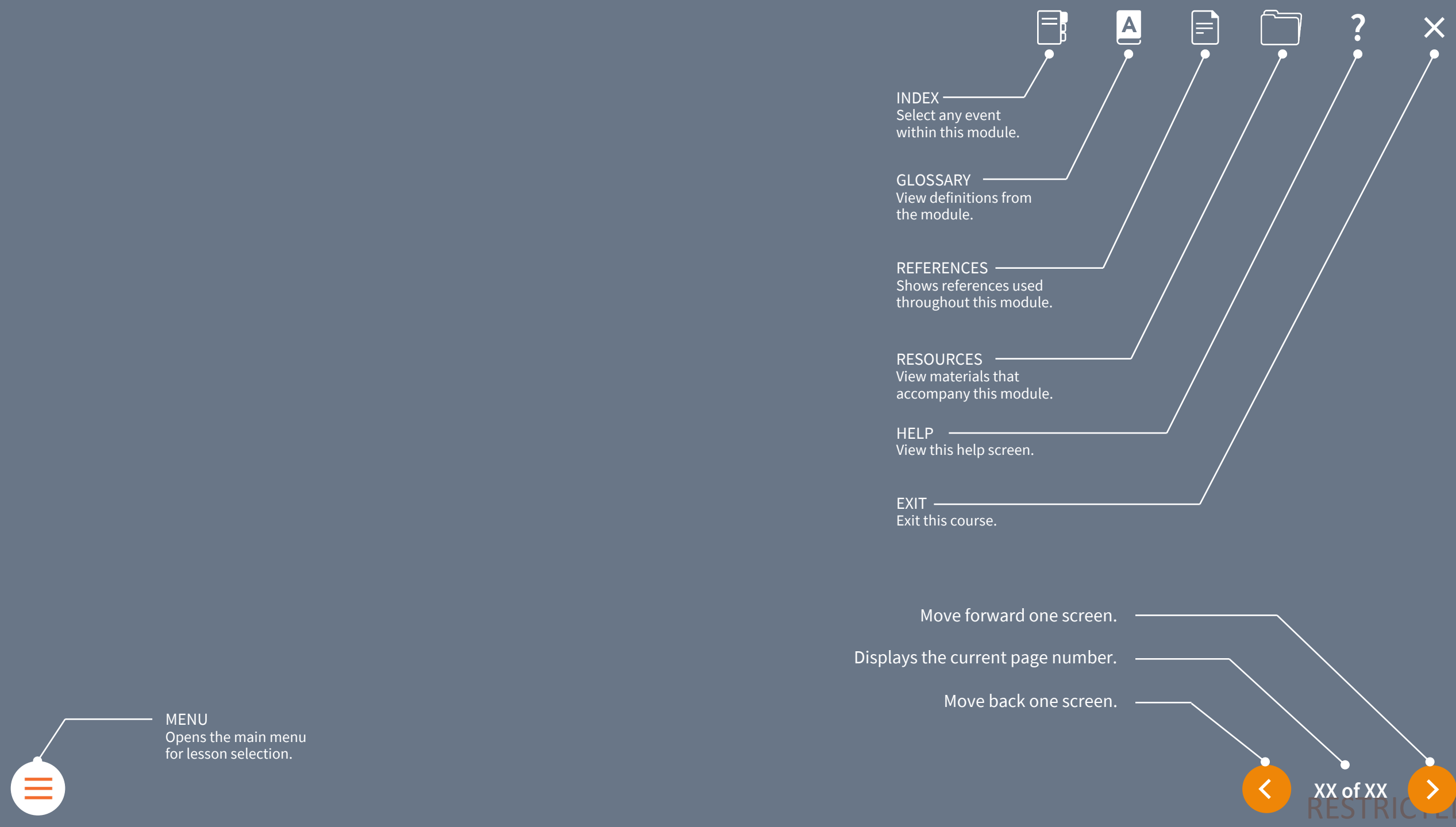
INDEX
Select any event within this module.
GLOSSARY
View definitions from the module.
REFERENCES
Shows references used throughout this module.
RESOURCES
View materials that accompany this module.
HELP
View this help screen.
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Exit this course.
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Opens the main menu for lesson selection.
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Index

Glossary

6-minute walking distance (6MWD): The distance a person is able to walk in 6 minutes on a hard, flat surface.

etiology: the cause or causes of a disease or abnormal condition

Hemodynamic parameters: Basic measures of cardiovascular function, such as arterial pressure.

Idiopathic PAH: PAH due to an unknown cause

N-terminal pro-brain natriuretic peptide (NT-proBNP): A hormone secreted by the left or right ventricle of the heart; bloodstream concentration of NT-proBNP increase with heart damage.

pulmonary vascular resistance (PVR): The vascular resistance of the pulmonary circulation, equal to the difference between the mean pulmonary arterial pressure and the left atrial filling pressure divided by the cardiac output.

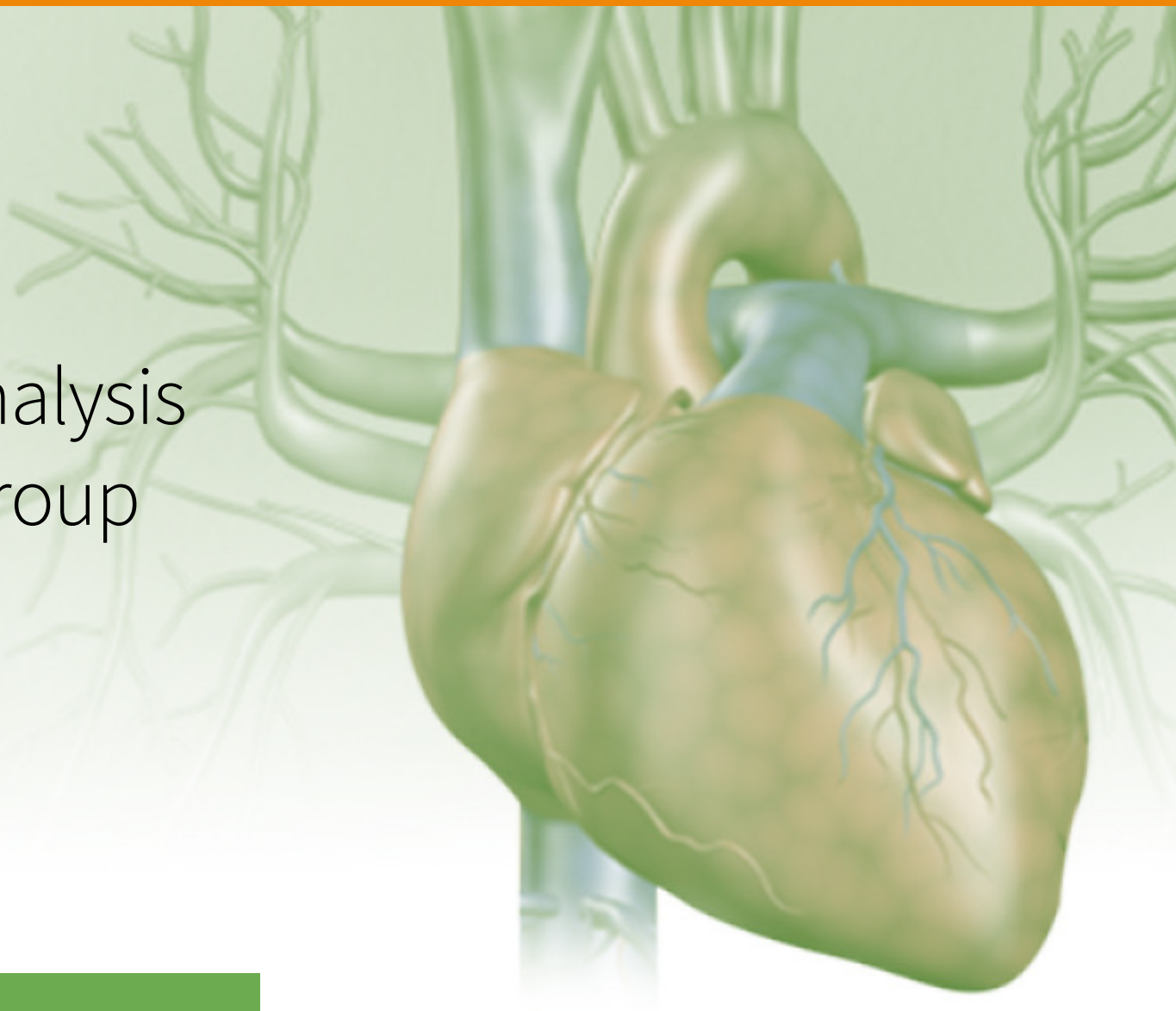
World Health Organization functional classification (WHO FC): a tool used to measure disease severity in PH patients across classes. Assessment in a higher class indicates a more severe disease.

ADEMPAS LEARNING SYSTEM

MODULE:

PAH Adempas Treatment Analysis With Treatment-Naïve Subgroup

Select start to begin.



Start

Introduction

Meet Aisha.

Up until a year ago, Aisha had no problem keeping up with her busy life as a wife, mother, and writer. She was previously diagnosed with essential hypertension (for which she takes lisinopril 20 mg daily). Other than that, she had no medical problems until—at age 42—she started to find herself more winded than usual. Even her daily activities around the house like vacuuming and carrying her laundry up the stairs started to leave her short of breath. Even though she recovered when she paused to rest, Aisha decided to speak with her doctor.

Aisha was referred to a pulmonary hypertension (PH) specialist for evaluation of her shortness of breath and diagnosed with Pulmonary Arterial Hypertension (PAH).

This module will provide you with a review of PAH and a walkthrough of the PATENT-1 and PATENT-2 data for PAH treated with Adempas (riociguat). While we will walkthrough the full data set from the study, particular attention will be given to the treatment-naïve subgroup analysis.

Aisha

All individuals in this module are actors.

Learning Objectives

At the completion of this lesson, you should be able to:

- Define PAH and its clinical outcomes
- Describe the baseline characteristics and results from PATENT-1 including the subgroup analysis of treatment-naïve patients
- Identify the outcomes of the PATENT-2 long-term study including the subgroup analysis of treatment-naïve patients

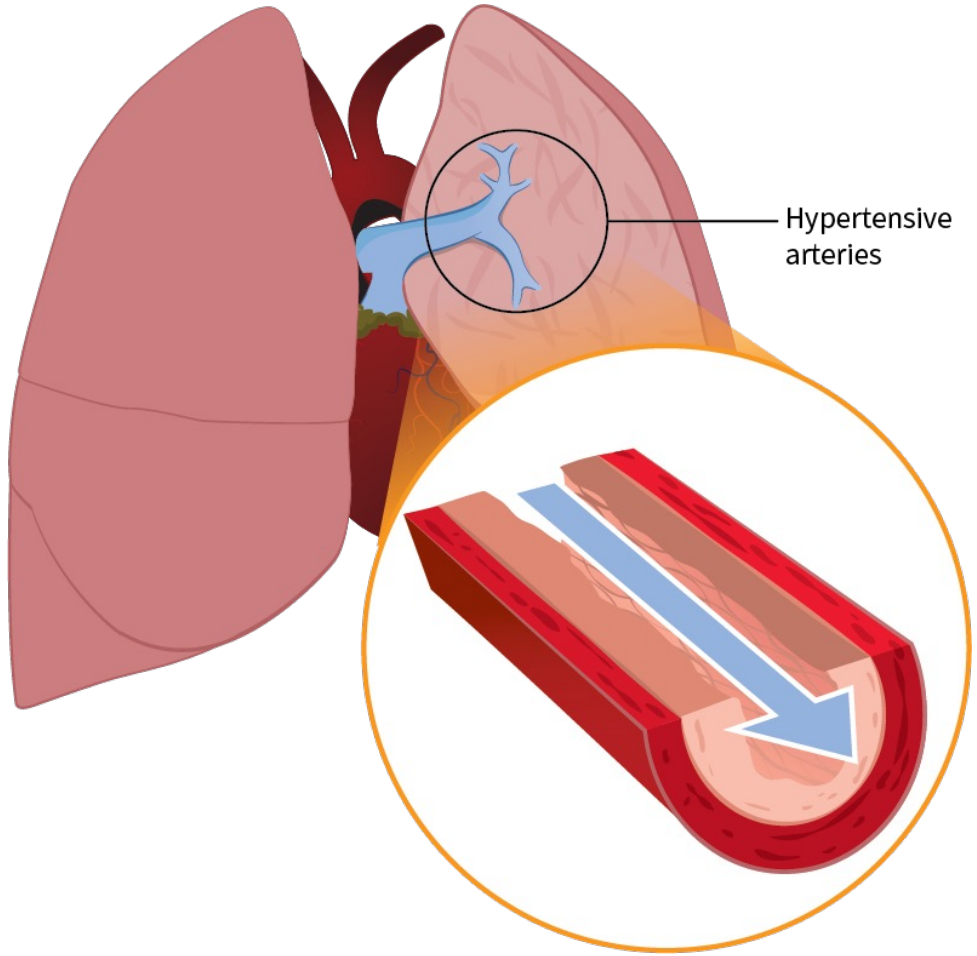
Review: What Is PAH?

Pulmonary arterial hypertension (PAH) is a subgroup of pulmonary hypertension (PH) and is defined as abnormally high pressure (≥25 mm Hg) in the pulmonary artery, the blood vessel that carries blood from the heart to the lungs.

In PAH, blood vessels in the lungs narrow or are blocked, making it difficult for blood to flow through them. This results in increased blood pressure, and a variety of associated symptoms like faintness, shortness of breath, and chest pain.

Who does it affect, and what is the outlook for individuals diagnosed with this condition? Select the buttons below to find out.

Select the buttons to learn more about PAH.

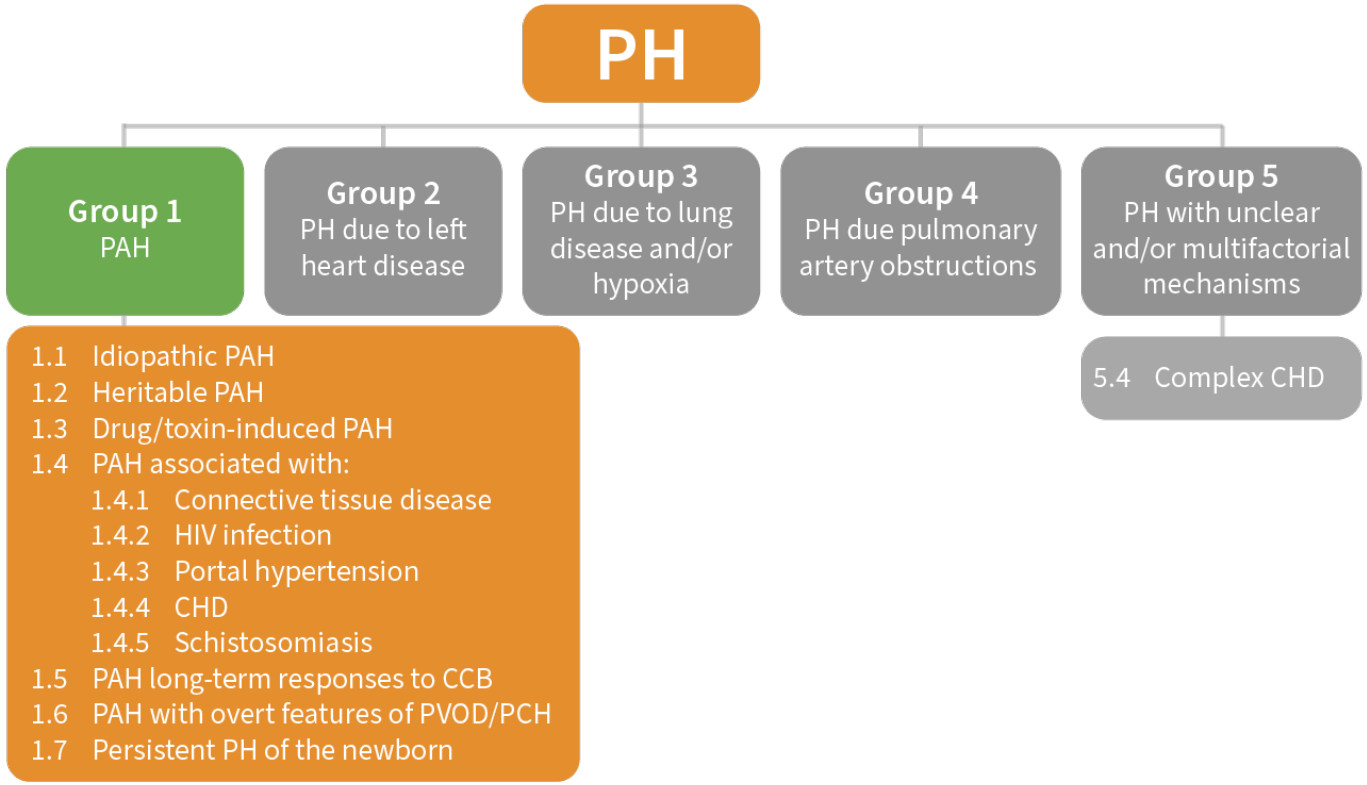


+ Classification, Prevalence, & Outcomes

+ Risk Factors

Classification, Prevalence, Incidence, & Clinical Outcomes

- The classification of PAH has developed over time. PAH now comprises Group 1 of PH, including **idiopathic PAH**, heritable PAH, drug- and toxin-induced PAH, as well as PAH associated with congenital heart disease (CHD) and connective tissue disease (CTD).
- According to a global estimate, the incidence of PAH in adults ranges from 1.5-32 ppm, and the prevalence ranges from 12.4-268 ppm.
- 1-year survival for PAH is variable based on sub-group and risk factors. It ranges from 67%-99%.



All individuals in this module are actors.

What Are the Risk Factors for PAH?

- **Age:** Risk increases with age. Diagnosis occurs predominantly between the ages of 30 and 60.
- **Sex:** PAH is twice as common in females as in males.
- **Environment:** Exposure to asbestos or certain infections caused by parasites may increase risk of PAH.
- **Family history and genetics:** Can be heritable, but also occurs in individuals with no known family history. Family history of blood clots increases risk of PAH. Certain genetic disorders can also increase risk (eg, congenital heart disease, Down Syndrome, connective tissue disorder).
- **Lifestyle habits:** Smoking, illegal drug use (such as cocaine and methamphetamine), and appetite suppressants can increase risk.
- **Medicine:** Some prescribed medicines used to treat cancer and depression may increase the risk of PAH.

How Can We Assess Risk of PAH?

The 2022 European Society of Cardiology/European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and treatment of PAH recommend the use of **2 models for assessing risk** of worsening symptoms and mortality in PAH patients. These models are a more granular and comprehensive approach to PH risk assessment than simply leveraging the **World Health Organization functional classification (WHO FC)**. The ESC/ERS **provides specific treatment approaches based on the risk assessment model outcomes**. In both models, risk is assessed using WHO FC, **6-minute walking distance (6MWD)**, **N-terminal pro-brain natriuretic peptide (NT-proBNP)**, and **hemodynamic parameters**. As you will soon see, these same markers are used in the PATENT-1 and PATENT-2 studies to assess treatment efficacy.

3-strata model: Used to assess risk at diagnosis

- This model helps determine treatment escalation, risk assessment, and general treatment strategies for PH patients upon diagnosis
- Use the table to the right to help determine risk at diagnosis. Note the WHO FC, 6MWD, and biomarker categories

4-strata model: Used to assess risk at follow-up

- The 4-strata model is used to facilitate more granular treatment strategies. Stable patients are assessed every 3-6 months with this model; unstable patients should be assessed more frequently
- This model is developed to be customizable and adjustable to specific patient needs, PAH **etiology**, risk category, demographics, and comorbidities. Assessment frequency and treatment strategies should be chosen based on these needs and factors

3-Strata Model

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5-20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	Peak VO_2 >15 mL/min/kg (>65 % pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 mL/min/kg (35–65 % pred.) VE/VCO_2 slope 36–44	Peak VO_2 <11 mL/min/kg (<35 % pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mm Hg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mm Hg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mm Hg Moderate or large pericardial effusion
cMRI[e]	RVEF >54 % SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54 % SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37 % SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mm Hg CI ≥2.5 $L/min/m^2$ SVI >38 mL/m^2 SvO_2 >65 %	RAP 8–14 mm Hg CI 2.0–2.4 $L/min/m^2$ SVI 31–38 mL/m^2 SvO_2 60–65 %	RAP >14 mm Hg CI <2.0 $L/min/m^2$ SVI <31 mL/m^2 SvO_2 <60 %

Select the button for a closer look at the 3-Strata model.

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5-20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO FC	I, II	III	IV
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Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mm Hg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mm Hg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mm Hg Moderate or large pericardial effusion
cMRI[e]	RVEF >54 % SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54 % SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37 % SVI <26 mL/m^2 RVESVI >54 mL/m^2
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a Occasional syncope during heavy exercise or occasional orthostatic syncope in a stable patient. b Repeated episodes of syncope even with little or regular physical activity. c Observe that 6MWD is dependent upon age, height, and burden of comorbidities. d To harmonize with the four-strata model shown in the 2022 ERS/ESC guidelines, the BNP and NT-proBNP cut-off levels have been updated from the 2015 version based on data from the REVEAL registry, acknowledging that the European validation studies have used the original cut-off levels. e cMRI parameters adapted from the 2022 ESC/ERS guidelines. 6MWD = 6-minute walking distance; BNP = brain natriuretic peptide; CI = cardiac index; cMRI = cardiac magnetic resonance imaging; CPET = cardiopulmonary exercise testing; HF = heart failure; NT-proBNP = N-terminal pro-brain natriuretic peptide; PAH = pulmonary arterial hypertension; pred = predicted; RA = right atrium; RAP = right atrial pressure; sPAP = systolic pulmonary arterial pressure; SvO2 = mixed venous oxygen saturation; RVESVI = right ventricular end-systolic volume index; RVEF = right ventricular ejection fraction; SVI = stroke volume index; TAPSE = tricuspid annular plane systolic excursion; VE/VCO2 = ventilatory equivalents for carbon dioxide; VO2 = oxygen uptake; WHO FC = World Health Organization Functional Class.

PATENT-1: Study Design

The PATENT-1 study was a randomized, double-blind, multinational, multicenter, placebo-controlled, 12-week, Phase 3 study that explored the efficacy of Adempas treatment in adults with PAH.

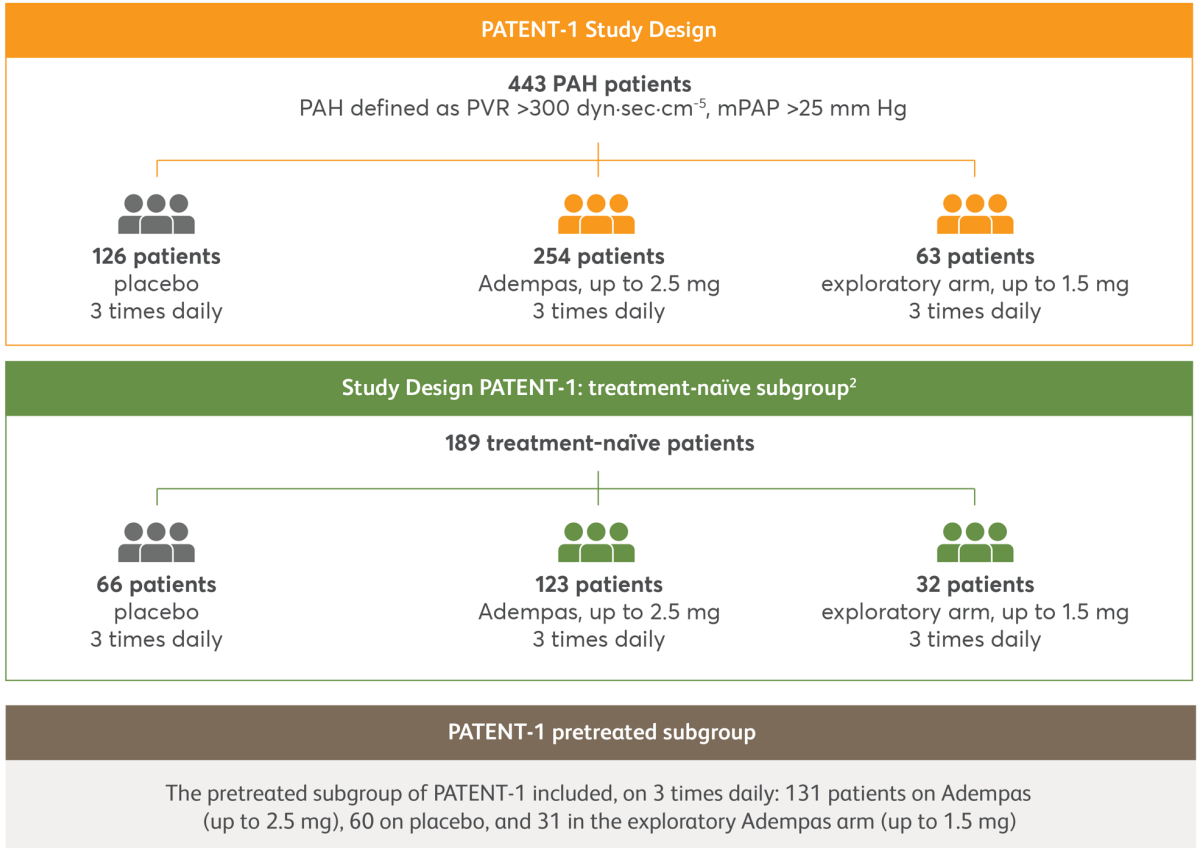
- The overall study population (N=443) was assigned to 1 of 3 treatment groups: **Placebo (n=126), Adempas up to 2.5 mg (n=254),** and Adempas up to 1.5 mg (n=63). Efficacy data were only measured for the Adempas up to 2.5 mg and placebo arms

PATENT-1 Study endpoints are as follows:

- **Primary: Change from baseline to Week 12 in 6MWD**
- Secondary: Change from baseline to Week 12 in WHO FC, time to clinical worsening event, **pulmonary vascular resistance (PVR)**, and NT-proBNP

After the study's conclusion, an **exploratory post-hoc subgroup analysis** examined data from two subgroups: **treatment-naïve (n=189)** and pretreated (n=191).

The treatment-naïve population—which had never been treated for PAH prior to this study—exhibited improvements across critical parameters. This subgroup is of particular interest and will be highlighted throughout this module.



PATENT-1: Baseline Characteristics in PAH Patients Treated With Adempas

This table shows the baseline characteristics of patients enrolled in PATENT-1. Patients in the treatment-naïve subgroup were slightly younger, on average, than patients in the overall population.

The pretreated subgroup had a larger percentage of Adempas-treated patients in WHO FC III (65%) than the treatment-naïve subgroup (45%). In the treatment-naïve subgroup, the majority of Adempas-treated patients were in WHO FC II (53%).

Take a moment to look at the mean 6MWD at baseline for each population. The Adempas-treated patients in the treatment-naïve subgroup had a mean 6MWD of 370 ± 66 meters at baseline. The Adempas-treated patients in the overall population had a mean 6MWD of 361 ± 68 meters whereas the pretreated subgroup's mean 6MWD was 353 ± 69 meters.

Now let's dive into the study's outcomes and data.

	Overall Population		Treatment-naïve		Pretreated	
Characteristic	**Adempas 2.5 mg—maximum (n=254)**	**Placebo (n=126)**	**Adempas 2.5 mg—maximum (n=123)**	**Placebo (n=66)**	**Adempas 2.5 mg—maximum (n=131)**	**Placebo (n=60)**
Female sex, n (%)	203 (80%)	98 (78%)	94 (76%)	52 (79%)	109 (83%)	46 (77%)
Age, years, mean (SD)	51 (17)	51 (17)	48 (17)	48 (18)	54 (15)	53 (15)
WHO FC, n (%)*						
I	5 (2%)†	4 (3%)	3 (2%)	4 (6%)	2 (2%)	0†
II	108 (43%)	60 (48%)	65 (53%)	35 (53%)	43 (33%)	25 (42%)†
III	140 (55%)	58 (46%)†	55 (45%)	25 (38%)	85 (65%)	33 (56%)†
IV	1 (0.4%)	3 (2%)	0	2 (3%)	1 (1%)	1 (2%)†
Missing	0	1 (1%)	0	0	0	0
6MWD, m, mean (SD)	361 (68)	368 (75)	370 (66)	360 (80)	353 (69)	376 (68)

*Data may not add up to 100% owing to rounding.
†n=59.

PATENT-1: Change in 6MWD

Recall our study's primary endpoint was the mean change from baseline at Week 12 in 6MWD—the distance a person is able to walk in 6 minutes on a hard, flat surface.

Select the buttons to view the full data set, the treatment-naïve subgroup analysis, and the subgroup comparison.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

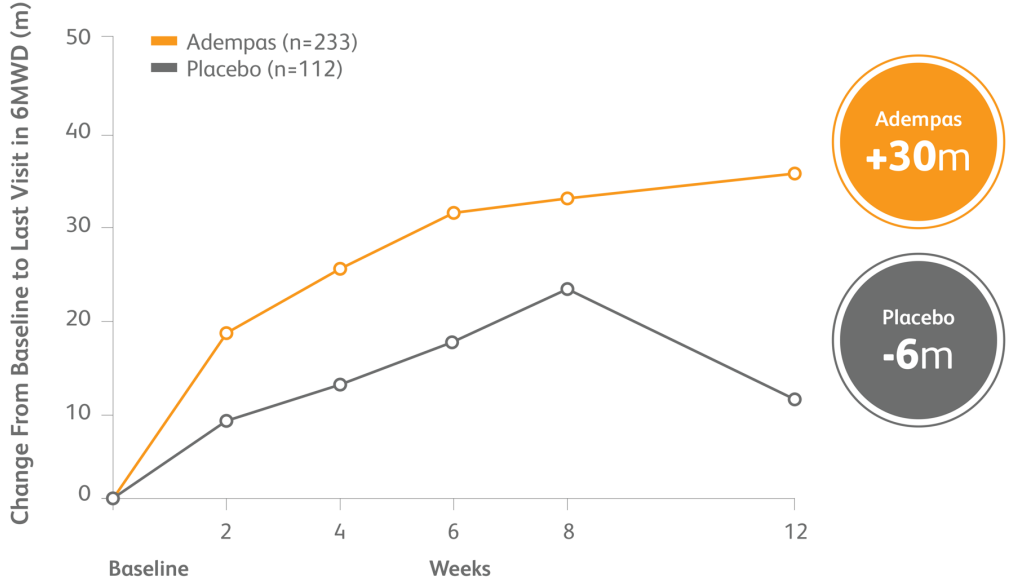
+ PATENT-1 Full Data Set

+ Treatment-Naïve Subgroup

+ Subgroup Comparison

Mean Change From Baseline in 6MWD at Week 12 for Overall Population (N=443)

36 m 6MWD vs placebo at Week 12 (95 % CI: 20 m–52 m; p<0.0001) for adults with PAH (WHO Group 1).



In the full data set at Week 12, there was a **significantly higher mean increase from baseline in the Adempas-treated group than in the placebo group**. There was a mean **30-meter increase from baseline in 6MWD** in the Adempas 2.5 mg maximum group (n=254) and a 6-meter *decrease* in the placebo group (n=126). This equates to 36-meter least squares mean treatment difference (95% CI: 20-52 meters, *P*<0.0001).

PATENT-1: Change in 6MWD

Recall our study's primary endpoint was the mean change from baseline at Week 12 in 6MWD—the distance a person is able to walk in 6 minutes on a hard, flat surface.

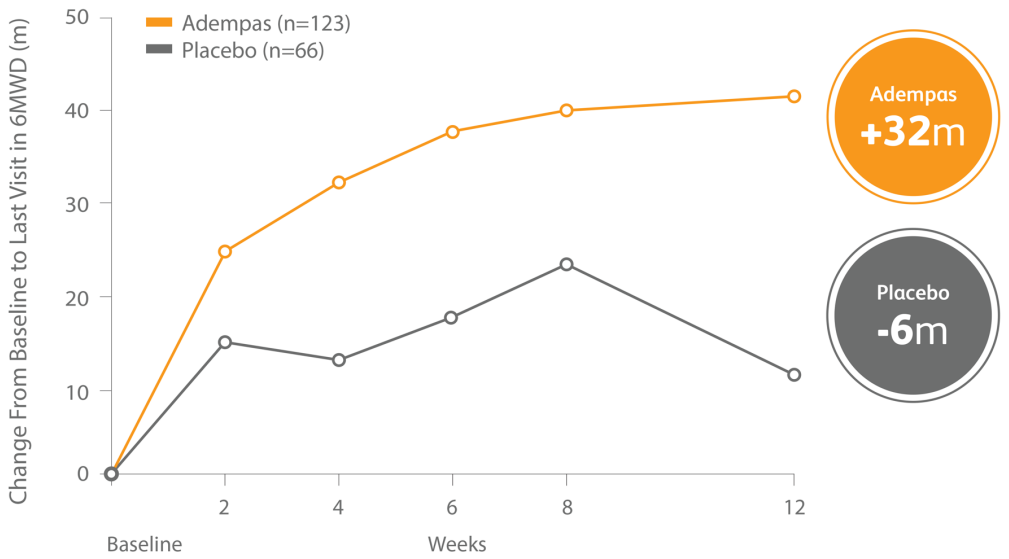
Select the buttons to view the full data set, the treatment-naïve subgroup analysis, and the subgroup comparison.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set
+ Treatment-Naïve Subgroup
+ Subgroup Comparison

Change from Baseline in 6MWD for Treatment-Naïve Subgroup (n=189)

38 m 6MWD vs placebo at Week 12 (95% CI: 14 m–62 m) for adults with PAH (WHO Group 1).



Recall that the baseline mean 6MWD in the treatment-naïve subgroup was 370 ± 66 meters. In the exploratory post-hoc subgroup analysis of the mean change in 6MWD from baseline to Week 12, there was a **32-meter increase from baseline** in the treatment-naïve patients in the Adempas 2.5 mg maximum group (n=123) and a 6-meter decrease in the treatment-naïve patients in the placebo group (n=66). This equates to 38-meter least squares mean treatment difference (95% CI: 14-62 meters). Please note that this analysis is considered exploratory and was not designed to detect statistically significant differences in subgroups.

PATENT-1: Change in 6MWD

Recall our study's primary endpoint was the mean change from baseline at Week 12 in 6MWD—the distance a person is able to walk in 6 minutes on a hard, flat surface.

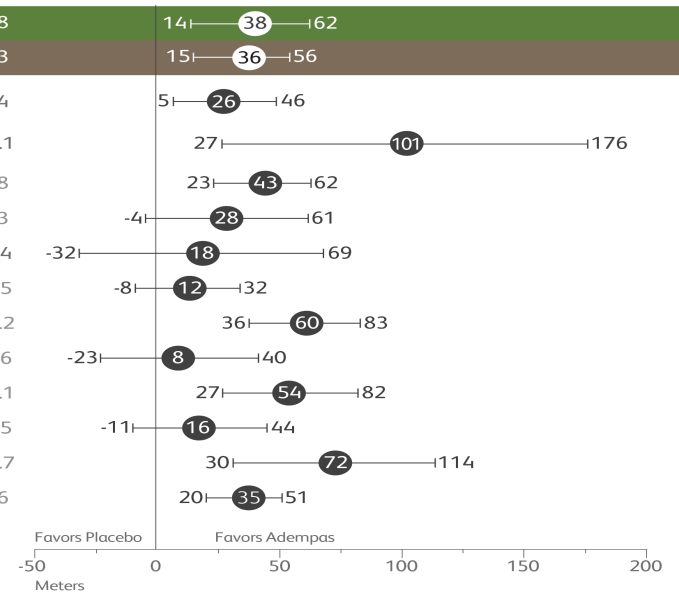
Select the buttons to view the full data set, the treatment-naïve subgroup analysis, and the subgroup comparison.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set
+ Treatment-Naïve Subgroup
+ Subgroup Comparison

Mean Treatment Difference in Change From Baseline to Week 12* in 6MWD by Prespecified Subgroup[a]

	Number of Patients	Mean Change in 6MWD (m)		Least Squares Difference in Means (m) (95% CI)
		Adempas	Placebo	
Therapy Naïve	189	32.2	-5.8	14, 38, 62
Pretreated	191	27.1	-5.3	15, 36, 56
Pretreated With ERA	167	22.6	-0.4	5, 26, 46
Pretreated With PCA	27	55.7	-40.1	27, 101, 176
Idiopathic/Familial	241	34.9	-7.8	23, 43, 62
Connective Tissue Disease	96	18.2	-8.3	-4, 28, 61
Associated (other forms) PAH	43	28.6	10.4	-32, 18, 69
WHO FC I/II at Baseline	177	30	17.5	-8, 12, 32
WHO FC III/IV at Baseline	202	29.3	-30.2	36, 60, 83
Pretreated & WHO FC I/II at Baseline	70	29	20.6	-23, 8, 40
Pretreated & WHO FC III/IV at Baseline	120	26.2	-25.1	27, 54, 82
Therapy Naïve & WHO FC I/II at Baseline	107	30.6	15.5	-11, 16, 44
Therapy Naïve & WHO FC III/IV at Baseline	82	34.1	-36.7	30, 72, 114
Overall	380	29.6	-5.6	20, 35, 51



In an exploratory analysis, the mean change in 6MWD from baseline to Week 12 and the least-squares difference in means was analyzed for each prespecified subgroup. In the pretreated population (n=191), the least squares mean treatment difference for patients treated with Adempas and placebo was 36 meters (95% CI, 15 m-56 m). The mean change from baseline was 27 meters in the pretreated Adempas treatment group (n=131), and there was a 5-meter reduction in the pretreated placebo group (n=60).

ERA = endothelin receptor antagonist; PCA = prostacyclin analogues.

[a]The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

PATENT-1: Change in WHO FC

Adempas treatment provided strong improvement in WHO FC from baseline to Week 12.

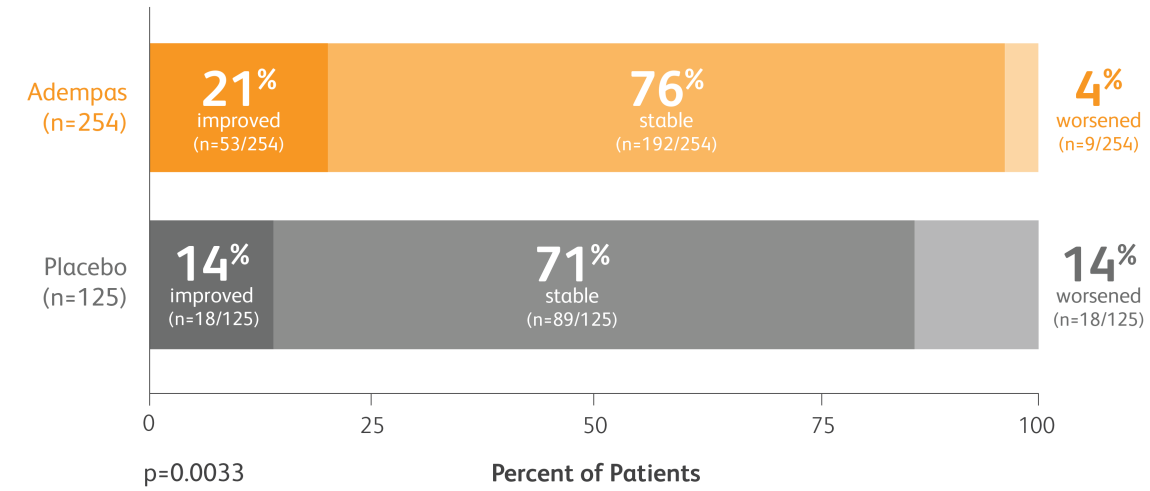
Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Change in WHO FC From Baseline to Week 12 for Overall Population (N=443)



Overall, WHO FC was improved in 50% more patients treated with Adempas compared to patients in the placebo group.

In the overall population, of patients treated with Adempas 76% were stable, 21% were improved, and 4% were deteriorated in WHO FC at Week 12. In the placebo group, 71% of patients were stable, 14% were improved, and 14% were deteriorated in WHO FC at Week 12.

PATENT-1: Change in WHO FC

Adempas treatment provided strong improvement in WHO FC from baseline to Week 12.

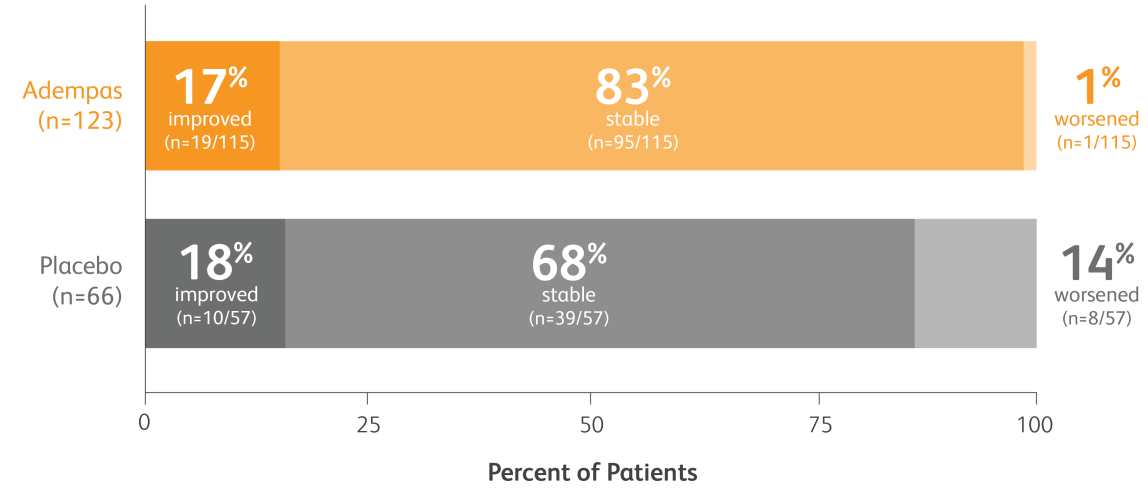
Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Change in WHO FC from Baseline to Week 12 for Treatment-Naïve Subgroup[a] (n=189)



In the exploratory post-hoc analysis of the change in WHO FC from baseline to Week 12, **83% of patients** in the treatment-naïve subgroup **were stable, 17% were improved**, and **1% deteriorated.** In the placebo group, 68% of patients were stable, 18% improved, and 14% deteriorated in WHO FC at Week 12 compared to baseline.

In the pretreated subgroup, of those patients treated with Adempas **25% had improved** (n=30/119) WHO FC at Week 12, **72% remained stable** (n=86/119), and **3% deteriorated** (n=43/119). 15% of placebo-treated patients improved (n=8/55), 78% remained stable (n=43/55), and 6% deteriorated (n=3/55) within the pretreated subpopulation.

[a]The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

PATENT-1: Change in Hemodynamic Parameters

In patients treated with Adempas, hemodynamic parameters—including change in NT-proBNP and PVR—improved from baseline to Week 12.

Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Change in Hemodynamic Parameters for Overall Population (N=443)

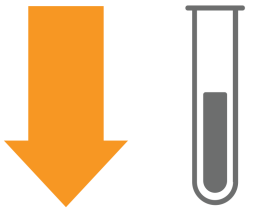
PVR

Secondary endpoint
p<0.001[3]

–226 dyn·sec·cm^{-5}
(95% CI: -281 to -170)

NT-proBNP

Secondary endpoint
p<0.001[3]



–432 ng/L
(95% CI: -782 to -82)

Right heart catheterization was performed at the beginning and end of the PATENT-1 study to gather data on hemodynamic parameters like PVR and NT-proBNP. NT-proBNP is a substance produced by the heart and is useful for continued assessments in PAH.

The mean change in PVR and NT-proBNP levels from baseline at Week 12 was adjusted for the placebo data. In the overall population, **both PVR and NT-proBNP levels were reduced** at Week 12 with PVR decreasing by 226 dyn-s-cm^{-5} and NT-proBNP decreasing by 432 ng/L. These data are reported as least-squares mean difference in the full dataset.

PATENT-1: Change in Hemodynamic Parameters

In patients treated with Adempas, hemodynamic parameters—including change in NT-proBNP and PVR—improved from baseline to Week 12.

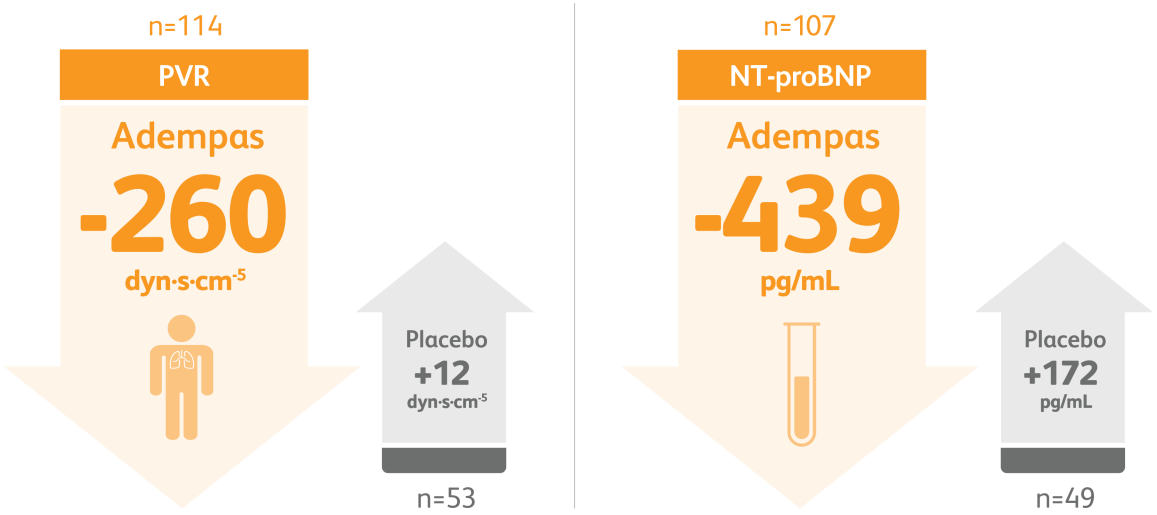
Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Change in Hemodynamic Parameters for Treatment-Naïve Subgroup[a] (n=189)



The PVR and NT-proBNP data from the PATENT-1 treatment-naïve exploratory post-hoc subgroup analysis are reported as change from baseline at Week 12. **PVR and NT-proBNP levels decreased in the treatment-naïve Adempas treatment subgroup** whereas the placebo group saw an increase.

In the pretreated subgroup, change in PVR was -188 dyn-s-cm^{-5} in Adempas-treated patients (n=117) and -36 dyn-s-cm^{-5} in the placebo group (n=52). NT-proBNP levels decreased in the Adempas-treated pretreated subgroup population (n=105) by 196 pg/mL. In the pretreated placebo group (n=50), NT-proBNP increased by 137 pg/mL.

[a]The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

PATENT-1: Clinical Worsening

Adempas significantly reduced events associated with clinical worsening.

Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Clinical Worsening*† at 12 Weeks for Overall Population (N=443)

The clinical worsening data is presented as a percentage of patients who experienced clinical worsening events. Individual patients may have experienced more than one event associated with clinical worsening.

At 12 weeks, the **percentage of patients receiving Adempas who experienced clinical worsening events (1.2%) was significantly lower than those receiving placebo (6.3%)**.

*Time to clinical worsening was a combined endpoint defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of pulmonary hypertension, start of new PAH-specific treatment, persistent decrease in 6MWD, and persistent worsening of WHO FC.
† Patients may have had more than one event of clinical worsening

PATENT-1: Clinical Worsening

Adempas significantly reduced events associated with clinical worsening.

Select the buttons to view the full data set and the subgroup analysis.

NOTE: *When sharing the subgroup data with a customer, please ensure the PATENT-1 full data set findings are shared first.*

+ PATENT-1 Full Data Set

+ Subgroup Analysis

Clinical Worsening*† at 12 Weeks for Treatment-Naïve Subgroup[a] (n=189)

In the overall population data, 1.2% of patients treated with Adempas experienced events associated with clinical worsening. Note that **only 1.6% of patients in the Adempas-treated treatment-naïve subgroup experienced events associated with clinical worsening, and 6.1% of patients in the placebo group experienced events associated with clinical worsening.**

In the pretreated subgroup, one patient on Adempas (n=1/131, 0.8%) experienced clinical worsening and 4 patients (6.7%, n=4/60), in the placebo-treated pretreated subgroup experienced clinical worsening.

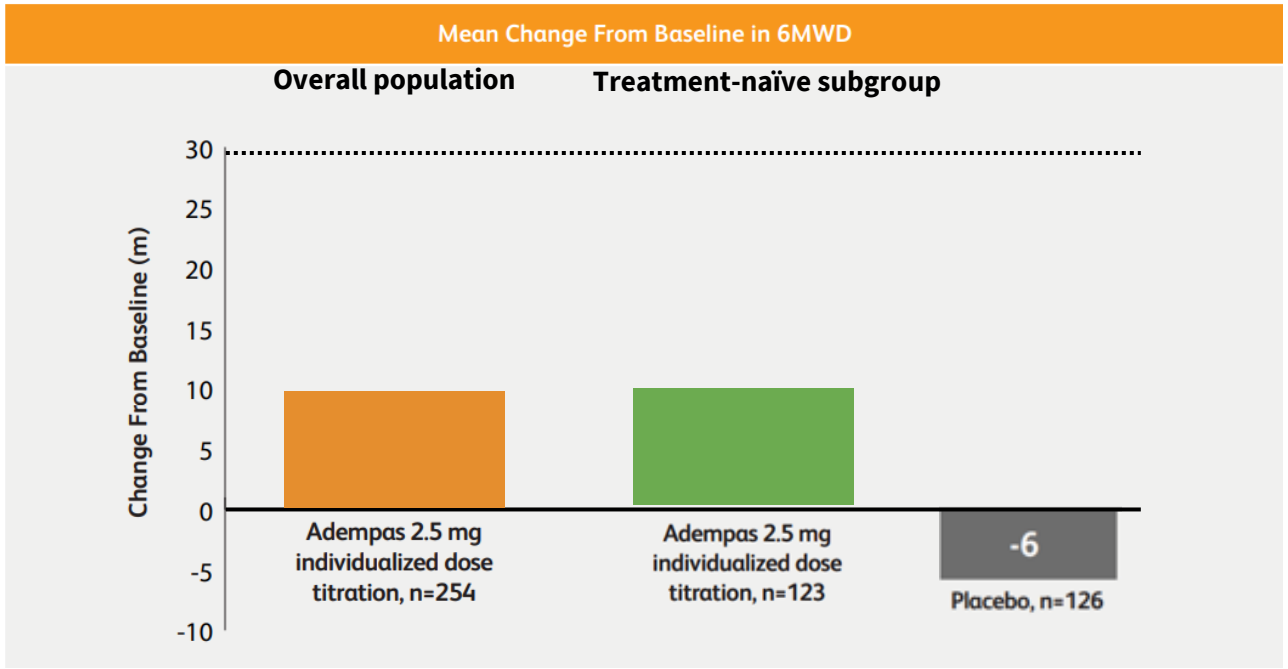
*Time to clinical worsening was a combined endpoint defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of pulmonary hypertension, start of new PAH-specific treatment, persistent decrease in 6MWD, and persistent worsening of WHO FC.

† Patients may have had more than one event of clinical worsening

[a] The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

Check What You Know: Change From Baseline in 6MWD

Let's make sure you grasped these key takeaways. Based on the PATENT-1 study data, **drag the orange bars to the correct mean change in 6MWD from baseline to 12 weeks** for the overall population and treatment-naïve data. ***Select submit when you are done.***



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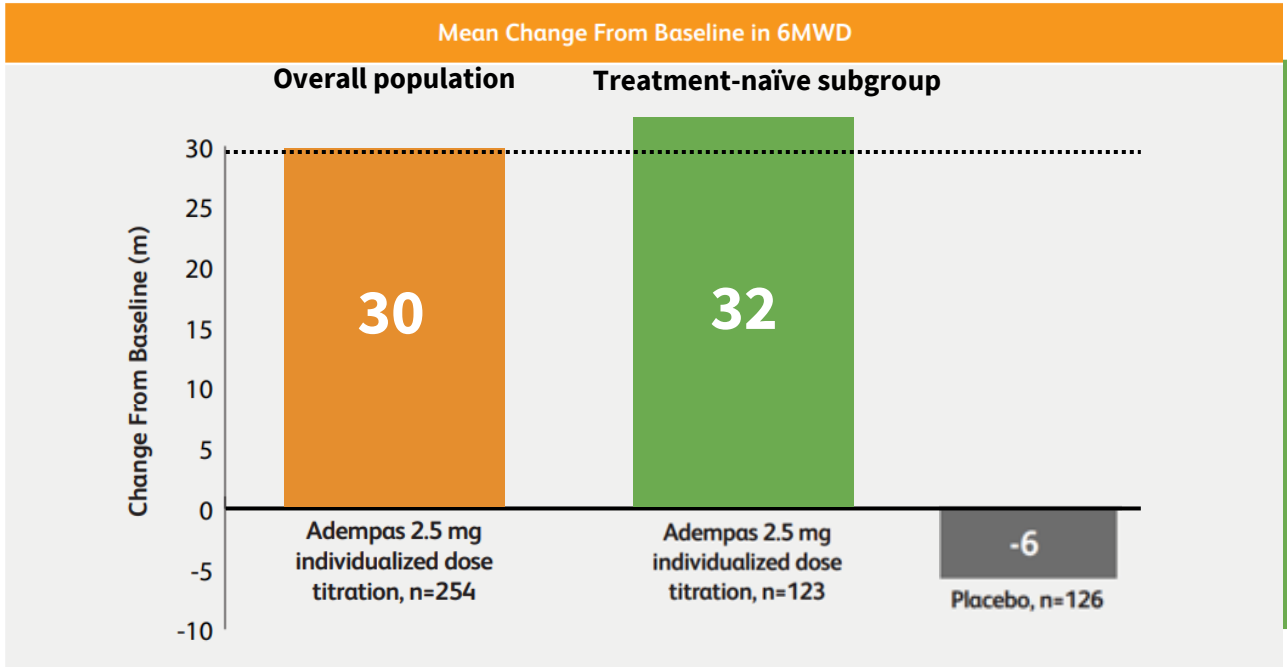

That is correct!

The mean 6MWD improved from baseline in patients in both the treatment-naïve subgroup and overall population. The mean 6MWD in the treatment-naïve group increased 32 meters from baseline, and in the overall population the mean 6MWD increased 30 meters from baseline.

Submit | Reset | Try Again | Show Correct Answers | Show My Answers

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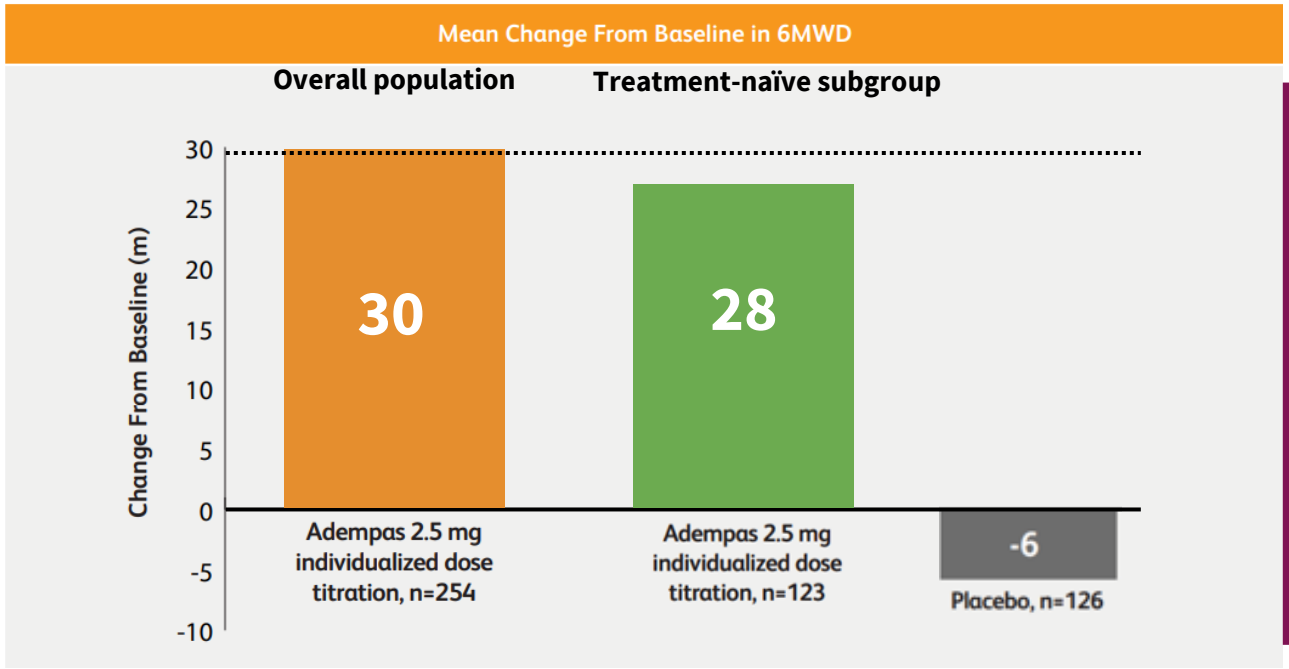

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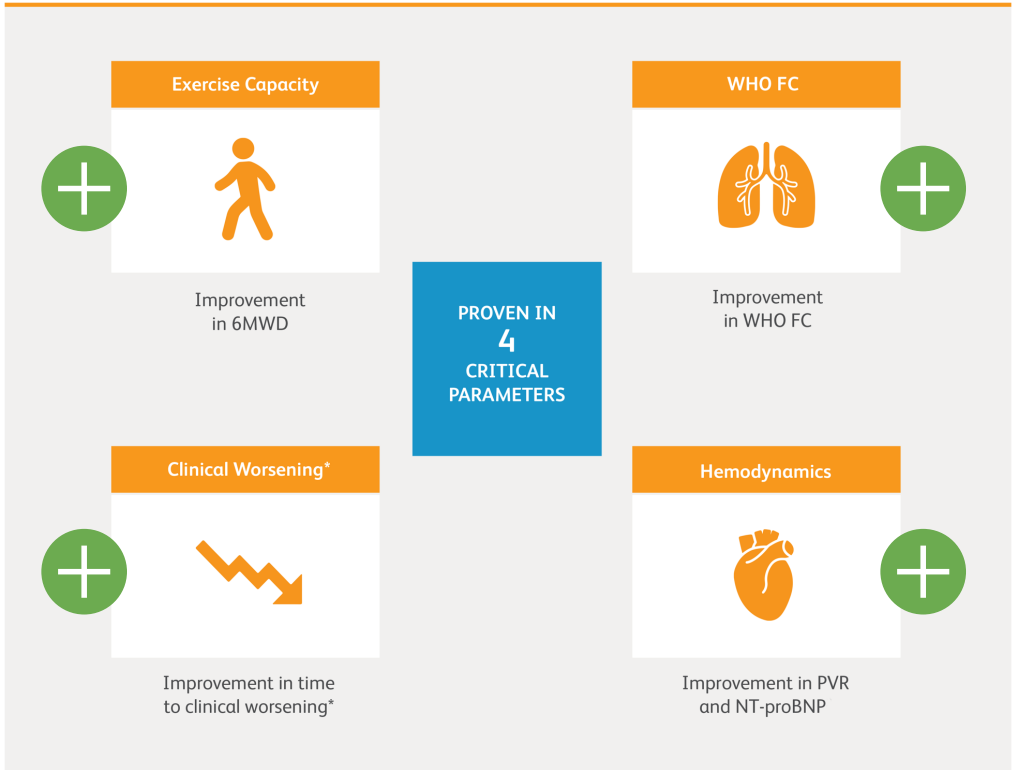
Submit | Reset | Try Again | Show Correct Answers | Show My Answers

PATENT-1: Critical Parameters

Recall the categories for risk assessment from the 3-strata module (6MWD, WHO FC, Hemodynamics/Biomarkers). Adempas delivers significant improvements across these 3 parameters, in addition to improvement in time to clinical worsening. ***Select each critical parameter tile to review the data.***



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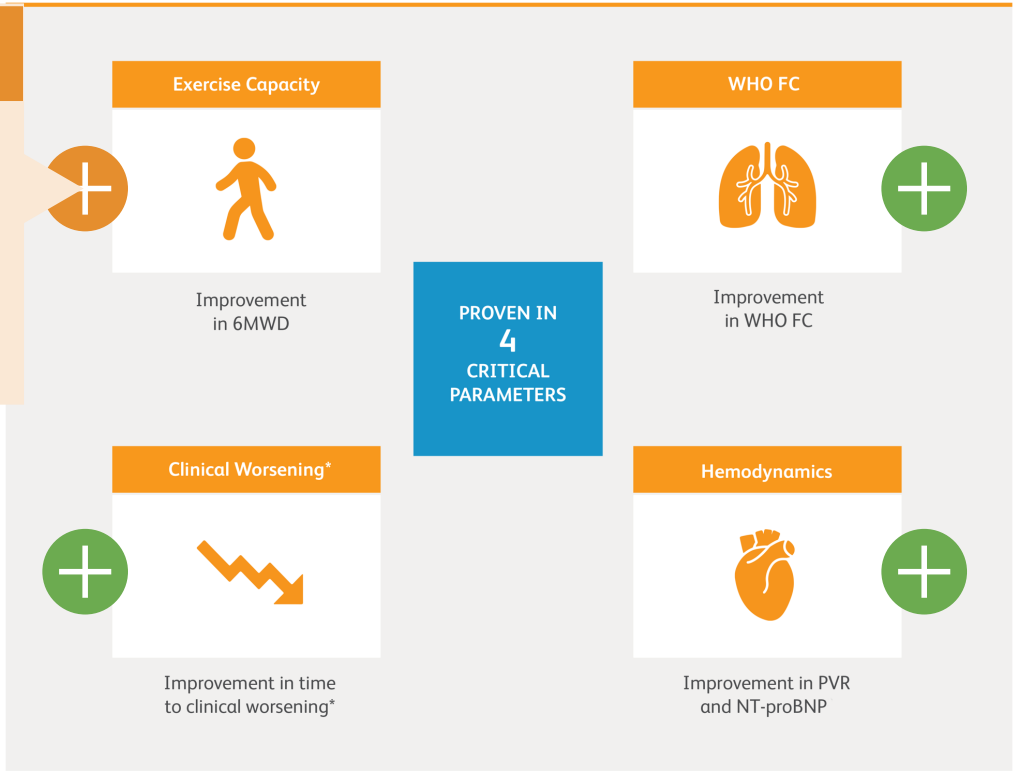
Exercise Capacity

- There was a mean **30-meter increase from baseline** at Week 12 in 6MWD in the Adempas up to 2.5 mg treatment group
- Between the Adempas up to 2.5 mg treatment group and the placebo population**, there was a 36-meter least squares difference in treatment means**



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PATENT-1: Critical Parameters

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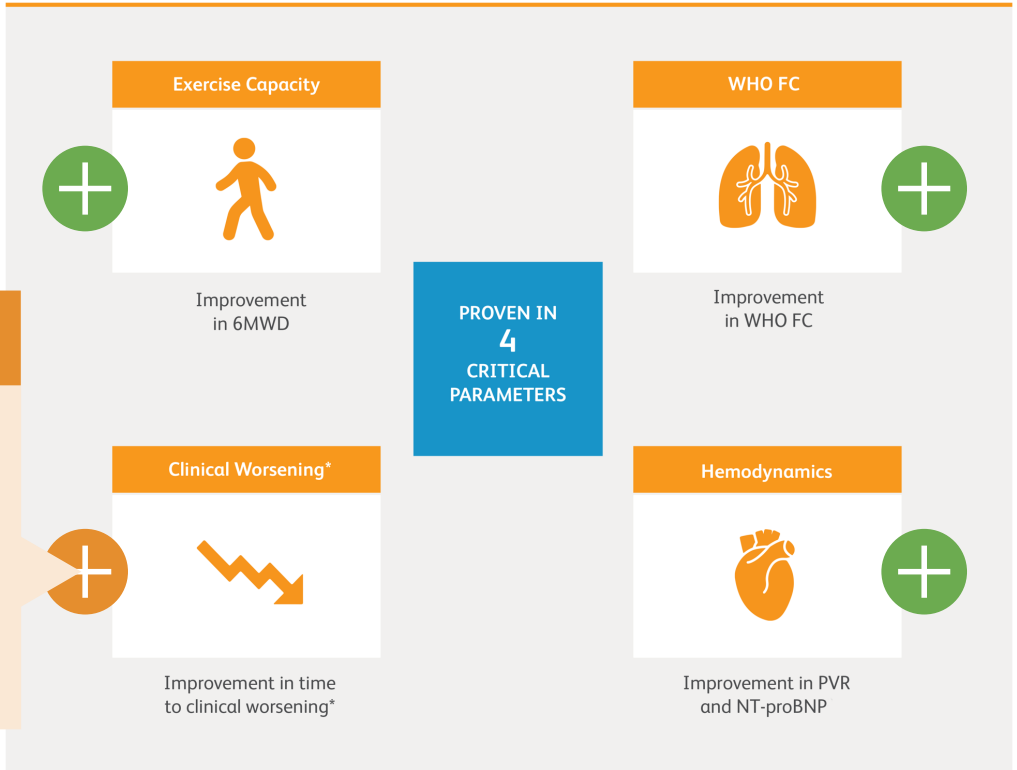
Clinical Worsening

- At 12 weeks, patients treated with Adempas demonstrated **significantly fewer events of clinical worsening** than the placebo Group
- **1.2% of patients in the Adempas up to 2.5mg** treatment group experienced clinical worsening vs **6.3% of patients in the placebo group**



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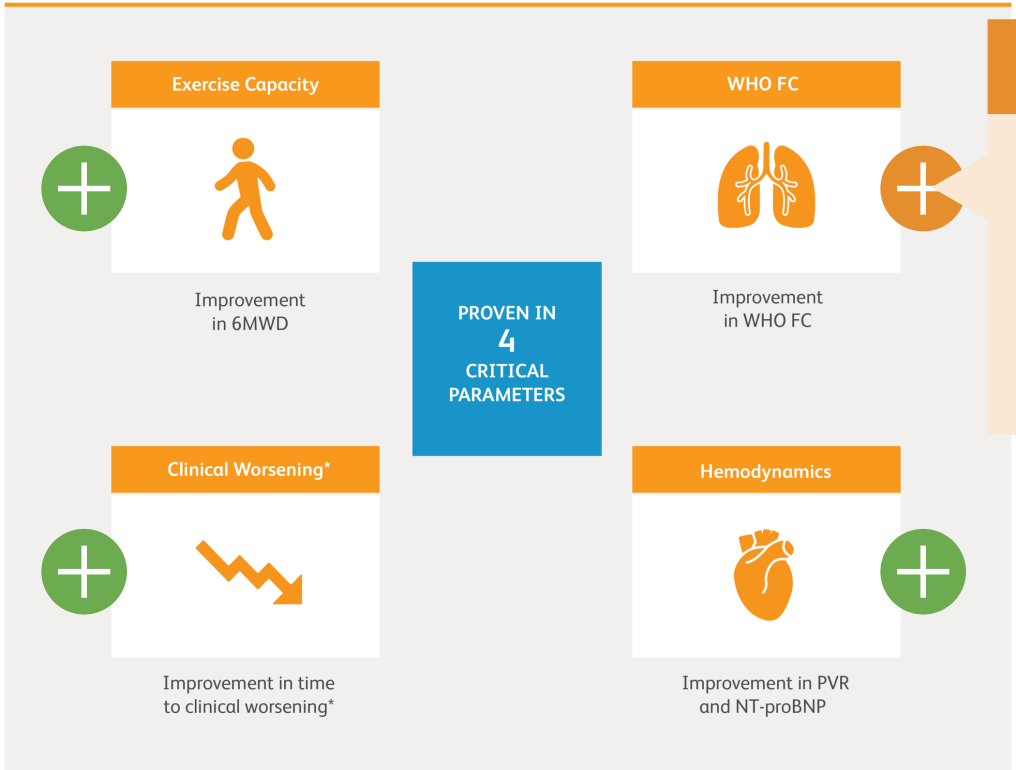

WHO FC

- **50% more patients in the Adempas group had an improved WHO FC** compared to the placebo group
- At Week 12, **21% of Adempas patients had improved WHO FC**, 76% had a stable WHO FC, and only 4% had a deteriorated WHO FC.

*Time to clinical worsening was a combined endpoint defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of pulmonary hypertension, start of new PAH-specific treatment, persistent decrease in 6MWD, and persistent worsening of WHO FC.

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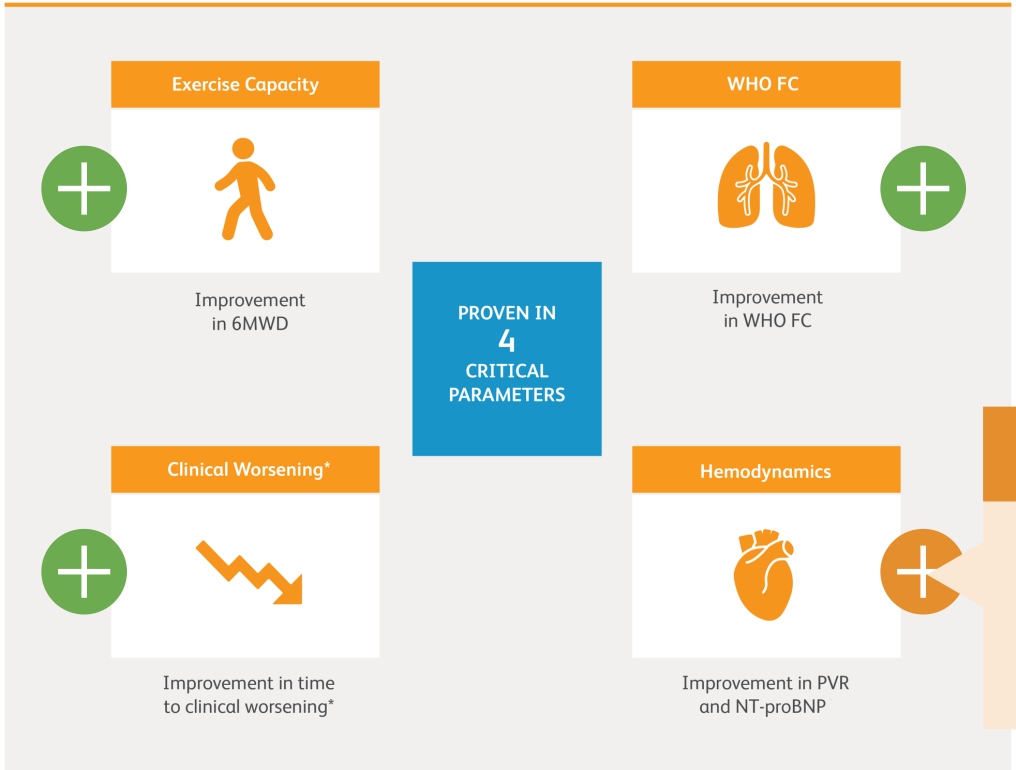


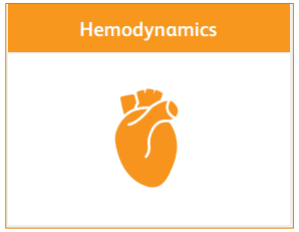
Hemodynamics

- Both **PVR and NT-proBNP levels improved** in Adempas patients

*Time to clinical worsening was a combined endpoint defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of pulmonary hypertension, start of new PAH-specific treatment, persistent decrease in 6MWD, and persistent worsening of WHO FC.

Did You Get All That?

Let's make sure you grasped these key takeaways. Based on the PATENT-1 data, **drag each critical parameter to the corresponding arrow** to indicate whether each parameter improved or worsened with Adempas treatment at Week 12. ***Select submit when you are done.***



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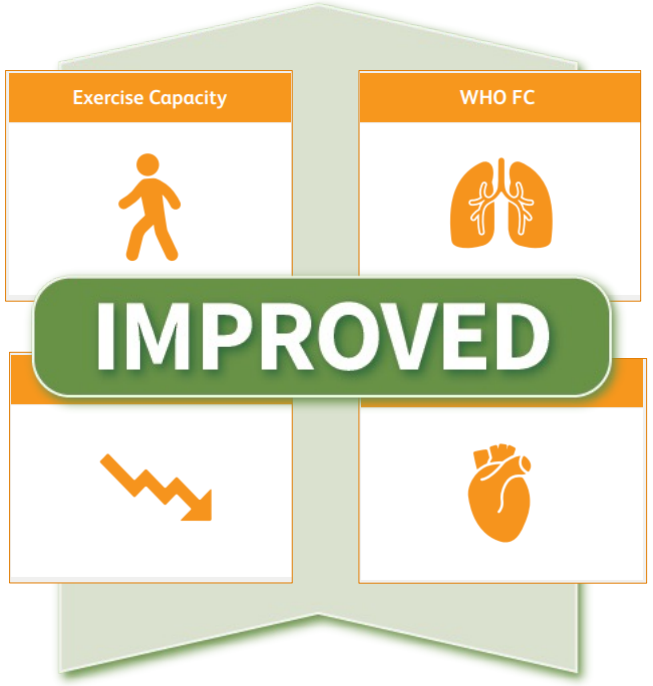

That is correct!

In the PATENT-1 study, all 4 critical parameters listed (exercise capacity, WHO FC, clinical worsening, and hemodynamics) improved in patients treated with Adempas at Week 12.

Submit | Reset | Try Again | Show Correct Answers | Show My Answers

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IMPROVED

That is incorrect.

In the PATENT-1 study, all 4 critical parameters listed (exercise capacity, WHO FC, clinical worsening, and hemodynamics) improved in patients treated with Adempas at Week 12.

Submit | Reset | Try Again | Show Correct Answers | Show My Answers

PATENT-2: Study Design

PATENT-2 was an open-label, randomized, long-term extension trial of PATENT-1, which examined the long-term safety of Adempas treatment. It enrolled 396 patients (98%) who completed the PATENT-1 study and consisted of an 8-week, double-blind, dose-adjustment phase followed by an open-label trial for 2 years. ***Select the buttons to learn more about the study design and limitations.***

+ PATENT-2 Study Endpoints
+ Study Limitations
+ PATENT-2 Treatment Groups

PATENT-1[3,5] → PATENT-2[5]

Patients completing PATENT-1, n=405 (91 %)	An open-label extension study Patients entering PATENT-2, n=396 (98%) (9 patients from PATENT-1 did not enter PATENT-2)	
Adempas 2.5 mg maximum n=237 (93 %) →	Entered PATENT-2 at the same dose they were receiving on the last day of PATENT-1, (n=231)	73 withdrew (8 transitioned to commercial Adempas, 27 adverse events, 23 deaths [5 additional deaths during follow-up], 2 lack of efficacy, 8 withdrawal by patient, 2 protocol violations, 2 lost to follow-up, 1 other)
Adempas 1.5 mg maximum n=57 (90 %) →	Initiated on Adempas 1 mg and adjusted to maximum 2.5 mg, (n=56)	13 withdrew (1 transitioned to commercial Adempas, 5 adverse events, 4 deaths [1 additional death during follow-up], 1 lack of efficacy, 1 withdrawal by patient, 1 lost to follow-up)
Placebo n=111 (88 %) →	After an 8-week dose-adjustment phase, all patients received an individually adjusted dose of Adempas (maximum 2.5 mg), (n=109)	35 withdrew (4 transitioned to commercial Adempas, 9 adverse events, 14 deaths [3 additional deaths during follow-up], 3 non-compliance, 4 withdrawal by patient, 1 lack of efficacy)

Adult patients with symptomatic PAH were eligible for inclusion if they had successfully completed PATENT-1 without ongoing study drug–related serious Adverse Events (AEs).

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+ PATENT-2 Study Endpoints

+ Study Limitations

+ PATENT-2 Treatment Groups

PATENT-1[3,5] → PATENT-2[5]

PATENT-2 Study Endpoints

- The **primary endpoint was the safety and tolerability of long-term Adempas therapy**, assessed by the recording of adverse events, serious adverse events, discontinuations, and deaths
- Exploratory endpoints included change from baseline in **6MWD, WHO FC, and NT-proBNP**

Placebo n=111 (88%)	After an 8-week dose-adjustment phase, all patients received an individually adjusted dose of Adempas (maximum 2.5 mg), (n=109)	35 withdrew (4 transitioned to commercial Adempas, 9 adverse events, 14 deaths [3 additional deaths during follow-up], 3 non-compliance, 4 withdrawal by patient, 1 lack of efficacy)

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+ PATENT-2 Study Endpoints

+ Study Limitations

+ PATENT-2 Treatment Groups

Study Limitations

- The limitations of this study, in common with all open-label, long-term extension studies, were the lack of a comparator group and the fact that efficacy parameters were analyzed descriptively
- Enrollment was limited only to those patients who met strict inclusion criteria, completed PATENT-1, and elected to enroll in the extension study
- Patient dropout might also have resulted in bias toward those who responded well to Adempas treatment
- Additionally, 199 (50%) of 396 patients were receiving additional PAH-specific therapy, meaning it is impossible to unequivocally attribute all of the efficacy and safety findings to Adempas
- For the Cox proportional hazards analysis, exclusion of patients who died or withdrew between baseline and follow-up might have affected the results of the analysis

PATENT-2: Study Design

PATENT-2 was an open-label, randomized, long-term extension trial of PATENT-1, which examined the long-term safety of Adempas treatment. It enrolled 396 patients (98%) who completed the PATENT-1 study and consisted of an 8-week, double-blind, dose-adjustment phase followed by an open-label trial for 2 years. ***Select the buttons to learn more about the study design and limitations.***

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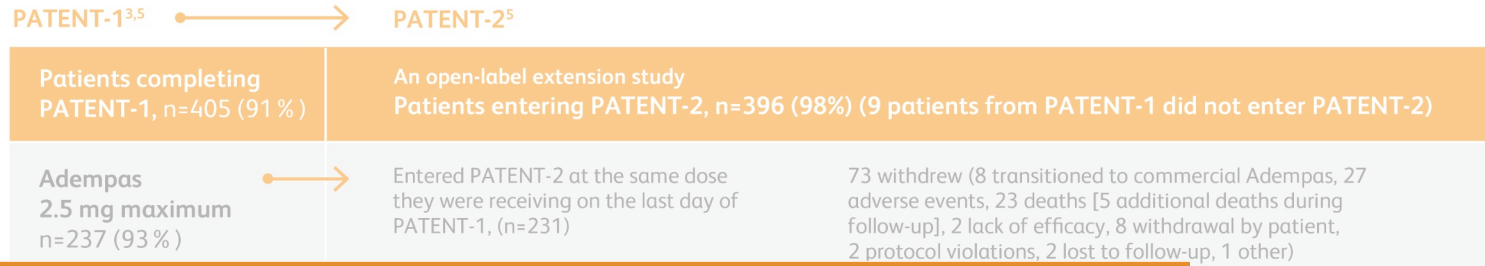


PATENT-2 Treatment Groups

- The PATENT-1 full treatment group (Adempas up to 2.5 mg) continued to receive a maximum dosage of 2.5 mg Adempas 3x daily over the course of PATENT-2
- The **PATENT-1 experimental** (Adempas up to 1.5 mg) **and placebo groups had their doses adjusted to a maximum of 2.5 mg Adempas 3x daily** for PATENT-2

Adult patients with symptomatic PAH were eligible for inclusion if they had successfully completed PATENT-1 without ongoing study drug–related serious Adverse Events (AEs).

PATENT-2: Estimated Survival and Clinical Worsening

Recall the primary endpoint for the PATENT-2 Study was the **safety and tolerability of long-term Adempas therapy.** The mean treatment duration for the total population that continued from PATENT-1 into the open-label extension study was 1,146 days (±479). The top figure displays the probability of survival of patients in PATENT-2 at Year 2. **The probability of survival of all patients in the PATENT-2 study was 97% at Year 1, and 93% at Year 2**. Without a control group, these data must be interpreted cautiously.

The bottom figure displays clinical worsening data from the PATENT-2 study. Only **25% of patients in the treatment-naïve subgroup experienced clinical worsening events**. 29% of patients in the pretreated subgroup (n=58/199) and 27% of patients in the overall population (n=108/396) experienced clinical worsening events.

Probability of survival

Clinical worsening events at 2 years[5] *†

*Time to clinical worsening was a combined endpoint defined as death (all-cause mortality), heart/lung transplantation, atrial septostomy, hospitalization due to persistent worsening of pulmonary hypertension, start of new PAH-specific treatment, persistent decrease in 6MWD, and persistent worsening of WHO Functional Class.
† Patients can have more than one event.

PATENT-2 Patient Characteristics at PATENT-1 Baseline

The patient characteristics of each population subgroup for PATENT-2 was gathered at the beginning of the PATENT-1 study and the end of the PATENT-1 study. Collectively these are referred to as the PATENT-1 baseline (Week 1 for those receiving riociguat treatment in PATENT-1, Week 12 for those receiving placebo treatment in PATENT-1). The treatment-naïve subgroup and the overall population had a similar distribution in PAH etiology. **Most patients had** idiopathic PAH (64% of patients in the treatment-naïve subgroup; 62% of patients in the overall population) with the second most common PAH etiology being associated with connective tissue disease (CTD) (17% of patients in treatment-naïve subgroup; 24% of patients in the overall population)

At the PATENT-1 baseline, the mean 6MWD was 367 meters in the overall population and 369 meters in the treatment-naïve subgroup.

At the PATENT-1 baseline, 44% of patients in the treatment-naïve subgroup were in WHO FC III. 54% of patients in the overall population started in WHO FC III. **The majority (51%) of patients in the treatment-naïve subgroup were in WHO FC II.**

PATENT-2 Patient Characteristics at PATENT-1 Baseline

	Overall population	Treatment Naïve	Pretreated
Subjects, n	396	197	199
Mean Age, years (range)	50 (18-80)	47 (18-80)	53 (18-79)
Female, n (%)	317 (80%)	153 (78%)	164 (82%)
PAH etiology, n (%) Idiopathic	245 (62%)	126 (64%)	119 (60%)
Familial	9 (2%)	8 (4%)	1 (1%)
Associated with connective tissue disease	94 (24%)	34 (17%)	60 (30%)
Associated with systemic sclerosis*	55 (14%)	17 (9%)	38 (19%)
Congenital heart disease	33 (8%)	19 (10%)	14 (7%)
Portopulmonary hypertension	12 (3%)	9 (5%)	3 (2%)
Anorexigen or amphetamine use	3 (1%)	1 (1%)	2 (1%)
Mean 6MWD	367 m	369 m	365 m
WHO FC I/II/III/IV	3%[†‡]/43%[†‡]/54%[†‡]/1%[†‡]	5%[†]/51%[†]/44%[†]/1%[†]	2%[†§]/34%[†§]/64%[†§]/1%[†§]

*Based on a post hoc search of medical histories.
[†]Data do not add up to 100% due to rounding.
[‡]n=395.
[§]n=198.

PATENT-2: Safety Signals & Adverse Events

No new safety signals were identified after 2 years of treatment in PATENT-2. **Adverse events were similar across studies.**

Take a moment to review the adverse event data across categories in each population. The most common adverse event in PATENT-2 in the treatment-naïve subgroup population, the pretreated subgroup population, and the overall population was nasopharyngitis.

10% or less of patients in PATENT-2 experienced the most common serious adverse events. These serious adverse events included syncope (10%), worsening PAH (10%), and right ventricular failure (8%). Of the 10% of patients who experienced syncope, 6% of those were in the treatment-naïve subgroup and 14% were in the pretreated subgroup.

Discontinuation due to adverse events was 11% in the overall population (7% treatment-naïve and 16% pretreated).

Most common adverse events in PATENT-1[3]

	Adempas 2.5 mg, 3x a day n=254
Headache	27 % (69)
Dyspepsia	19 % (48)
Peripheral edema	17 % (44)
Nausea	16 % (40)
Dizziness	16 % (40)
Diarrhea	14 % (35)
Nasopharyngitis	10 % (26)
Vomiting	10 % (26)
Dyspnea	6 % (16)
Cough	5 % (12)
Hypotension	10 % (25)

Most common adverse events in PATENT-2[5]

	Overall n=396	Treatment Naïve n=197	Pretreated n=199
Headache	21 % (82)	15 % (29)	27 % (53)
Peripheral edema	25 % (98)	21 % (42)	28 % (56)
Nausea	19 % (76)	14 % (27)	25 % (49)
Dizziness	26 % (101)	25 % (50)	26 % (51)
Diarrhea	21 % (84)	14 % (28)	28 % (56)
Nasopharyngitis	30 % (118)	27 % (53)	33 % (65)
Vomiting	17 % (67)	13 % (26)	21 % (41)
Dyspnea	16 % (64)	13 % (25)	20 % (39)
Cough	22 % (88)	23 % (45)	22 % (43)
Upper respiratory	16 % (64)	22 % (43)	11 % (21)

PATENT-2: Change in 6MWD at 2 Years

Select the buttons to view the comparative graphs.

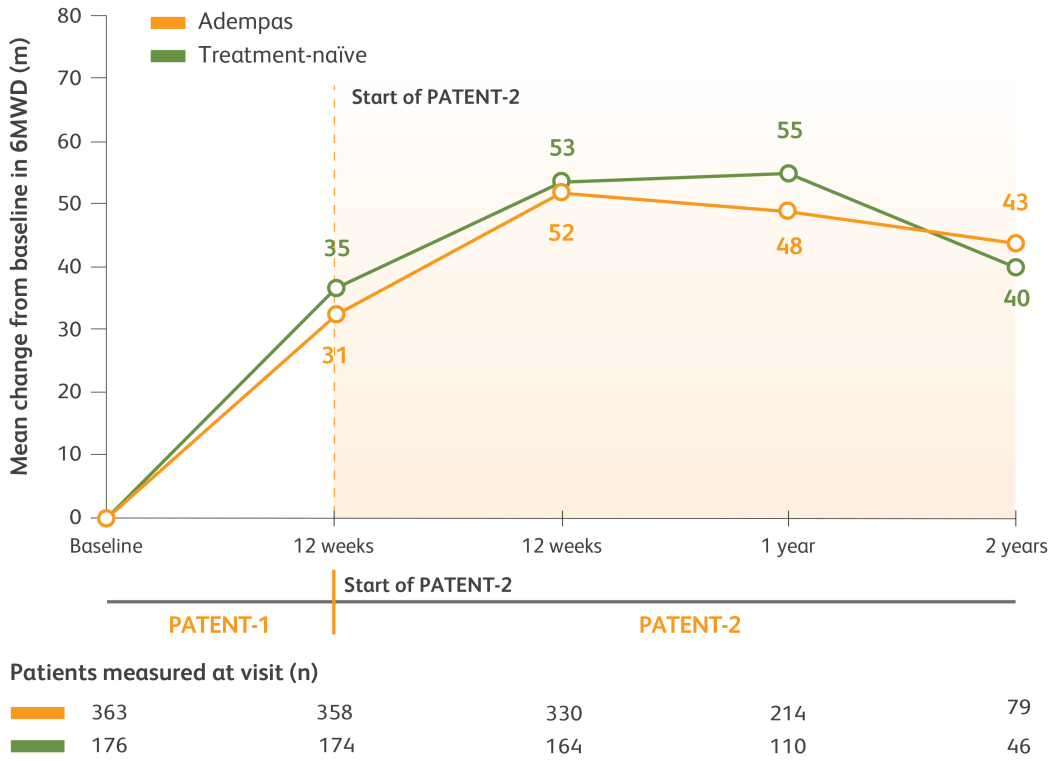
+ Adempas vs Treatment-Naïve

+ Adempas vs Placebo

In the exploratory post-hoc analysis, the mean change in 6MWD from baseline to Year 1 and Year 2 for each subgroup was analyzed. At Year 1, the mean change in 6MWD from baseline increased 48 meters in the overall population and 55 meters in the treatment-naïve subgroup. **At Year 2, the mean change from baseline in 6MWD increased 43 meters in the overall population,** and 40 meters in the treatment-naïve subgroup.

At 2 years, the mean 6MWD in the pretreated subgroup increased 48 meters from baseline.

Mean Change From Baseline in 6MWD Adempas vs Treatment-Naïve Populations[a]



[a]The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

PATENT-2: Change in 6MWD at 2 Years

Select the buttons to view the comparative graphs.

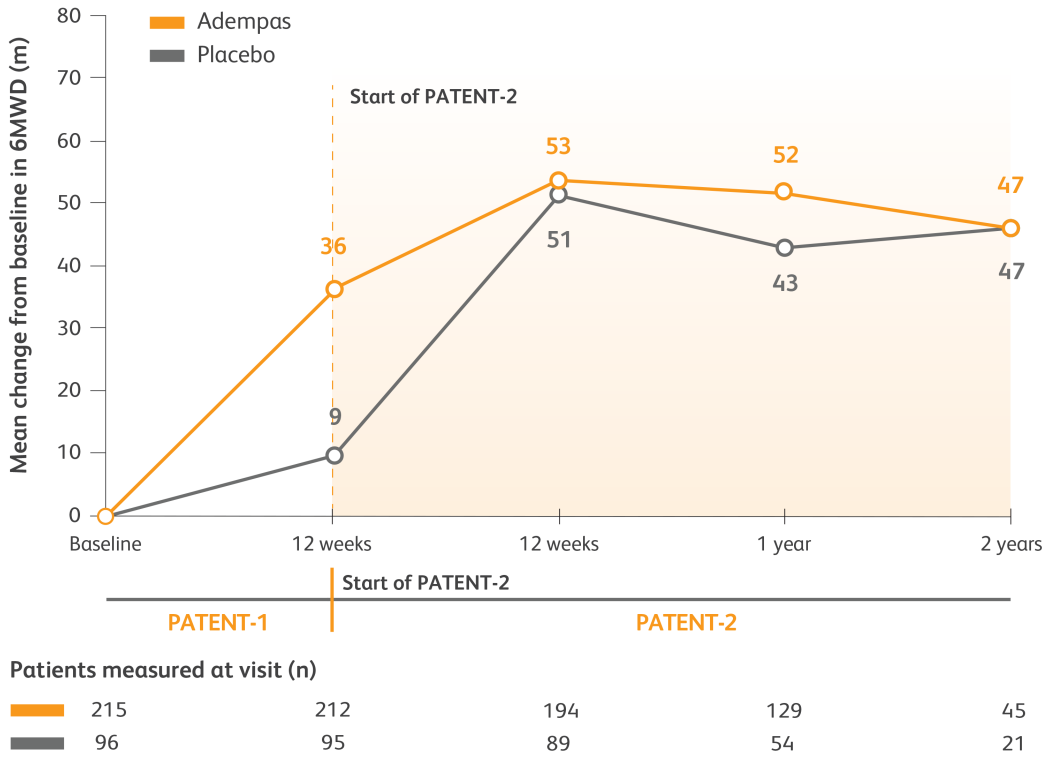
+ Adempas vs Treatment-Naïve

+ Adempas vs Placebo

At Year 1, the mean change in 6MWD in the Adempas group increased 52 meters from the baseline, whereas the placebo population's mean 6MWD increased 43 meters.

The placebo population from PATENT-1 began treatment with Adempas at the start of the PATENT-2 extension trial. At 12 weeks, **the mean 6MWD of the former placebo population increased to be similar to the mean 6MWD of the overall Adempas population**. At Year 2, both groups showed a 47-meter increase in 6MWD mean change from baseline.

Change in 6MWD at 2 Years by PATENT-1 Treatment Arm Adempas vs Placebo Populations[a]



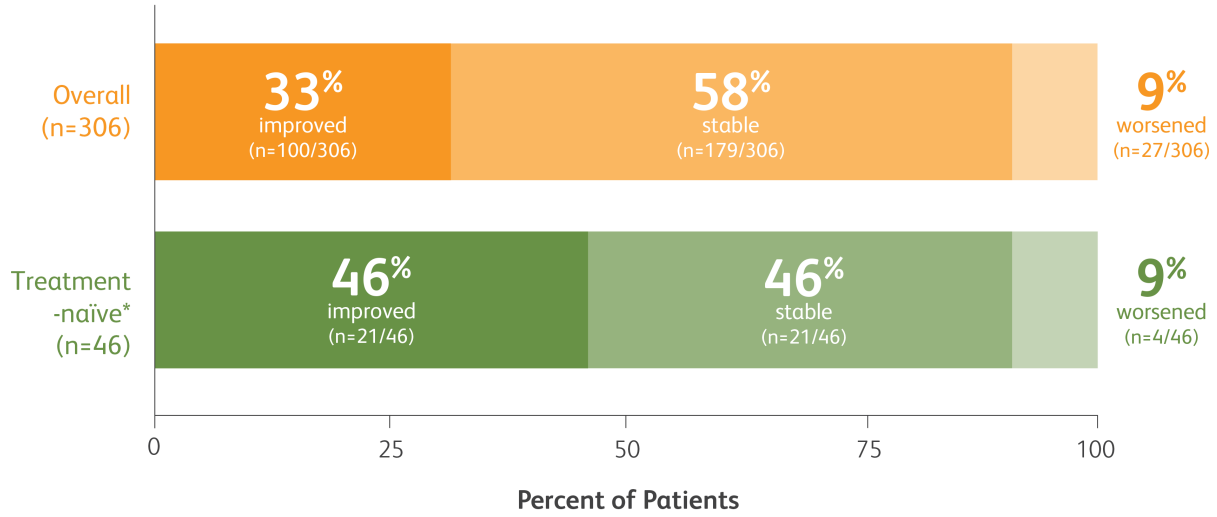
[a]The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in subgroups.

PATENT-2: Change in WHO FC at 2 Years

At 2 years, 33% of patients in the overall population had an improved WHO FC, and **46% of patients in the treatment-naïve subgroup had an improved WHO FC.** Similarly, 46% of patients in the pretreated subgroup (n=16/35) had an improved WHO FC; 49% (n=17/35) remained stable and 6% (n=2/35) worsened in the pretreated subgroup.

In the overall population, 58% of patients remained stable and 9% worsened WHO FC. For the treatment-naïve subgroup, 46% remained stable, while 9% worsened WHO FC.

Change in WHO FC at 2 Years for Overall Population and Treatment-Naïve Subgroup



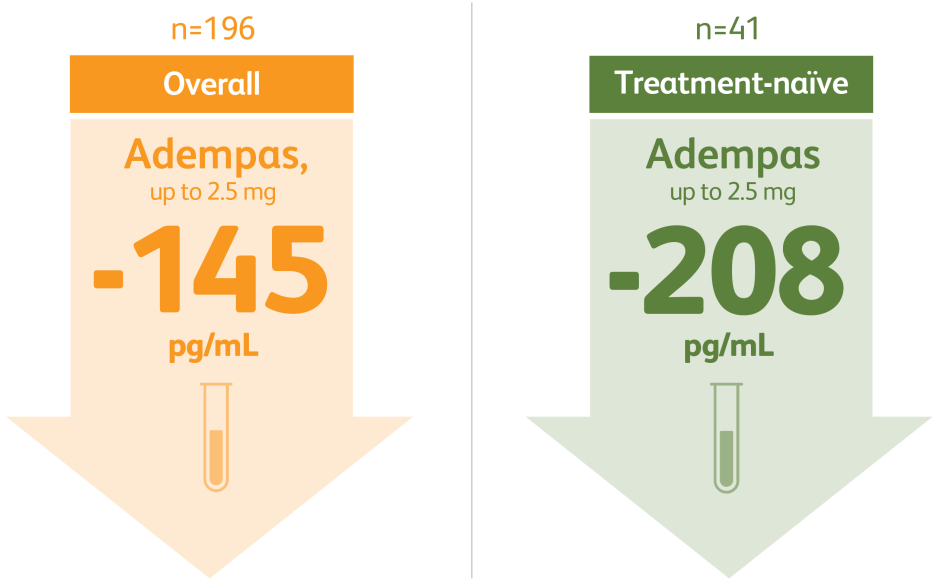
*Values are rounded to nearest integer so may not necessarily add up to 100%.
The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in these subgroups.

PATENT-2: Change in NT-proBNP at 2 years

At 2 years, NT-proBNP levels were improved in patients treated with Adempas in both the overall population and the treatment-naïve subgroup.

The treatment-naïve subgroup population NT-proBNP levels decreased by 208 pg/ML, whereas the overall population NT-proBNP levels decreased by 145 pg/mL. The pretreated population NT-proBNP levels increased by 30 pg/ML.

Change in NT-proBNP at 2 Years for Overall Population and Treatment-Naïve Subgroup



The data in this analysis should be considered exploratory and not designed to detect statistically significant differences in these subgroups.

Check What You Know: PATENT-2 Outcomes

Were you able to **retain the outcomes of the treatment-naïve subgroup and the overall population**?
Drag each exploratory endpoint to the population that showed improvement in that endpoint at Year 2 in PATENT-2. The same endpoint may apply to both populations. ***Select submit when you are done.***

Treatment-Naïve	Overall Population

6MWD NT-proBNP WHO FC Clinical worsening

6MWD NT-proBNP WHO FC Clinical worsening

Submit Reset Try Again Show Correct Answers Show My Answers

Check What You Know: PATENT-2 Outcomes

Were you able to **retain the outcomes of the treatment-naïve subgroup and the overall population**?
Drag each exploratory endpoint to the population that showed improvement in that endpoint at Year 2 in PATENT-2. The same endpoint may apply to both populations. ***Select submit when you are done.***

Treatment-Naïve	Overall Population
6MWD	6MWD
NT-proBNP	NT-proBNP
WHO FC	WHO FC
Clinical worsening	Clinical worsening

That is correct!

The treatment-naïve subgroup and the overall population showed improvement in all the listed study endpoints.

Submit | Reset | Try Again | Show Correct Answers | Show My Answers

Check What You Know: PATENT-2 Outcomes

Were you able to **retain the outcomes of the treatment-naïve subgroup and the overall population**?
Drag each exploratory endpoint to the population that showed improvement in that endpoint at Year 2 in PATENT-2. The same endpoint may apply to both populations. ***Select submit when you are done.***

Treatment-Naïve

- 6MWD
- NT-proBNP

Overall Population

- Clinical worsening

That is incorrect.

The treatment-naïve subgroup and the overall population showed improvement in all the listed study endpoints.

- 6MWD
- WHO FC
- Clinical worsening

Submit | Reset | Try Again | Show Correct Answers | Show My Answers

Summary

Take a moment to review key information from the lesson:

- Pulmonary arterial hypertension (PAH) is a condition in which blood vessels in the lungs narrow or are blocked. This increases blood pressure.
  - Symptoms: faintness, shortness of breath, and chest pain
  - Risk factors: sex (female), age (30-60 years old), family history of blood clots or genetic predisposition, illegal drug use, unhealthy lifestyle habits
  - Prevalence and incidence: Incidence of PAH in adults ranges from 1.5-32 ppm, and the prevalence ranges from 12.4-268 ppm
- Assessing PAH risk uses parameters such as 6MWD, WHO FC, and NT-proBNP levels
  - 3-strata model is used for assessing risk at diagnosis
  - 4-strata model is used for assessing risk at follow-up
- PATENT-1 Study: Exploratory post-hoc analysis (N=443)
  - Least squares mean treatment difference in 6MWD at Week 12: +36 meters (95% CI: 20-52 m) overall population, +38 meters (95% CI: 14-62 m) treatment-naïve, and +27 meters (95% CI: 15-56m) pretreated
  - WHO FC at Week 12:
    - 21% improved, 76% stable, 4% worsened in overall population
    - 17% improved, 83% stable, 1% worsened in treatment-naïve
    - 25% improved, 72% stable, 3% worsened in pretreated
  - Mean change in PVR at Week 12: -226 dyn·sec·cm^{-5} in overall population , -260 dyn·sec·cm^{-5} in treatment-naïve, -188 dyn·sec·cm^{-5} in pretreated
  - Mean change in NT-proBNP at Week 12: -432 ng/L in overall population, -439 pg/mL in treatment-naïve, -196 pg/mL in pretreated
  - Clinical worsening: 1.2% of overall population, 1.6% of treatment-naïve population, and 0.8% of pretreated
- PATENT-2: Long-term extension study including exploratory post-hoc analysis (N=405)
  - Probability of survival at Year 2: 93% with Adempas
  - Clinical worsening: 27% of overall population, 25% of treatment-naïve, 29% of pretreated
  - Mean change in 6MWD at Year 2: 43 meters in overall population, 40 meters in treatment-naïve, 48 meters in pretreated
  - Mean change in NT-proBNP at Year 2: -145 pg/L in overall population, -208 pg/L in treatment-naïve, and +30 pg/mL
  - WHO FC at Year 2:
    - 33% improved, 58% stable, and 9% worsened in overall population
    - 46% improved, 46% stable, and 9% worsened in treatment-naïve population
    - 46% improved, 49% stable, and 6% worsened in pretreated population

Self-Check

Which of the following are risk factors for PAH?

Select all that apply.

A Smoking

B Female sex

C Male sex

D Older age (30-60 years)

E Certain genetic disorders

Submit Review

Self-Check

Which of the following are risk factors for PAH?

Select all that apply.

- A Smoking
- B Female sex
- C Male sex
- D Older age (30-60 years)
- E Certain genetic disorders

That is correct!

Risk factors for PAH include female sex, older age (30-60 years), certain genetic disorders (eg, Down syndrome, congenital heart disease, and Gaucher disease), and unhealthy lifestyle habits such as smoking.

Submit Review

Self-Check

Which of the following are risk factors for PAH?

Select all that apply.

- A Smoking
- B Female sex
- C Male sex
- D Older age (30-60 years)
- E Certain genetic disorders

That is incorrect. Select Review if you would like to revisit the screen related to this question.

Risk factors for PAH include female sex, older age (30-60 years), certain genetic disorders (eg, Down syndrome, congenital heart disease, and Gaucher disease), and unhealthy lifestyle habits such as smoking.

Submit Review

Self-Check

In the PATENT-1 exploratory post-hoc treatment-naïve subgroup analysis, what was the least squares mean treatment difference between Adempas and placebo for the change in 6MWD at Week 12?

Select the best answer.

A -6 meters

B 15 meters

C 36 meters

D 38 meters

Submit Review

Self-Check

In the PATENT-1 exploratory post-hoc treatment-naïve subgroup analysis, what was the least squares mean treatment difference between Adempas and placebo for the change in 6MWD at Week 12?

Select the best answer.

A -6 meters

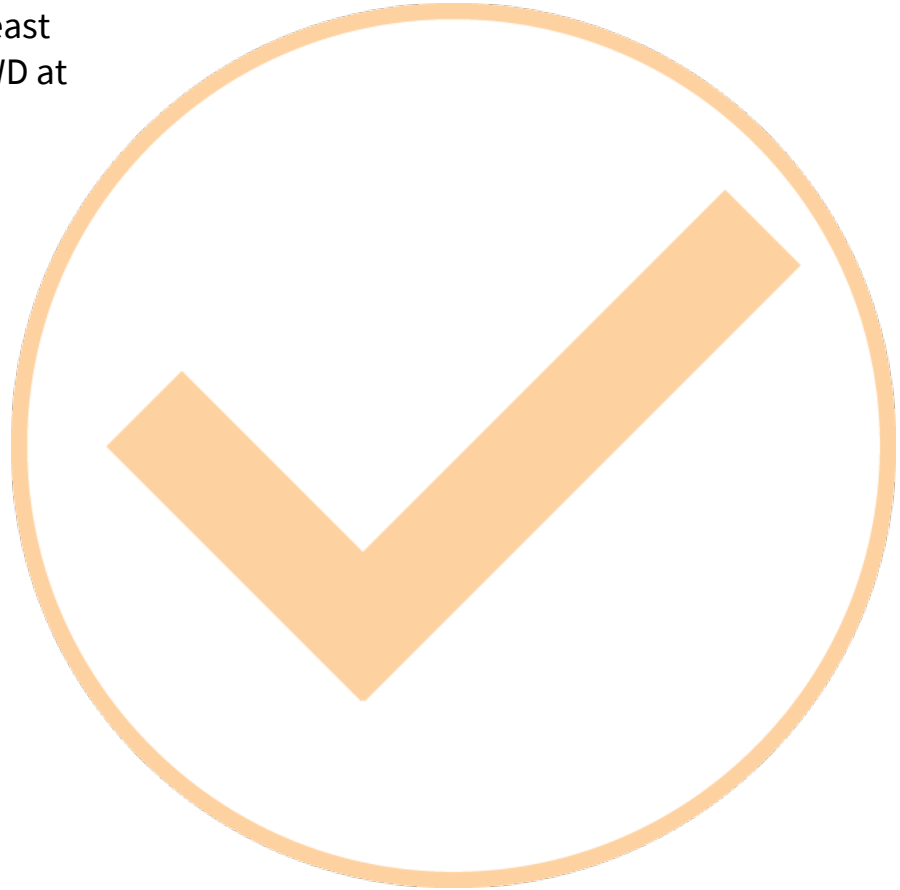
B 15 meters

C 36 meters

D 38 meters

That is correct!

The treatment-naïve subgroup had a 38 m least squares mean treatment difference for the change in 6MWD from baseline, and the overall population had a 36 m least squares mean treatment difference.



Submit Review

Self-Check

In the PATENT-1 exploratory post-hoc treatment-naïve subgroup analysis, what was the least squares mean treatment difference between Adempas and placebo for the change in 6MWD at Week 12?

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C 36 meters

D 38 meters

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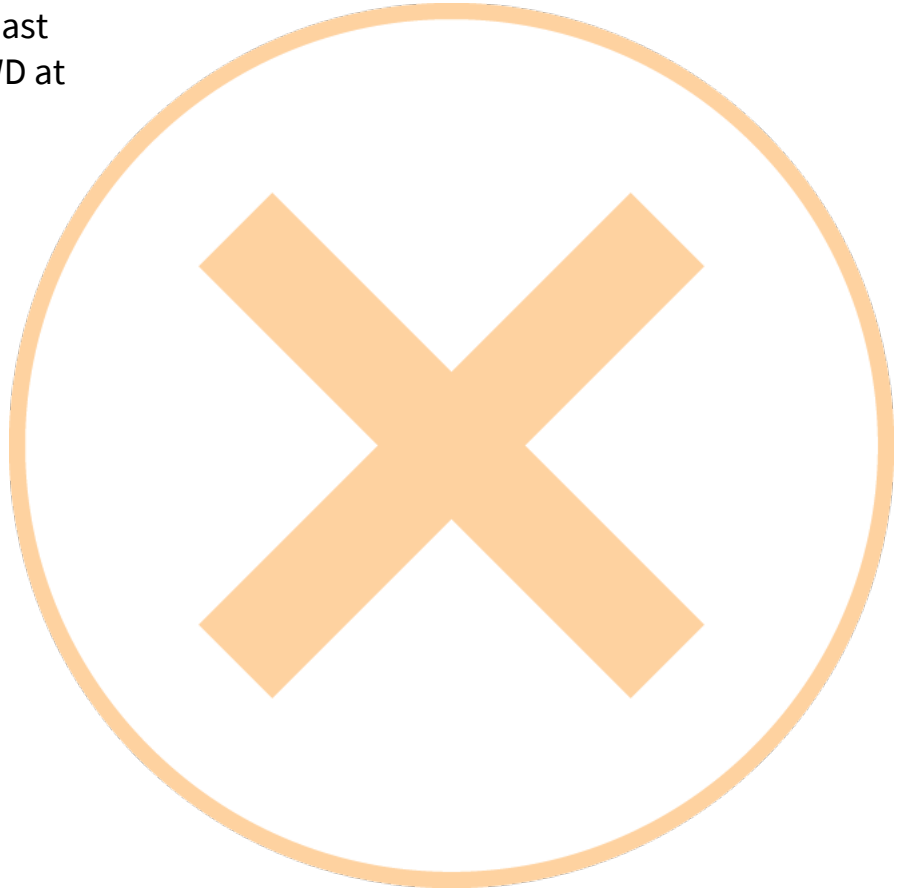
The treatment-naïve subgroup had a 38 m least squares mean treatment difference for the change in 6MWD from baseline, and the overall population had a 36 m least squares mean treatment difference.



Submit Review

Self-Check

Which of the following were outcomes of the PATENT-2 exploratory post-hoc analysis of the overall population?

Select all that apply.

A 93% probability of survival at Year 2

B 27% clinical worsening

C 40 6MWD mean change from baseline

D 43 6MWD mean change from baseline

E 33% improvement in WHO FC

Submit Review

Self-Check

Which of the following were outcomes of the PATENT-2 exploratory post-hoc analysis of the overall population?

Select all that apply.

- A 93% probability of survival at Year 2
- B 27% clinical worsening
- C 40 6MWD mean change from baseline
- D 43 6MWD mean change from baseline
- E 33% improvement in WHO FC

That is correct!

The PATENT-2 exploratory post-hoc analysis showed improvements in critical categories with Adempas treatment.

Submit Review

Self-Check

Which of the following were outcomes of the PATENT-2 exploratory post-hoc analysis of the overall population?

Select all that apply.

A 93% probability of survival at Year 2

B 27% clinical worsening

C 40 6MWD mean change from baseline

D 43 6MWD mean change from baseline

E 33% improvement in WHO FC

Submit Review

That is incorrect. Select Review if you would like to revisit the screen related to this question.

The PATENT-2 exploratory post-hoc analysis showed improvements in critical categories with Adempas treatment. The treatment-naïve population data showed a 40m 6MWD mean change from baseline, and the overall population data showed a 43m change.

Self-Check

In the PATENT-2 exploratory post hoc treatment-naïve subgroup analysis, what was the change in NT-proBNP at 2 years?

Select the best answer.

A -145 pg/mL

B -208 pg/mL

C -259 pg/mL

D -439 pg/mL

Submit Review

Self-Check

In the PATENT-2 exploratory post hoc treatment-naïve subgroup analysis, what was the change in NT-proBNP at 2 years?

Select the best answer.

A -145 pg/mL

B -208 pg/mL

C -259 pg/mL

D -439 pg/mL

That is correct!

The treatment-naïve subgroup showed a -208 pg/mL change in NT-proBNP at 2 years.

Submit Review

Self-Check

In the PATENT-2 exploratory post hoc treatment-naïve subgroup analysis, what was the change in NT-proBNP at 2 years?

Select the best answer.

A -145 pg/mL

B -208 pg/mL

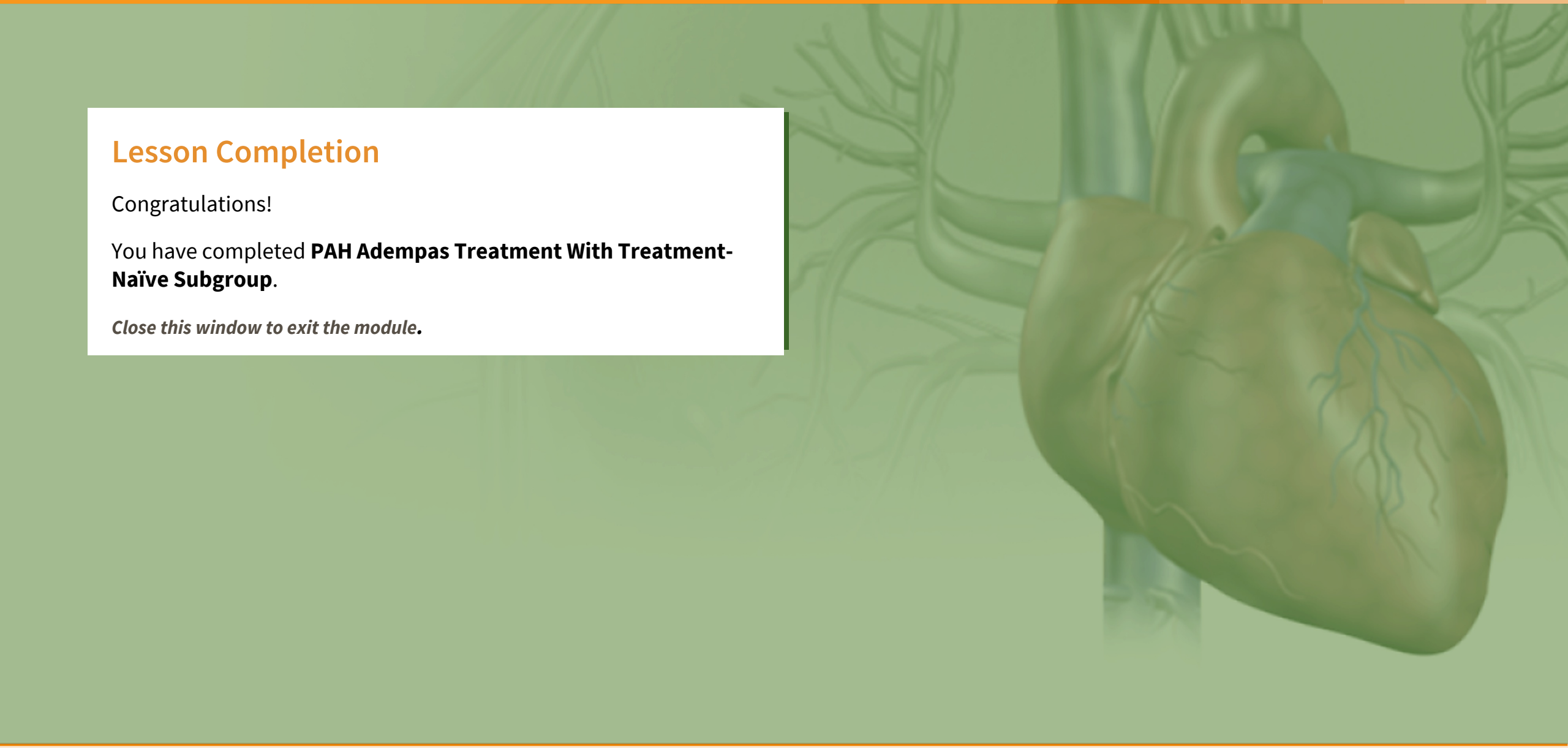
C -259 pg/mL

D -439 pg/mL

That is incorrect. Select Review if you would like to revisit the screen related to this question.

The treatment-naïve subgroup showed a -208 pg/mL change in NT-proBNP at 2 years. The PATENT-1 study data showed -439 pg/mL change at Week 12.

Submit Review



Lesson Completion

Congratulations!

You have completed **PAH Adempas Treatment With Treatment-Naïve Subgroup**.

***Close this window to exit the module*.**

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Glossary

6-minute walking distance (6MWD): The distance a person is able to walk in 6 minutes on a hard, flat surface.

etiology: The cause or causes of a disease or abnormal condition

Hemodynamic parameters: Basic measures of cardiovascular function, such as arterial pressure.

Idiopathic PAH: PAH due to an unknown cause.

N-terminal pro-brain natriuretic peptide (NT-proBNP): A hormone secreted by the left or right ventricle of the heart; bloodstream concentration of NT-proBNP increase with heart damage.

pulmonary vascular resistance (PVR): The vascular resistance of the pulmonary circulation, equal to the difference between the mean pulmonary arterial pressure and the left atrial filling pressure divided by the cardiac output.

World Health Organization functional classification (WHO FC): a tool used to measure disease severity in PH patients across classes. Assessment in a higher class indicates a more severe disease.