Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Pulmonary Hypertension
Interventions:	Drug: Oral treprostinil (UT-15C) sustained release tablets Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
354 subjects were randomized with 350 subjects receiving a dose of study drug and subsequently analyzed from 20 October 2006 to 17 September 2008 at 70 sites across the United States, Canada, Europe, Israel, and Australia.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Participant Flow: Overall Study

	Placebo Arm	**Active**
STARTED	**176**	**174**
COMPLETED	**167**	**153**
NOT COMPLETED	**9**	**21**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.
Total	Total of all reporting groups

Baseline Measures

	Placebo Arm	Active	Total
Number of Participants [units: participants]	**176**	**174**	**350**
Age [units: participants]			
<=18 years	**5**	**3**	**8**
Between 18 and 65 years	**149**	**151**	**300**
>=65 years	**22**	**20**	**42**
Age [units: years] Mean ± Standard Deviation	**49.5 ± 13.3**	**51.1 ± 12.3**	**50.3 ± 12.8**
Gender [units: participants]			
Female	**140**	**148**	**288**
Male	**36**	**26**	**62**
Distance Traversed (meters) During Six Minute Walk Test at Baseline [units: meters] Mean ± Standard Deviation	**345.4 ± 75.5**	**346.1 ± 71.4**	**345.7 ± 73.4**
Baseline WHO Functional Classification [1] **[units: participants]**			

WHO Functional Class I	**1**	**2**	**3**
WHO Functional Class II	**31**	**41**	**72**
WHO Functional Class III	**139**	**127**	**266**
WHO Functional Class IV	**5**	**4**	**9**
PAH Etiology [units: participants]			
Idiopathic / familial PAH	**119**	**113**	**232**
PAH associated with collagen vasular disease	**43**	**49**	**92**
PAH associated wtih congenital heart defect	**11**	**11**	**22**
PAH associated with HIV infection	**3**	**1**	**4**
Background PAH Therapy [units: participants]			
ERA	**51**	**55**	**106**
PDE5-I	**43**	**45**	**88**
ERA and PDE5-I	**82**	**74**	**156**

[1] Class I: PH without limitation of physical activity (PA); no undue dyspnea or fatigue, chest pain, or near syncope.

Class II: PH resulting in slight limitation of PA; comfortable at rest; ordinary PA causes undue dyspnea or fatigue, chest pain or near syncope.

Class III: PH resulting in marked limitation of PA; comfortable at rest; ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.

Class IV: PH with inability to carry out any PA without symptoms and signs of right heart failure. Dyspnea and/or fatigue may be present at rest. Discomfort is increased by any PA.

Outcome Measures

Hide All Outcome Measures

1. Primary: Six Minute Walk Distance (6MWD) [Time Frame: Baseline and 16 Weeks]

Measure Type	Primary
Measure Title	Six Minute Walk Distance (6MWD)
Measure Description	Placebo corrected change in six minute walk distance (6MWD) from Baseline to Week 16, correlates with the historical clinical standard for assessing patient functional status in the treatment of PAH and is considered an objective measure of patient functional status by the American Thoracic Society (ATS).

	The six minute walk test was to be conducted 3 to 6 hours after the previous dose of study drug.
Time Frame	Baseline and 16 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**176**	**174**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**362.5 (302.0 to 400.0)**	**362.5 (304.0 to 397.0)**
6MWD at Week 16	**367.0 (283.0 to 420.5)**	**381.0 (323.0 to 420.0)**
Change in 6MWD from Baseline to Week 16	**4.8 (-22.0 to 35.5)**	**14.5 (-10.0 to 47.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.072
Hodges-Lehmann [4]	11.0

95% Confidence Interval	(0 to 22)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Borg Dyspnea Score [Time Frame: Baseline and 16 Weeks]

Measure Type	Secondary
Measure Title	Borg Dyspnea Score
Measure Description	The Borg dyspnea score is a 10-point scale rating the maximum level of dyspnea experienced during the 6-minute walk test. The Borg dyspnea score was assessed immediately following the 6-minute walk test. Scores ranged from 0 (for no shortness of breath) to 10 (for greatest shortness of breath ever experienced).
Time Frame	Baseline and 16 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
One subject in the placebo arm did not have a Baseline Borg score value.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**175**	**174**
Borg Dyspnea Score [units: units on a scale] Mean ± Standard Deviation		
Borg dyspnea score at Baseline	**4.26 ± 2.25**	**4.22 ± 2.24**
Borg dyspnea score at Week 16	**4.64 ± 2.62**	**4.18 ± 2.59**
Change in Borg dyspnea score from BL to Wk 16	**0.38 ± 2.06**	**-0.03 ± 2.13**

Statistical Analysis 1 for Borg Dyspnea Score

Groups [1]	All groups
Method [2]	Wilcoxon rank-sum test
P Value [3]	0.062
Hodges-Lehmann (H-L) [4]	0.0
95% Confidence Interval	(-1.0 to 0.0)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in Borg dyspnea score from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Clinical Worsening Assessment [Time Frame: Baseline and 16 Weeks]

Measure Type	Secondary
Measure Title	Clinical Worsening Assessment

Measure Description	Definition of clinical worsening required one of the following: 1. Death (all causes excluding accident) 2. Transplantation or atrial septostomy 3. Clinical deterioration as defined by: a. Hospitalization as a result of PAH, or b. ≥ 20% decrease in 6-minute walk distance from Baseline (or too ill to walk) and a decrease in WHO functional class And c. Initiation of new PAH specific therapy (i.e., ERA, PDE5I, prostacyclin).
Time Frame	Baseline and 16 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**176**	**174**
Clinical Worsening Assessment [units: participants]	**12**	**8**

Statistical Analysis 1 for Clinical Worsening Assessment

Groups [1]	All groups
Method [2]	Fisher Exact
P Value [3]	0.491

[1]	Additional details about the analysis, such as null hypothesis and power calculation:

	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

4. Secondary: Dyspnea-Fatigue Index [Time Frame: Baseline and 16 Weeks]

Measure Type	Secondary
Measure Title	Dyspnea-Fatigue Index
Measure Description	The dyspnea-fatigue index has three components, each rated on a scale of 0 to 4, for the magnitude of the task that evokes dyspnea or fatigue, the magnitude of the pace (or effort) with which the task is performed and the associated functional impairment in general activities. The ratings for each component were added to form an aggregate score, which could range from 0, for the worst condition, to 12, for the best.
Time Frame	Baseline and 16 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Five subjects in the placebo arm and three subjects in the active arm did not have a Baseline dypsnea-fatigue index score.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**171**	**171**

Dyspnea-Fatigue Index [units: units on a scale] Mean ± Standard Deviation		
Dyspnea-fatigue index at Baseline	**5.5 ± 2.2**	**5.7 ± 2.1**
Dyspnea-fatigue index at Week 16	**5.1 ± 2.5**	**5.7 ± 2.5**
Change in dyspnea-fatigue index from BL to Wk 16	**-0.4 ± 1.9**	**0.0 ± 1.9**

Statistical Analysis 1 for Dyspnea-Fatigue Index

Groups [1]	All groups
Method [2]	Wilcoxon sum-rank test
P Value [3]	0.011
Hodges-Lehmann (H-L) [4]	0.0
95% Confidence Interval	(0.0 to 1.0)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in dyspnea-fatigue index from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: World Health Organization Functional Classification for PAH [Time Frame: Week 16]

Measure Type	Secondary
Measure Title	World Health Organization Functional Classification for PAH
Measure Description	Class I: Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope. Class II: Patients with pulmonary hypertension resulting in slight limitation of physical activity. These patients are comfortable at rest, but ordinary physical

	activity causes undue dyspnea or fatigue, chest pain or near syncope. Class III: Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope. Class IV: Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present even at rest. Discomfort is increased by any physical activity.
Time Frame	Week 16
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**176**	**174**
World Health Organization Functional Classification for PAH [units: participants]		
WHO Class I	**1**	**2**
WHO Class II	**48**	**58**
WHO Class III	**114**	**103**
WHO Class IV	**13**	**11**

No statistical analysis provided for World Health Organization Functional Classification for PAH

6. Secondary: Six Minute Walk Distance (6MWD) [Time Frame: Baseline and 12 weeks]

Measure Type	Secondary
Measure Title	Six Minute Walk Distance (6MWD)
Measure Description	Placebo corrected change in six minute walk distance (6MWD) from Baseline to Week 12, correlates with the historical clinical standard for assessing patient functional status in the treatment of PAH and is considered an objective measure of patient functional status by the American Thoracic Society (ATS). The six minute walk test was to be conducted 3 to 6 hours after the previous dose of study drug.
Time Frame	Baseline and 12 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**176**	**174**
Six Minute Walk Distance (6MWD) [units: meters] Median (Full Range)		
6MWD at Baseline	**362.5 (302.0 to 400.0)**	**362.5 (304.0 to 397.0)**
6MWD at Week 12	**366.4 (280.5 to 424.0)**	**378.0 (320.0 to 425.0)**
Change in 6MWD from Baseline to Week 12	**5.8 (-23.5 to 29.5)**	**16.5 (-15.0 to 51.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.015
Hodges-Lehmann (H-L) [4]	13.0
95% Confidence Interval	(3.0 to 23.0)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 12
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

7. Secondary: Six Minute Walk Distance (6MWD) [Time Frame: Baseline and 8 weeks]

Measure Type	Secondary
Measure Title	Six Minute Walk Distance (6MWD)
Measure Description	Placebo corrected change in six minute walk distance (6MWD) from Baseline to Week 8, correlates with the historical clinical standard for assessing patient functional status in the treatment of PAH and is considered an objective measure of patient functional status by the American Thoracic Society (ATS). The six minute walk test was to be conducted 3 to 6 hours after the previous dose of study drug.
Time Frame	Baseline and 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**176**	**174**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**362.5 (302.0 to 400.0)**	**362.5 (304.0 to 397.0)**
6MWD at Week 8	**368.5 (294.5 to 416.0)**	**379.0 (310.0 to 415.0)**
Change in 6MWD from Baseline to Week 8	**7.0 (-22.0 to 30.5)**	**15.0 (-9.0 to 42.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.051
Hodges-Lehmann [4]	9.0
95% Confidence Interval	(0.0 to 18.0)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 8
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

[4]	Other relevant estimation information:
	No text entered.

8. Secondary: Six Minute Walk Distance (6MWD) [Time Frame: Baseline and 4 weeks]

Measure Type	Secondary
Measure Title	Six Minute Walk Distance (6MWD)
Measure Description	Placebo corrected change in six minute walk distance (6MWD) from Baseline to Week 4, correlates with the historical clinical standard for assessing patient functional status in the treatment of PAH and is considered an objective measure of patient functional status by the American Thoracic Society (ATS). The six minute walk test was to be conducted 3 to 6 hours after the previous dose of study drug.
Time Frame	Baseline and 4 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**176**	**174**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**362.5 (302.0 to 400.0)**	**362.5 (304.0 to 397.0)**

6MWD at Week 4	**363.0 (299.0 to 410.5)**	**370.5 (312.0 to 410)**
Change in 6MWD from Baseline to Week 4	**2.1 (-17.5 to 24.5)**	**5.5 (-8.0 to 31.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.238
Hodges-Lehmann (H-L) [4]	4
95% Confidence Interval	(-2.4 to 12.0)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 4
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

9. Secondary: Change in Symptoms of PAH From Baseline to Week 16 [Time Frame: Baseline and 16 weeks]

Measure Type	Secondary
Measure Title	Change in Symptoms of PAH From Baseline to Week 16
Measure Description	Defined symptoms of PAH including fatigue, dyspnea, edema, dizziness, syncope, chest pain, and orthopnea were assessed at Baseline prior to starting study drug and during the Treatment Phase at Week 16. Severity grade values (i.e., 0, 1, 2, or 3 in increasing severity) were assigned for each symptom. The outcome data describes the change in severity values from Baseline to Week 16 for each defined symptom of PAH.
Time Frame	Baseline and 16 weeks

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**176**	**174**
Change in Symptoms of PAH From Baseline to Week 16 [units: units on a scale] Mean ± Standard Error		
Change in fatigue symptoms	**0.0 ± 0.0**	**0.01 ± 0.10**
Change in dypsnea symptoms	**0.00 ± 0.00**	**-0.01 ± 0.09**
Change in edema symptoms	**0.00 ± 0.00**	**-0.06 ± 0.10**
Change in dizziness symptoms	**0.00 ± 0.00**	**-0.16 ± 0.11**
Change in syncope symptoms	**0.00 ± 0.00**	**-0.10 ± 0.09**
Change in chest pain symptoms	**0.00 ± 0.00**	**-0.09 ± 0.11**
Change in orthopnea symptoms	**0.00 ± 0.00**	**-0.20 ± 0.10**

No statistical analysis provided for Change in Symptoms of PAH From Baseline to Week 16

10. Post-Hoc: Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartiles: Quartile 1 (126-302 Meters) [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartiles: Quartile 1 (126-302 Meters)

Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The study population was divided into quartiles by Baseline 6MWD. The subjects in this subgroup were in quartile 1 (126 - 302 meters).

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**45**	**43**
Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartiles: Quartile 1 (126-302 Meters) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**247.0 (191.0 to 288.0)**	**255.0 (204.0 to 289.0)**
6MWD at Week 16	**241.0 (141.0 to 286.0)**	**265.0 (189.0 to 325.0)**
Change in 6MWD from Baseline to Week 16	**-5.6 (-39.0 to 16.0)**	**17.0 (-13.0 to 43.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartiles: Quartile 1 (126-302 Meters)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.121
Hodges-Lehmann (H-L) [4]	24
95% Confidence Interval	(0 to 45)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

11. Post-Hoc: Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 2 (303 - 362 Meters) [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 2 (303 - 362 Meters)
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The study population was divided into quartiles by Baseline 6MWD. The subjects in this subgroup were in quartile 2 (303 - 362 meters).

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**43**	**44**
Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 2 (303 - 362 Meters) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**332.0 (323.0 to 354.0)**	**339.0 (323.5 to 350.5)**
6MWD at Week 16	**348.0 (300.0 to 376.0)**	**359.0 (329.5 to 400.5)**
Change in 6MWD from Baseline to Week 16	**12.0 (-22.0 to 37.0)**	**17.0 (-0.4 to 53.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 2 (303 - 362 Meters)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.069
Hodges-Lehmann (H-L) [4]	15
95% Confidence Interval	(-7 to 41)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.

[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

12. Post-Hoc: Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 3 (363 - 397 Meters) [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 3 (363 - 397 Meters)
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The study population was divided into quartiles by Baseline 6MWD. The subjects in this subgroup were in quartile 3 (363 - 397 meters).

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**42**	**45**
Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 3 (363 - 397 Meters) [units: meters] Median (Inter-Quartile Range)		

6MWD at Baseline	**385.0** **(378.0 to 390.0)**	**383.0** **(376.0 to 390.0)**
6MWD at Week 16	**388.0** **(358.0 to 429.0)**	**396.0** **(370.0 to 417.0)**
Change in 6MWD from Baseline to Week 16	**6.5** **(-22.0 to 43.0)**	**13.0** **(-8.0 to 44.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 3 (363 - 397 Meters)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.889
Hodges-Lehmann (H-L) [4]	4
95% Confidence Interval	(-15 to 24)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

13. Post-Hoc: Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 4 (398 - 450 Meters) [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
	Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 4

Measure Title	(398 - 450 Meters)
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The study population was divided into quartiles by Baseline 6MWD. The subjects in this subgroup were in quartile 4 (398 - 450 meters).

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**46**	**42**
Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 4 (398 - 450 Meters) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**425.5 (410.0 to 440.0)**	**425.0 (412.0 to 430.0)**
6MWD at Week 16	**442.0 (411.0 to 468.0)**	**438.5 (395.0 to 483.0)**
Change in 6MWD from Baseline to Week 16	**15.0 (-6.0 to 49.0)**	**15.0 (-20.0 to 59.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Baseline 6MWD Quartile: Quartile 4 (398 - 450 Meters)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.966
Hodges-Lehmann (H-L) [4]	0
95% Confidence Interval	(-23 to 24)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

14. Post-Hoc: Change in Six Minute Walk Distance (6MWD) From Baseline in Subjects Who Received Oral Treprostinil by Last Study Drug Dose and Reason for Discontinuation [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Change in Six Minute Walk Distance (6MWD) From Baseline in Subjects Who Received Oral Treprostinil by Last Study Drug Dose and Reason for Discontinuation
Measure Description	In general, the dose of study drug was increased in 0.5 mg increments every 3 days, in the absence of dose-limiting drug-related AEs, to ensure the subject received the optimal clinical dose throughout the study.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Of 174 subjects randomized to receive oral treprostinil, 153 subjects who completed the study and 6

additional subjects who did not complete the study but discontinued the study due to adverse events were included in this analysis.

Reporting Groups

	Description
Less Than 1 mg or Discontinuation Due to Adverse Events	Subjects in this group received less than or equal to 1 mg oral treprostinil twice daily or discontinued treatment due to adverse events.
1.25 - 3.25 mg	Subjects in this group recieved 1.25 to 3.25 mg oral treprostinil twice daily.
3.5 - 16 mg	Subjects in this group received 3.5 to 16 mg oral treprostinil twice daily.

Measured Values

	Less Than 1 mg or Discontinuation Due to Adverse Events	1.25 - 3.25 mg	3.5 - 16 mg
Number of Participants Analyzed [units: participants]	**58**	**49**	**52**
Change in Six Minute Walk Distance (6MWD) From Baseline in Subjects Who Received Oral Treprostinil by Last Study Drug Dose and Reason for Discontinuation [units: meters] Median (Inter-Quartile Range)	**3.8 (-8.0 to 26.0)**	**18.0 (-3.0 to 56.0)**	**34.0 (3.0 to 52.0)**

No statistical analysis provided for Change in Six Minute Walk Distance (6MWD) From Baseline in Subjects Who Received Oral Treprostinil by Last Study Drug Dose and Reason for Discontinuation

15. Post-Hoc: Six Minute Walk Distance (6MWD) by Lowest Dose Strength Available at Randomization: Smallest Dose Available 1 mg [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Lowest Dose Strength Available at Randomization: Smallest Dose Available 1 mg
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup had a minimum tablet strength of 1 mg for initiation of study drug dosing and dose titration.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**51**	**51**
Six Minute Walk Distance (6MWD) by Lowest Dose Strength Available at Randomization: Smallest Dose Available 1 mg [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**348.0 (282.0 to 385.0)**	**349.0 (311.0 to 380.0)**
6MWD at Week 16	**350.0 (243.0 to 431.0)**	**379.0 (324.7 to 405.0)**
Change in 6MWD from Baseline to Week 16	**15.0 (-26.0 to 55.0)**	**22.0 (5.0 to 45.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Lowest Dose Strength Available at Randomization: Smallest Dose Available 1 mg

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.853

Hodges-Lehmann (H-L) [4]	5
95% Confidence Interval	(-16 to 28)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

16. Post-Hoc: Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomizaiton: Dose Strength 0.5 mg [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomizaiton: Dose Strength 0.5 mg
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup had a minimum tablet strength of 0.5 mg for initiation of study drug dosing and dose titration.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**99**	**100**
Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomizaiton: Dose Strength 0.5 mg [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**366.0 (302.0 to 410.0)**	**370.0 (297.0 to 411.0)**
6MWD at Week 16	**370.0 (283.0 to 430.0)**	**375.5 (301.0 to 439.5)**
Change in 6MWD from Baseline to Week 16	**7.0 (-19.0 to 30.0)**	**7.0 (-19.0 to 46.5)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomizaiton: Dose Strength 0.5 mg

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.327
Hodges-Lehmann (H-L) [4]	7
95% Confidence Interval	(-7 to 21)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

17. Post-Hoc: Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomization: Study Drug Dose 0.25 mg [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomization: Study Drug Dose 0.25 mg
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup had a minimum tablet strength of 0.25 mg for initiation of study drug dosing and dose titration.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**26**	**23**
Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomization: Study Drug Dose 0.25 mg **[units: meters]** **Median (Inter-Quartile Range)**		
6MWD at Baseline	**374.0** **(319.0 to 408.0)**	**384.0** **(306.0 to 405.0)**
6MWD at Week 16	**374.0**	**398.0**

	(320.0 to 399.0)	**(340.0 to 438.0)**
Change in 6MWD from Baseline to Week 16	**-1.0 (-30.0 to 12.0)**	**21.0 (-7.0 to 78.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Lowest Study Drug Dose Strength Available at Randomization: Study Drug Dose 0.25 mg

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.085
Hodges-Lehmann (H-L) [4]	29.5
95% Confidence Interval	(1 to 73)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

18. Post-Hoc: Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup were receiving treatment with an ERA for 90 days or greater at the time of randomization.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	**Active**
Number of Participants Analyzed [units: participants]	**51**	**55**
Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**382.0 (325.0 to 403.0)**	**372.0 (325.0 to 398.0)**
6MWD at Week 16	**377.0 (303.0 to 423.0)**	**385.0 (306.4 to 422.0)**
Change in 6MWD from Baseline to Week 16	**-3.0 (-22.0 to 30.0)**	**4.0 (-16.0 to 40.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.615
Hodges-Lehmann (H-L) [4]	5
95% Confidence Interval	(-12 to 24)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

19. Post-Hoc: Six Minute Walk Distance (6MWD) by Background PAH Therapy: PDE5-I [Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Background PAH Therapy: PDE5-I
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup were receiving treatment with a PDE5-I for 90 days or greater at the time of randomization.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed		

[units: participants]	**43**	**45**
Six Minute Walk Distance (6MWD) by Background PAH Therapy: PDE5-I **[units: meters]** **Median (Inter-Quartile Range)**		
6MWD at Baseline	**360.0** **(302.0 to 397.0)**	**348.0** **(296.0 to 390.0)**
6MWD at Week 16	**357.0** **(318.0 to 424.0)**	**373.0** **(307.0 to 411.0)**
Change in 6MWD from Baseline to Week 16	**8.0** **(-31.0 to 47.0)**	**23.0** **(-3.0 to 47.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Background PAH Therapy: PDE5-I

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.230
Hodges-Lehmann (H-L) [4]	17
95% Confidence Interval	(-6 to 40)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

20. Post-Hoc: Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA and PDE5-I [

Time Frame: Baseline and 16 weeks]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA and PDE5-I
Measure Description	No text entered.
Time Frame	Baseline and 16 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The subjects in this subgroup were receiving treatment with an ERA and PDE5-I for 90 days or greater at the time of randomization.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo Arm	Active
Number of Participants Analyzed [units: participants]	**82**	**74**
Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA and PDE5-I [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**351.5 (290.0 to 400.0)**	**358.5 (300.0 to 412.0)**
6MWD at Week 16	**359.2 (243.0 to 418.0)**	**381.0 (325.0 to 425.0)**
Change in 6MWD from Baseline to Week 16	**8.0 (-20.0 to 35.0)**	**14.5 (-13.0 to 47.0)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by Background PAH Therapy: ERA and PDE5-I

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.209
Hodges-Lehmann (H-L) [4]	10
95% Confidence Interval	(-6 to 28)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change in 6MWD from Baseline to Week 16
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse events were recorded throughout the 16 week study which was conducted between October 2006 and September 2008.
Additional Description	No text entered.

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Serious Adverse Events

	Placebo Arm	Active
Total, serious adverse events		
# participants affected / at risk	**33/176 (18.75%)**	**32/174 (18.39%)**
Blood and lymphatic system disorders		
anemia [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
international normalized ratio increased [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
Cardiac disorders		
right ventricular failure [*1]		
# participants affected / at risk	**2/176 (1.14%)**	**6/174 (3.45%)**
# events	**2**	**7**
atrial flutter [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**2/174 (1.15%)**
# events	**1**	**2**
chest pain [*1]		
# participants affected / at risk	**2/176 (1.14%)**	**0/174 (0.00%)**
# events	**2**	**0**
aortic stenosis [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
bradycardia [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
cardiac arrest [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
cardiac failure [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
cardiac failure congestive [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**

# events	0	1
low cardiac output syndrome [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
pericarditis constrictive [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
bradyarrhythmia [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
Gastrointestinal disorders		
nausea [*1]		
# participants affected / at risk	2/176 (1.14%)	0/174 (0.00%)
# events	2	0
vomiting [*1]		
# participants affected / at risk	2/176 (1.14%)	0/174 (0.00%)
# events	2	0
diarrhea hemorrhagic [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
gastroenteritis viral [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
intestinal obstruction [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
Mallory-Weiss syndrome [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
large intestinal hemorrhage [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
General disorders		
syncope [*1]		
# participants affected / at risk	3/176 (1.70%)	2/174 (1.15%)
# events	3	4

hypersensitivity [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
Hepatobiliary disorders		
hepatitis [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
hepatitis toxic [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
liver function test abnormal [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
hepatic enzyme increased [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
Infections and infestations		
lower respiratory tract infection [*1]		
# participants affected / at risk	1/176 (0.57%)	1/174 (0.57%)
# events	1	1
infection [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
pyrexia [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
central line infection [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
streptococcal infection [*1]		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
respiratory tract infection [*1]		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
Metabolism and nutrition disorders		

hyperparathyroidism secondary [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
iron deficiency anemia [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
Musculoskeletal and connective tissue disorders		
myalgia [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
pain in extremity [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
spinal osteoarthritis [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
tibia fracture [*1]		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
breast cancer [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
ovarian cyst [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
Nervous system disorders		
multiple sclerosis [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
subarachnoid hemorrhage [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
subdural hematoma [*1]		
# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**

# events	1	0
Psychiatric disorders		
suicide attempt * 1		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
Renal and urinary disorders		
renal failure acute * 1		
# participants affected / at risk	0/176 (0.00%)	3/174 (1.72%)
# events	0	4
Respiratory, thoracic and mediastinal disorders		
Pulmonary arterial hypertension * 1		
# participants affected / at risk	8/176 (4.55%)	9/174 (5.17%)
# events	8	9
dyspnea * 1		
# participants affected / at risk	3/176 (1.70%)	1/174 (0.57%)
# events	3	1
pneumonia * 1		
# participants affected / at risk	2/176 (1.14%)	0/174 (0.00%)
# events	2	0
cough * 1		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
hypoxia * 1		
# participants affected / at risk	0/176 (0.00%)	1/174 (0.57%)
# events	0	1
Vascular disorders		
hypotension * 1		
# participants affected / at risk	2/176 (1.14%)	0/174 (0.00%)
# events	2	0
epistaxis * 1		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
fluid overload * 1		
# participants affected / at risk	1/176 (0.57%)	0/174 (0.00%)
# events	1	0
fluid retention * 1		

# participants affected / at risk	**1/176 (0.57%)**	**0/174 (0.00%)**
# events	**1**	**0**
pulmonary hemorrhage * 1		
# participants affected / at risk	**0/176 (0.00%)**	**1/174 (0.57%)**
# events	**0**	**1**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse events were recorded throughout the 16 week study which was conducted between October 2006 and September 2008.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Placebo Arm	Subjects were randomly allocated to receive oral placebo twice daily.
Active	Subjects in this arm were randomly allocated to receive oral treprostinil twice daily.

Other Adverse Events

	Placebo Arm	**Active**
Total, other (not including serious) adverse events		
# participants affected / at risk	**157/176 (89.20%)**	**173/174 (99.43%)**
Cardiac disorders		
chest pain * 1		
# participants affected / at risk	**14/176 (7.95%)**	**12/174 (6.90%)**
# events	**15**	**12**
palpitations * 1		
# participants affected / at risk	**9/176 (5.11%)**	**17/174 (9.77%)**
# events	**9**	**18**
Ear and labyrinth disorders		

dizziness [*1]		
# participants affected / at risk	28/176 (15.91%)	30/174 (17.24%)
# events	33	33
Gastrointestinal disorders		
nausea [*1]		
# participants affected / at risk	60/176 (34.09%)	112/174 (64.37%)
# events	65	126
diarrhea [*1]		
# participants affected / at risk	48/176 (27.27%)	106/174 (60.92%)
# events	49	115
vomiting [*1]		
# participants affected / at risk	14/176 (7.95%)	76/174 (43.68%)
# events	18	82
constipation [*1]		
# participants affected / at risk	8/176 (4.55%)	9/174 (5.17%)
# events	8	9
dyspepsia [*1]		
# participants affected / at risk	8/176 (4.55%)	9/174 (5.17%)
# events	10	9
General disorders		
fatigue [*1]		
# participants affected / at risk	17/176 (9.66%)	25/174 (14.37%)
# events	18	25
pain [*1]		
# participants affected / at risk	6/176 (3.41%)	17/174 (9.77%)
# events	7	17
syncope [*1]		
# participants affected / at risk	11/176 (6.25%)	7/174 (4.02%)
# events	14	9
abdominal pain [*1]		
# participants affected / at risk	5/176 (2.84%)	8/174 (4.60%)
# events	5	8
oropharyngeal pain [*1]		
# participants affected / at risk	8/176 (4.55%)	3/174 (1.72%)
# events	8	3
Metabolism and nutrition disorders		
decreased appetite [*1]		

# participants affected / at risk	2/176 (1.14%)	13/174 (7.47%)
# events	2	13
Musculoskeletal and connective tissue disorders		
pain in jaw * 1		
# participants affected / at risk	21/176 (11.93%)	75/174 (43.10%)
# events	22	77
pain in extremity * 1		
# participants affected / at risk	17/176 (9.66%)	54/174 (31.03%)
# events	17	62
myalgia * 1		
# participants affected / at risk	6/176 (3.41%)	24/174 (13.79%)
# events	6	26
back pain * 1		
# participants affected / at risk	10/176 (5.68%)	13/174 (7.47%)
# events	10	13
arthralgia * 1		
# participants affected / at risk	4/176 (2.27%)	18/174 (10.34%)
# events	4	19
abdominal pain upper * 1		
# participants affected / at risk	8/176 (4.55%)	8/174 (4.60%)
# events	8	8
musculoskeletal pain * 1		
# participants affected / at risk	3/176 (1.70%)	9/174 (5.17%)
# events	4	9
Nervous system disorders		
headache * 1		
# participants affected / at risk	65/176 (36.93%)	150/174 (86.21%)
# events	69	164
insomnia * 1		
# participants affected / at risk	7/176 (3.98%)	15/174 (8.62%)
# events	7	15
migraine * 1		
# participants affected / at risk	0/176 (0.00%)	8/174 (4.60%)
# events	0	8
Psychiatric disorders		
anxiety * 1		

# participants affected / at risk	4/176 (2.27%)	8/174 (4.60%)
# events	4	10
Respiratory, thoracic and mediastinal disorders		
nasopharyngitis * 1		
# participants affected / at risk	16/176 (9.09%)	13/174 (7.47%)
# events	16	14
upper respiratory tract infection * 1		
# participants affected / at risk	17/176 (9.66%)	11/174 (6.32%)
# events	21	11
dyspnea * 1		
# participants affected / at risk	12/176 (6.82%)	13/174 (7.47%)
# events	12	14
cough * 1		
# participants affected / at risk	11/176 (6.25%)	11/174 (6.32%)
# events	11	11
nasal congestion * 1		
# participants affected / at risk	10/176 (5.68%)	11/174 (6.32%)
# events	10	11
Skin and subcutaneous tissue disorders		
rash * 1		
# participants affected / at risk	8/176 (4.55%)	10/174 (5.75%)
# events	8	11
Vascular disorders		
flushing * 1		
# participants affected / at risk	27/176 (15.34%)	85/174 (48.85%)
# events	28	87
edema peripheral * 1		
# participants affected / at risk	17/176 (9.66%)	15/174 (8.62%)
# events	19	15
abdominal distention * 1		
# participants affected / at risk	10/176 (5.68%)	11/174 (6.32%)
# events	10	11
pulmonary arterial hypertension * 1		
# participants affected / at risk	11/176 (6.25%)	10/174 (5.75%)
# events	12	10
epistaxis * 1		
# participants affected / at risk	9/176 (5.11%)	7/174 (4.02%)

# events	10	7

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA (12.0)

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
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