Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Pulmonary Hypertension
Interventions:	Drug: Oral treprostinil (UT-15C) Sustained Release Tablets Other: 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
349 subjects participated in the study from 24 October 2006 to 29 April 2011 at 52 of 77 sites across the United States, Puerto Rico, Canada, Europe, Israel, India, Mexico, and China. The primary endpoint was analyzed using the primary analysis population which included 228 subjects who had access to 0.25 mg tablets at the time of randomization.

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	These subjects were randomly allocated to receive matching oral placebo twice daily (every 12 hours +/- 1 hour) and were included in the primary analysis population. Dose increases were made in the absence of dose-limiting drug-related AEs, to ensure the subject received the optimal clinical dose throughout the study.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily (every 12 hours +/- 1 hour) and were included in the primary analysis population. Dose increases were made in the absence of dose-limiting drug-related AEs, to ensure the subject received the optimal clinical dose throughout the study.

Participant Flow: Overall Study

	Placebo	UT-15C (Oral Treprostinil)
STARTED	116	233
COMPLETED	98 [1]	182 [2]
NOT COMPLETED	18	51

[1] 98 subjects receiving placebo completed the study on study drug
[2] 182 subjects receiving oral treprostinil completed the study on study drug

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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population
Total	Total of all reporting groups

Baseline Measures

	Placebo	UT-15C (Oral Treprostinil)	Total
Number of Participants [units: participants]	77	151	228
Age [units: participants]			
<=18 years	1	9	10
Between 18 and 65 years	69	141	210
>=65 years	7	1	8
Age [units: years] Mean ± Standard Deviation	42.5 ± 13.5	37.8 ± 13.5	39.4 ± 13.7

Gender [units: participants]			
Female	**58**	**108**	**166**
Male	**19**	**43**	**62**
PAH Etiology [units: participants]			
Idiopathic or heritable PAH	**56**	**114**	**170**
PAH associated w collagen vascular disease	**17**	**26**	**43**
PAH associated w repaired congenital heart defect	**3**	**10**	**13**
PAH associated w HIV infection	**1**	**1**	**2**
Baseline Six Minute Walk Distance [units: meters] Mean ± Standard Deviation	**327.6 ± 70.7**	**331.3 ± 64.9**	**330.0 ± 66.8**
WHO Functional Classification [1] [units: participants]			
WHO Class I	**1**	**1**	**2**
WHO Class II	**24**	**52**	**76**
WHO Class III	**52**	**98**	**150**

[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 Week 12]

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 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. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 12. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 12
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.
Analyses were conducted using the modified intention to treat (mITT) group, which includes subjects with access to 0.25 mg tablets at randomization (n=228). All alpha was spent on this subgroup, thereby maintaining an overall type I error rate of 0.05. For sensitivity purposes, efficacy analyses were also performed on all enrolled subjects (n=349).

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**77**	**151**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**339 (282 to 381)**	**350 (283 to 386)**

6MWD at Week 12	**343 (246 to 403)**	**370 (300 to 418)**
Change in 6MWD from Baseline to Week 12	**-5 (-41 to 49)**	**25 (-16 to 63)**

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

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0125
Hodges-Lehmann (H-L) [4]	23
95% Confidence Interval	(4 to 41)

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Using an allocation ratio of 2:1 between oral treprostinil and placebo, a fixed sample size of approximately 195 subjects with access to 0.25 mg tablets at randomization would provide at least 90% power at a significance level of 0.01 (two-sided hypothesis) to detect a between-treatment difference in the change from Baseline to Week 12 in distance traversed during the 6-minute walk, assuming a true underlying treatment difference of 45 meters with a SD of 75 meters in both treatment groups.
[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:
	P-Value
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Six Minute Walk Distance (6MWD) [Time Frame: Baseline and Week 11]

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 11, a time expected to correlate with trough treprostinil concentration. The six minute walk test was to be conducted 8 to 13 hours after the previous

	dose of study drug. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 11. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 11
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.
Analyses were conducted using the modified intention to treat (mITT) group, which includes subjects with access to 0.25 mg tablets at randomization (n=228). All alpha was spent on this subgroup, thereby maintaining an overall type I error rate of 0.05. For sensitivity purposes, efficacy analyses were also performed on all enrolled subjects (n=349).

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**339 (282 to 381)**	**350 (283 to 386)**
6MWD at Week 11	**335 (254 to 400)**	**350 (290 to 400)**
Change in 6MWD from Baseline to Week 11	**0 (-54 to 36)**	**8 (-25 to 50)**

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

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0653
Hodges-Lehmann (H-L) [4]	13
95% Confidence Interval	(-2 to 33)

[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]	Other relevant estimation information:
	No text entered.

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

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. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 8. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.

Time Frame	Baseline and Week 8
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.
Analyses were conducted using the modified intention to treat (mITT) group, which includes subjects with access to 0.25 mg tablets at randomization (n=228). All alpha was spent on this subgroup, thereby maintaining an overall type I error rate of 0.05. For sensitivity purposes, efficacy analyses were also performed on all enrolled subjects (n=349).

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**339 (282 to 381)**	**350 (283 to 386)**
6MWD at Week 8	**347 (240 to 398)**	**355 (300 to 408)**
Change in 6MWD from Baseline to Week 8	**0 (-36 to 35)**	**17 (-15 to 54)**

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

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0307

Hodges-Lehmann (H-L) [4]	17
95% Confidence Interval	(1 to 33)

[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]	Other relevant estimation information:
	No text entered.

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

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. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 4. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 4
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.
Analyses were conducted using the modified intention to treat (mITT), which includes subjects who

had access to 0.25 mg tablets at randomization (n=228). All alpha was spent on this subgroup, thereby maintaining an overall type I error rate of 0.05. For sensitivity purposes, efficacy analyses were also performed on all enrolled subjects (n=349).

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
Six Minute Walk Distance (6MWD) [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**339 (282 to 381)**	**350 (283 to 386)**
6MWD at Week 4	**350 (254 to 387)**	**360 (285 to 400)**
Change in 6MWD from Baseline to Week 4	**0 (-28 to 17)**	**7 (-15 to 42)**

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

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0518
Hodges-Lehmann (H-L) [4]	12
95% Confidence Interval	(0 to 24)

[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]	Other relevant estimation information:
	No text entered.

5. Secondary: Clinical Worsening Assessment [Time Frame: Baseline and Week 12]

Measure Type	Secondary
Measure Title	Clinical Worsening Assessment
Measure Description	Definition of clinical worsening included patients who met at least one of the following criteria during the 12 weeks of the study: 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. greater than or equal to 20% decrease in 6MWD 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, PDE5-I, prostacyclin)
Time Frame	Baseline and Week 12
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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
Clinical Worsening Assessment [units: participants]	**8**	**15**

Statistical Analysis 1 for Clinical Worsening Assessment

Groups [1]	All groups
Method [2]	Fisher Exact
P Value [3]	1.000

[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.

6. Secondary: World Health Organization Functional Classification for PAH [Time Frame: Baseline and Week 12]

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	Baseline and Week 12
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.
Subjects with a WHO functional classification assessment at Week 12.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
World Health Organization Functional Classification for PAH [units: participants]		
WHO Class I	**1**	**2**
WHO Class II	**29**	**59**
WHO Class III	**38**	**75**
WHO Class IV	**9**	**15**

Statistical Analysis 1 for World Health Organization Functional Classification for PAH

Groups [1]	All groups
Method [2]	Wilcoxon rank sum test
P Value [3]	0.7380

Hodges-Lehmann (H-L) [4]	0
95% Confidence Interval	(0 to 0)

[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:
	In cases where the “value corresponding to overall poorest relative change” was imputed for walk distance, a value of “IV” was used for the WHO functional classification for PAH.
[4]	Other relevant estimation information:
	The values for the estimated parameter and 95% confidence interval were calculated.

7. Secondary: Borg Dyspnea Score [Time Frame: Baseline and Week 12]

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 Week 12
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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.

UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**77**	**151**
Borg Dyspnea Score [units: units on a scale] Median (Inter-Quartile Range)		
Borg dyspnea score at Baseline	**3 (2 to 6)**	**3 (2 to 4)**
Borg dyspnea score at Week 12	**3 (2 to 5)**	**3 (1 to 5)**
Change in Borg dyspnea score from Baseline to Wk12	**0 (-1 to 1)**	**0 (-1 to 1)**

Statistical Analysis 1 for Borg Dyspnea Score

Groups [1]	All groups
Method [2]	Wilcoxon rank-sum test
P Value [3]	0.4887
Hodges-Lehmann (H-L) [4]	0
95% Confidence Interval	(-1 to 0)

[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]	Other relevant estimation information:
	No text entered.

8. Secondary: Dyspnea-Fatigue Index [Time Frame: Baseline and Week 12]

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 Week 12
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.
Two subjects (one in the placebo arm and one in the oral treprostinil arm) from the primary analysis population (n=228) did not have a Baseline dyspnea-fatigue index score and were not included in this analysis.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**76**	**150**
Dyspnea-Fatigue Index [units: units on a scale] Mean ± Standard Deviation		
Dyspnea-fatigue index at Baseline	**5.8 ± 2.4**	**6.2 ± 2.1**
Dyspnea-fatigue index at Week 12	**5.5 ± 2.9**	**5.9 ± 2.8**

Change in dyspnea-fatigue index from BL to Wk 12	**-0.3 ± 2.5**	**-0.3 ± 2.4**

Statistical Analysis 1 for Dyspnea-Fatigue Index

Groups [1]	All groups
Method [2]	Wilcoxon sum-rank test
P Value [3]	0.6116
Hodges-Lehmann (H-L) [4]	0
95% Confidence Interval	(0 to 1)

[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]	Other relevant estimation information:
	No text entered.

9. Secondary: Symptoms of PAH [Time Frame: Baseline and Week 12]

Measure Type	Secondary
Measure Title	Symptoms of PAH
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 12. Severity grade values (i.e., 0, 1, 2, or 3 in increasing severity) were assigned for each symptom.
Time Frame	Baseline and Week 12
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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**77**	**151**
Symptoms of PAH [units: units on a scale] Mean ± Standard Deviation		
Change in fatigue symptoms	**0.1 ± 1.0**	**0.0 ± 1.0**
Change in dyspnea symptoms	**-0.1 ± 0.9**	**-0.2 ± 0.9**
Change in edema symptoms	**0.3 ± 1.0**	**0.2 ± 1.1**
Change in dizziness symptoms	**0.0 ± 1.0**	**0.3 ± 1.0**
Change in syncope symptoms	**0.3 ± 1.0**	**0.3 ± 0.9**
Change in chest pain symptoms	**0.1 ± 0.9**	**0.2 ± 1.0**
Change in orthopnea symptoms	**0.2 ± 0.9**	**0.2 ± 1.0**

No statistical analysis provided for Symptoms of PAH

10. Post-Hoc: Six Minute Walk Distance by Baseline WHO Functional Classification III or IV [Time Frame: Baseline and Week 12]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance by Baseline WHO Functional Classification III or IV
Measure Description	Exploratory efficacy analyses were to determine the effect of Baseline WHO functional class on treatment effect for change in 6MWD. The Hodges-Lehmann median difference between treatment groups was

	used to estimate the treatment effect on 6MWD from Baseline to Week 12. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 12
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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**52**	**98**
Six Minute Walk Distance by Baseline WHO Functional Classification III or IV [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**333.5 (269 to 382.5)**	**330 (265 to 378)**
6MWD at Week 12	**316.5 (231.5 to 385)**	**354 (265 to 400)**
Change in 6MWD from Baseline to Week 12	**-8.5 (-50.5 to 40)**	**20.5 (-20 to 63)**

Statistical Analysis 1 for Six Minute Walk Distance by Baseline WHO Functional Classification III or IV

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0326
Hodges-Lehmann (H-L) [4]	26
95% Confidence Interval	(1 to 49)

[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]	Other relevant estimation information:
	No text entered.

11. Post-Hoc: Six Minute Walk Distance by Baseline WHO Functional Classification: I or II [Time Frame: Baseline and Week 12]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance by Baseline WHO Functional Classification: I or II
Measure Description	Exploratory efficacy analyses were to determine the effect of Baseline WHO functional class on treatment effect for change in 6MWD. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 12. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 12

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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**25**	**53**
Six Minute Walk Distance by Baseline WHO Functional Classification: I or II [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**370 (297 to 378)**	**366 (315 to 390)**
6MWD at Week 12	**379 (274 to 429)**	**391 (348 to 431)**
Change in 6MWD from Baseline to Week 12	**18 (-30 to 55)**	**27 (-5 to 67)**

Statistical Analysis 1 for Six Minute Walk Distance by Baseline WHO Functional Classification: I or II

Groups [1]	All groups
Method [2]	ANCOVA

P Value [3]	0.2275
Hodges-Lehmann (H-L) [4]	16.0
95% Confidence Interval	(-15 to 47)

[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]	Other relevant estimation information:
	No text entered.

12. Post-Hoc: Six Minute Walk Distance (6MWD) by PAH Etiology: Idiopathic or Heritable PAH [Time Frame: Baseline and Week 12]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) by PAH Etiology: Idiopathic or Heritable PAH
Measure Description	Exploratory efficacy analyses were to determine the effect of PAH etiology (idiopathic/heritable, associated with collagen vascular disease, and other etiologies) on treatment effect for change in 6MWD. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 12. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 12
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	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**56**	**114**
Six Minute Walk Distance (6MWD) by PAH Etiology: Idiopathic or Heritable PAH [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**332.5 (260 to 379)**	**346 (281 to 390)**
6MWD at Week 12	**310.5 (242.5 to 380)**	**380 (304 to 420)**
Change in 6MWD from BL to Wk 12	**-7.5 (-50.5 to 42)**	**25 (-13 to 67)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) by PAH Etiology: Idiopathic or Heritable PAH

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0024
Hodges-Lehmann (H-L) [4]	32
95% Confidence Interval	(10 to 55)

[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]	Other relevant estimation information:
	No text entered.

13. Post-Hoc: Six Minute Walk Distance (6MWD) for the Entire Study Population [Time Frame: Baseline and Week 12]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) for the Entire Study Population
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). This outcome measure was assessed using data collected from all subjects enrolled in the study, regardless of tablet strength availability at randomization. The six minute walk test was to be conducted 3 to 6 house after the previous dose of study drug. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Wk 12. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference i
Time Frame	Baseline and Week 12
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.
This analysis was performed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**116**	**233**
Six Minute Walk Distance (6MWD) for the Entire Study Population [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**338.5 (265.5 to 383.5)**	**347 (288 to 387)**
6MWD at Week 12	**329.5 (231.5 to 397.5)**	**370 (304 to 420)**
Change in 6MWD from Baseline to Week 12	**0 (-46 to 40)**	**25 (-12 to 63)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) for the Entire Study Population

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0001
Hodges-Lehmann (H-L) [4]	25.5
95% Confidence Interval	(10 to 41)

[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]	Other relevant estimation information:
	No text entered.

14. Post-Hoc: Six Minute Walk Distance (6MWD) for the Entire Study Population [Time Frame: Baseline and Week 11]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) for the Entire Study Population
Measure Description	Placebo corrected change in six minute walk distance (6MWD) from Baseline to Week 11, a time expected to correlate with trough treprostinil concentration. This outcome measure was assessed using data from all subjects enrolled in the study, regardless of tablet strength availability at the time of randomization. The six minute walk test was to be conducted 8 to 13 hours after the previous dose of study drug. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 11. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 11
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.
This analysis was performed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice

	daily.

Measured Values

	Placebo	UT-15C (Oral Treprostinil)
Number of Participants Analyzed [units: participants]	**116**	**233**
Six Minute Walk Distance (6MWD) for the Entire Study Population [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**338.5 (265.5 to 383.5)**	**347 (288 to 387)**
6MWD at Week 11	**326.5 (206 to 398)**	**351 (303 to 403)**
Change in 6MWD from Baseline to Week 11	**-2 (-58.5 to 36)**	**6 (-18 to 48)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) for the Entire Study Population

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0025
Hodges-Lehmann (H-L) [4]	17
95% Confidence Interval	(3 to 33)

[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]	Other relevant estimation information:
	No text entered.

15. Post-Hoc: Six Minute Walk Distance (6MWD) for the Entire Study Population [Time Frame: Baseline and Week 8]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) for the Entire Study Population
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). This outcome measure was assessed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization. The six minute walk test was to be conducted 3 to 6 house after the previous dose of study drug. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 8. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 8
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.
This analysis was performed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**

Number of Participants Analyzed [units: participants]	**116**	**233**
Six Minute Walk Distance (6MWD) for the Entire Study Population [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	**338.5 (265.5 to 383.5)**	**347 (288 to 387)**
6MWD at Week 8	**339.5 (227 to 392)**	**360 (300 to 411)**
Change in 6MWD from Baseline to Week 8	**1.0 (-38.5 to 34.5)**	**17.0 (-13 to 54)**

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) for the Entire Study Population

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0008
Hodges-Lehmann (H-L) [4]	20
95% Confidence Interval	(7 to 34)

[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]	Other relevant estimation information:
	No text entered.

16. Post-Hoc: Six Minute Walk Distance (6MWD) for the Entire Study Population [Time Frame:

Baseline and Week 4]

Measure Type	Post-Hoc
Measure Title	Six Minute Walk Distance (6MWD) for the Entire Study Population
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). This outcome measure was assessed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization. The six minute walk test was to be conducted 3 to 6 house after the previous dose of study drug. The Hodges-Lehmann median difference between treatment groups was used to estimate the treatment effect on 6MWD from Baseline to Week 4. A rank-based methodology was used instead of parametric-based methodology to avoid statistical bias caused by extreme outliers resulting from the handling of data that are missing due to death or clinical worsening of PAH. It is a more robust estimator than the between-treatment difference in medians.
Time Frame	Baseline and Week 4
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.
This analysis was performed using data from all subjects enrolled in the study, regardless of tablet strength availability at randomization.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily.

Measured Values

	Placebo	**UT-15C (Oral Treprostinil)**
Number of Participants Analyzed [units: participants]	**116**	**233**
Six Minute Walk Distance (6MWD) for the Entire Study		

Population [units: meters] Median (Inter-Quartile Range)		
6MWD at Baseline	338.5 (265.5 to 383.5)	347 (288 to 387)
6MWD at Week 4	339.5 (251 to 387)	358 (288 to 403.2)
Change in 6MWD from Baseline to Week 4	-4 (-31.5 to 20)	7 (-13 to 42)

Statistical Analysis 1 for Six Minute Walk Distance (6MWD) for the Entire Study Population

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.0025
Hodges-Lehmann (H-L) [4]	14
95% Confidence Interval	(3.9 to 25)

[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]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse events were recorded throughout the 12 week study which was conducted between October 2006 and April 2011.

Additional Description	No text entered.

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Serious Adverse Events

	Placebo	UT-15C (Oral Treprostinil)
Total, serious adverse events		
# participants affected / at risk	**15/77 (19.48%)**	**27/151 (17.88%)**
Cardiac disorders		
right ventricular failure [*1]		
# participants affected / at risk	**3/77 (3.90%)**	**10/151 (6.62%)**
# events	**3**	**12**
pulmonary hypertension [*1]		
# participants affected / at risk	**4/77 (5.19%)**	**3/151 (1.99%)**
# events	**4**	**3**
cardiac failure [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**2**
cardiac failure congestive [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
cardio-respiratory arrest [*1]		
# participants affected / at risk	**1/77 (1.30%)**	**0/151 (0.00%)**
# events	**1**	**0**
circulatory collapse [*1]		
# participants affected / at risk	**1/77 (1.30%)**	**0/151 (0.00%)**
# events	**1**	**0**
cor pulmonale acute [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
palpitations [*1]		

# participants affected / at risk	1/77 (1.30%)	0/151 (0.00%)
# events	1	0
pulmonary edema * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
sudden cardiac death * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
Gastrointestinal disorders		
diarrhea * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
diarrhea infectious * 1		
# participants affected / at risk	1/77 (1.30%)	0/151 (0.00%)
# events	1	0
gastritis * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
gastroenteritis * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
nausea * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
vomiting * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
General disorders		
death * 1		
# participants affected / at risk	2/77 (2.60%)	2/151 (1.32%)
# events	2	2
presyncope * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
sudden death * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1

syncope [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
Immune system disorders		
systemic lupus erythematosus [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
Infections and infestations		
septic shock [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
Musculoskeletal and connective tissue disorders		
chest pain [*1]		
# participants affected / at risk	**1/77 (1.30%)**	**2/151 (1.32%)**
# events	**1**	**2**
Nervous system disorders		
anterograde amnesia [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
headache [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
Renal and urinary disorders		
acute renal failure [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
urinary tract infection [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**1**
renal impairment [*1]		
# participants affected / at risk	**0/77 (0.00%)**	**1/151 (0.66%)**
# events	**0**	**2**
Respiratory, thoracic and mediastinal disorders		
pneumonia [*1]		
# participants affected / at risk	**3/77 (3.90%)**	**1/151 (0.66%)**

# events	4	1
pulmonary embolism * 1		
# participants affected / at risk	0/77 (0.00%)	2/151 (1.32%)
# events	0	2
hemoptysis * 1		
# participants affected / at risk	1/77 (1.30%)	1/151 (0.66%)
# events	1	1
paroxysmal noturnal dypsnea * 1		
# participants affected / at risk	1/77 (1.30%)	0/151 (0.00%)
# events	1	0
lower respiratory tract infection * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
respiratory tract infection * 1		
# participants affected / at risk	1/77 (1.30%)	0/151 (0.00%)
# events	1	0
Skin and subcutaneous tissue disorders		
skin ulcer * 1		
# participants affected / at risk	0/77 (0.00%)	1/151 (0.66%)
# events	0	1
Vascular disorders		
collagen-vascular disease * 1		
# participants affected / at risk	1/77 (1.30%)	0/151 (0.00%)
# events	1	0

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA (14.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse events were recorded throughout the 12 week study which was conducted between October 2006 and April 2011.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Placebo	These subjects were randomly allocated to receive placebo twice daily and were included in the primary analysis population.
UT-15C (Oral Treprostinil)	These subjects were randomly allocated to receive oral treprostinil twice daily and were included in the primary analysis population.

Other Adverse Events

	Placebo	UT-15C (Oral Treprostinil)
Total, other (not including serious) adverse events		
# participants affected / at risk	**68/77 (88.31%)**	**138/151 (91.39%)**
Cardiac disorders		
right ventricular failure [*1]		
# participants affected / at risk	**3/77 (3.90%)**	**10/151 (6.62%)**
# events	**3**	**12**
Endocrine disorders		
hypokalemia [*1]		
# participants affected / at risk	**2/77 (2.60%)**	**13/151 (8.61%)**
# events	**3**	**16**
Gastrointestinal disorders		
diarrhea [*1]		
# participants affected / at risk	**12/77 (15.58%)**	**46/151 (30.46%)**
# events	**12**	**54**
nausea [*1]		
# participants affected / at risk	**14/77 (18.18%)**	**45/151 (29.80%)**
# events	**14**	**50**
vomiting [*1]		
# participants affected / at risk	**12/77 (15.58%)**	**26/151 (17.22%)**
# events	**12**	**31**
gastritis [*1]		
# participants affected / at risk	**1/77 (1.30%)**	**7/151 (4.64%)**
# events	**1**	**7**
General disorders		
fatigue [*1]		
# participants affected / at risk	**6/77 (7.79%)**	**14/151 (9.27%)**

# events	6	15
decreased appetite [*1]		
# participants affected / at risk	4/77 (5.19%)	12/151 (7.95%)
# events	4	12
pain [*1]		
# participants affected / at risk	0/77 (0.00%)	7/151 (4.64%)
# events	0	7
asthenia [*1]		
# participants affected / at risk	4/77 (5.19%)	6/151 (3.97%)
# events	4	9
oropharyngeal pain [*1]		
# participants affected / at risk	4/77 (5.19%)	1/151 (0.66%)
# events	4	1
dizziness [*1]		
# participants affected / at risk	11/77 (14.29%)	17/151 (11.26%)
# events	11	19
Infections and infestations		
pyrexia [*1]		
# participants affected / at risk	8/77 (10.39%)	7/151 (4.64%)
# events	8	7
upper respiratory tract infection [*1]		
# participants affected / at risk	5/77 (6.49%)	8/151 (5.30%)
# events	5	8
Musculoskeletal and connective tissue disorders		
Pain in extremity [*1]		
# participants affected / at risk	6/77 (7.79%)	21/151 (13.91%)
# events	6	25
pain in jaw [*1]		
# participants affected / at risk	3/77 (3.90%)	17/151 (11.26%)
# events	3	18
abdominal pain [*1]		
# participants affected / at risk	4/77 (5.19%)	13/151 (8.61%)
# events	4	13
abdominal discomfort [*1]		
# participants affected / at risk	0/77 (0.00%)	9/151 (5.96%)
# events	0	9
upper abdominal pain [*1]		

# participants affected / at risk	2/77 (2.60%)	8/151 (5.30%)
# events	2	12
back pain * 1		
# participants affected / at risk	2/77 (2.60%)	7/151 (4.64%)
# events	2	8
arthralgia * 1		
# participants affected / at risk	1/77 (1.30%)	7/151 (4.64%)
# events	1	7
muscle spasms * 1		
# participants affected / at risk	4/77 (5.19%)	5/151 (3.31%)
# events	4	8
Nervous system disorders		
headache * 1		
# participants affected / at risk	15/77 (19.48%)	95/151 (62.91%)
# events	17	131
insomnia * 1		
# participants affected / at risk	2/77 (2.60%)	11/151 (7.28%)
# events	2	12
Respiratory, thoracic and mediastinal disorders		
nasopharyngitis * 1		
# participants affected / at risk	4/77 (5.19%)	9/151 (5.96%)
# events	4	12
pulmonary hypertension * 1		
# participants affected / at risk	5/77 (6.49%)	3/151 (1.99%)
# events	5	3
cough * 1		
# participants affected / at risk	9/77 (11.69%)	14/151 (9.27%)
# events	9	15
dyspnea * 1		
# participants affected / at risk	8/77 (10.39%)	7/151 (4.64%)
# events	8	8
Skin and subcutaneous tissue disorders		
rash * 1		
# participants affected / at risk	0/77 (0.00%)	7/151 (4.64%)
# events	0	7
Vascular disorders		

flushing [*1]		
# participants affected / at risk	**5/77 (6.49%)**	**23/151 (15.23%)**
# events	**5**	**25**
peripheral edema [*1]		
# participants affected / at risk	**5/77 (6.49%)**	**13/151 (8.61%)**
# events	**5**	**15**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA (14.0)

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
No text entered.