Iloprost Power 15 in Pulmonary Arterial Hypertension (PROWESS 15)

This study has been completed.

Sponsor:
Actelion

Information provided by (Responsible Party):
Actelion

ClinicalTrials.gov Identifier:
NCT00709956

First received: July 1, 2008
Last updated: September 10, 2015
Last verified: March 2015
History of Changes

Results First Received: October 7, 2010

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Crossover Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Pulmonary Arterial Hypertension
Interventions:	Drug: iloprost (5 µg) 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
On Day 1 all patients received a single inhalation dose of placebo. Patients who satisfied the selection criteria in the single-blind period of the study were entered into the double-blind period to receive iloprost 5 µg and matching placebo (Days 2 and 3) in a single dose, two-period crossover design.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Of the 70 randomized patients, 64 patients entered the double-blind period, (placebo/iloprost P15, 33 patients and iloprost P15/placebo, 31 patients). 1 patient in the iloprost P15/placebo treatment sequence was excluded from the per-protocol analysis which was defined as the primary analysis.

Reporting Groups

	Description
Iloprost (5µg) / Placebo	Single dose double-blind active iloprost (5µg) on study day 2 followed by single dose double-blind placebo on study day 3
Placebo / Iloprost (5 µg)	Single dose double-blind placebo on study day 2 followed by single dose double-blind active iloprost (5µg) on study day 3

Participant Flow: Overall Study

	Iloprost (5µg) / Placebo	Placebo / Iloprost (5 µg)
STARTED	33 [1]	37 [1]
Double-blind Crossover-period	31 [2]	33 [2]

COMPLETED	**30**	**33**
NOT COMPLETED	**3**	**4**
Withdrawal by Subject	**1**	**1**
Inclusion/exclusion criteria violation	**2**	**3**

[1] Day 1 Single-blind placebo run-in
[2] Days 2 and 3

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
Iloprost (5µg) / Placebo	Single dose double-blind active iloprost (5µg) on study day 2 followed by single dose double-blind placebo on study day 3
Placebo / Iloprost (5 µg)	Single dose double-blind placebo on study day 2 followed by single dose double-blind active iloprost (5µg) on study day 3
Total	Total of all reporting groups

Baseline Measures

	Iloprost (5µg) / Placebo	**Placebo / Iloprost (5 µg)**	**Total**
Number of Participants [units: participants]	**31**	**33**	**64**

Age **[units: participants]**			
<=18 years	**0**	**0**	**0**
Between 18 and 65 years	**22**	**24**	**46**
>=65 years	**9**	**9**	**18**
Age **[units: years]** **Mean (Standard Deviation)**	**55.5 (13.57)**	**55.8 (16.40)**	**55.7 (14.98)**
Gender **[units: participants]**			
Female	**23**	**28**	**51**
Male	**8**	**5**	**13**
Region of Enrollment **[units: participants]**			
United States	**28**	**30**	**58**
Austria	**2**	**2**	**4**
Germany	**1**	**1**	**2**

Outcome Measures

Hide All Outcome Measures

1. Primary: 6-minute-walk Distance (6MWD) [Time Frame: Study day 2 or study day 3]

Measure Type	Primary
Measure Title	6-minute-walk Distance (6MWD)

Measure Description	The 6-minute walk test was performed 20-40 minutes after treatment. This was a non-encouraged test (the person conducting the test did not encourage the patient to walk farther or faster) that measured the distance covered over a 6-minute walk. It was conducted by a trained member of the site staff who was listed on the site's delegation of authority sheet. For patients who had never performed a 6-minute walk test previously, a training test was requested before the qualifying tests for randomization.
Time Frame	Study day 2 or study day 3
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 analysis was per protocol, 64 patients started double blind phase of study, 63 completed.

Reporting Groups

	Description
6MWD After Placebo Treatment	No text entered.
6MWD After Iloprost (5 µg) Treatment	No text entered.

Measured Values

	6MWD After Placebo Treatment	**6MWD After Iloprost (5 µg) Treatment**
Number of Participants Analyzed [units: participants]	**63**	**63**
6-minute-walk Distance (6MWD) [units: meters] Least Squares Mean (95% Confidence Interval)	**330.0 (322.3 to 337.7)**	**328.6 (320.9 to 336.2)**

Statistical Analysis 1 for 6-minute-walk Distance (6MWD)

Groups [1]	All groups
Method [2]	Generalized linear model
P Value [3]	0.7883
Difference in least squares mean [4]	-1.5
95% Confidence Interval	-12.3 to 9.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	With a sample size of at least 63 patients and based on the assumptions on the primary endpoint (normal distribution, SD of the difference of 30 m) the study was designed to detect a significant treatment effect with 90% power, assuming a difference exceeding 12.5 m between the mean values of the 6MWD following the iloprost power 15 treatment and the one following the placebo treatment.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Subject (sequence), treatment, and period as fixed effect
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	If the primary endpoint reaches significance, treatment effect of the secondary endpoint is determined at a 2-sided nominal of 0.05. Since hierarchy of the endpoints to be tested has been predefined, no correction for multiple testing will be applied
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Borg Dyspnea Score [Time Frame: Study day 2 or study day 3]

Measure Type	Secondary
Measure Title	Borg Dyspnea Score

Measure Description	The Borg scale is a category-ratio scale, commonly used to evaluate the effects of exercise on dyspnea. The original and modified scales have ratio properties ranging from 0 = nothing at all to 10 = very, very severe, with descriptors from 0 to 10. Descriptors have been modified by others so that 10 has been labeled "extremely severe," or "the worst possible dyspnea imaginable." Reliability and validity have been reported in a general population and in patients with PAH as well as other respiratory conditions.
Time Frame	Study day 2 or study day 3
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 analysis was per protocol, 64 patients started double blind phase of study, 63 completed.

Reporting Groups

	Description
Borg Dyspnea Score After Placebo Treatment	No text entered.
Borg Dyspnea Score After Iloprost (5 µg) Treatment	No text entered.

Measured Values

	Borg Dyspnea Score After Placebo Treatment	**Borg Dyspnea Score After Iloprost (5 µg) Treatment**
Number of Participants Analyzed [units: participants]	**63**	**63**
Borg Dyspnea Score [units: scores on a scale] Mean (Standard Deviation)	**3.5 (2.23)**	**3.4 (2.25)**

No statistical analysis provided for Borg Dyspnea Score

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Due to data capture design constraints the time of adverse event (AE) onset was not collected, therefore the potential to assign potential causality to active treatment or placebo was not assessed. AE's can only be reported as shown, as prospectively planned in the protocol submitted to FDA. Includes all patients entered in the double-blind phase.

Reporting Groups

	Description
Iloprost (5µg) / Placebo	Single dose double-blind active iloprost (5µg) on study day 2 followed by single dose double-blind placebo on study day 3
Placebo / Iloprost (5 µg)	Single dose double-blind placebo on study day 2 followed by single dose double-blind active iloprost (5µg) on study day 3

Serious Adverse Events

	Iloprost (5µg) / Placebo	Placebo / Iloprost (5 µg)
Total, serious adverse events		
# participants affected / at risk	**0/31 (0.00%)**	**1/33 (3.03%)**
Cardiac disorders		
Right ventricular failure † 1		
# participants affected / at risk	**0/31 (0.00%)**	**1/33 (3.03%)**
# events	**0**	**1**
Respiratory, thoracic and mediastinal disorders		
Pulmonary arterial hypertension † 1		
# participants affected / at risk	**0/31 (0.00%)**	**1/33 (3.03%)**

# events	0	1

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	Due to data capture design constraints the time of adverse event (AE) onset was not collected, therefore the potential to assign potential causality to active treatment or placebo was not assessed. AE's can only be reported as shown, as prospectively planned in the protocol submitted to FDA. Includes all patients entered in the double-blind phase.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Iloprost (5µg) / Placebo	Single dose double-blind active iloprost (5µg) on study day 2 followed by single dose double-blind placebo on study day 3
Placebo / Iloprost (5 µg)	Single dose double-blind placebo on study day 2 followed by single dose double-blind active iloprost (5µg) on study day 3

Other Adverse Events

	Iloprost (5µg) / Placebo	**Placebo / Iloprost (5 µg)**
Total, other (not including serious) adverse events		
# participants affected / at risk	**16/31 (51.61%)**	**20/33 (60.61%)**

Gastrointestinal disorders		
Diarrhoea † 1		
# participants affected / at risk	**0/31 (0.00%)**	**2/33 (6.06%)**
Nausea † 1		
# participants affected / at risk	**0/31 (0.00%)**	**2/33 (6.06%)**
General disorders		
Pyrexia † 1		
# participants affected / at risk	**0/31 (0.00%)**	**2/33 (6.06%)**
Musculoskeletal and connective tissue disorders		
Muscle tightness † 1		
# participants affected / at risk	**0/31 (0.00%)**	**2/33 (6.06%)**
Pain in extremity † 1		
# participants affected / at risk	**2/31 (6.45%)**	**0/33 (0.00%)**
Nervous system disorders		
Dizziness † 1		
# participants affected / at risk	**2/31 (6.45%)**	**4/33 (12.12%)**
Headache † 1		
# participants affected / at risk	**3/31 (9.68%)**	**3/33 (9.09%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**4/31 (12.90%)**	**4/33 (12.12%)**
Dysphonia † 1		
# participants affected / at risk	**2/31 (6.45%)**	**0/33 (0.00%)**
Dyspnoea † 1		

# participants affected / at risk	1/31 (3.23%)	3/33 (9.09%)
Oropharyngeal pain † 1		
# participants affected / at risk	1/31 (3.23%)	3/33 (9.09%)
Rhinorrhoea † 1		
# participants affected / at risk	0/31 (0.00%)	3/33 (9.09%)
Throat irritation † 1		
# participants affected / at risk	5/31 (16.13%)	1/33 (3.03%)
Skin and subcutaneous tissue disorders		
Rash † 1		
# participants affected / at risk	0/31 (0.00%)	2/33 (6.06%)
Vascular disorders		
Flushing † 1		
# participants affected / at risk	4/31 (12.90%)	5/33 (15.15%)

† Events were collected by 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
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There is **NOT** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

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Responsible Party:	Actelion
ClinicalTrials.gov Identifier:	NCT00709956 History of Changes
Other Study ID Numbers:	**AC-063A301**
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Results First Received:	October 7, 2010
Last Updated:	September 10, 2015
Health Authority:	United States: Food and Drug Administration