Open Label Extension Study in Patients With Idiopathic Pulmonary Fibrosis Who Completed Protocol AC-052-321/ BUILD 3 / NCT00391443 (BUILD OL)

This study has been completed.

Sponsor:
Actelion

Information provided by (Responsible Party):
Actelion

ClinicalTrials.gov Identifier:
NCT00631475

First received: February 12, 2008
Last updated: September 9, 2015
Last verified: March 2015
History of Changes

Results First Received: June 19, 2012

Study Type:	Interven ional
Study Design:	Allocation: Non-Randomized; Endpoint Classification: Safety Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Idiopathic Pulmonary Fibrosis
Intervention:	Drug: Bosentan

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
Patients were enrolled at 61 centers in 15 countries (Australia, Belgium, Canada, Czech Republic, France, Germany, Ireland, Israel, Italy, Japan, South Korea, , Spain, Switzerland, UK, and USA. The first patient started on 5 March 2008 and the last patient, last visit was on 01 April 2010.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
In total, 128 of the 615 patients who received randomized treatment in BUILD 3 (NCT00391443) rolled over into the BUILD 3 OL extension.

Reporting Groups

	Description
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Participant Flow: Overall Study

	Bosentan Treatment
STARTED	128
COMPLETED	83
NOT COMPLETED	45
Death	18
Adverse Event	14
Withdrew consent	5
Preparation for lung transplant	8

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
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Baseline Measures

	Bosentan Treatment
Number of Participants [units: participants]	128
Age [units: years] Mean (Standard Deviation)	65.4 (8.2)
Age, Customized [units: participants]	
18-40 years	1
41-60 years	33
61-70 years	62
>70 years	32
Gender [units: participants]	
Female	31
Male	97
Region of Enrollment [units: participants]	
Australia	12
Belgium	1
Canada	14
Czech Republic	1
France	3
Germany	11
Ireland	1
Israel	4
Italy	2
Japan	8
Korea, Republic of	5
Spain	8
Switzerland	4
United Kingdom	3
United States	51

Outcome Measures

Hide All Outcome Measures

1. Primary: Extent of Exposure to Bosentan in Patients With Idiopathic Pulmonary Fibrosis (IPF) [Time Frame: Start of study to end of study, up to 21 months]

Measure Type	Primary
Measure Title	Extent of Exposure to Bosentan in Patients With Idiopathic Pulmonary Fibrosis (IPF)
Measure Description	Mean extent of exposure to bosentan treatment in months
Time Frame	Start of study to end of study, up to 21 mon hs
Safety Issue	Yes

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.
For two patients, the exact treatment stop date was missing and the duration could not be calculated, but these patients received at least 345 and 127 days of open label (OL) treatment.

Reporting Groups

	Description
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Measured Values

	Bosentan Treatment
Number of Participants Analyzed [units: participants]	**126**
Extent of Exposure to Bosentan in Patients With Idiopathic Pulmonary Fibrosis (IPF) [units: months] Mean (Standard Deviation)	**6.4 (4.6)**

No statistical analysis provided for Extent of Exposure to Bosentan in Patients With Idiopathic Pulmonary Fibrosis (IPF)

2. Secondary: Number of Patients Exposed to Bosentan Over Time [Time Frame: Start to end of study, up to 21 months]

Measure Type	Secondary
Measure Title	Number of Patients Exposed to Bosentan Over Time
Measure Description	Numbers of participants exposed to bosentan treatment over time
Time Frame	Start to end of study, up to 21 months
Safety Issue	Yes

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.
For two patients, the exact treatment stop date was missing and the duration could not be calculated, but these patients received at least 345 and 127 days of OL treatment, respectively.

Reporting Groups

	Description
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Measured Values

	Bosentan Treatment
Number of Participants Analyzed [units: participants]	**126**

Number of Patients Exposed to Bosentan Over Time [units: Participants]	
For at least 4 months	74
For at least 8 months	44
For at least 12 months	17
For at least 16 months	7
For at least 20 months	2

No statistical analysis provided for Number of Patients Exposed to Bosentan Over Time

3. Secondary: Adverse Events (AE) Leading to Discontinuation of Study Drug. [Time Frame: Start to end of study, up to 21 mon hs]

Measure Type	Secondary
Measure Title	Adverse Events (AE) Leading to Discon inuation of Study Drug.
Measure Description	Number of participants with at least one AE that led to permanent discontinuation of study treatment.
Time Frame	Start to end of study, up to 21 months
Safety Issue	Yes

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.
Study population

Reporting Groups

	Description
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Measured Values

	Bosentan Treatment
Number of Participants Analyzed [units: participants]	**128**
Adverse Events (AE) Leading to Discontinuation of Study Drug. [units: participants]	**32**

No statistical analysis provided for Adverse Events (AE) Leading to Discontinuation of Study Drug.

4. Secondary: Treatment-emergent Serious Adverse Events (SAE) [Time Frame: up to 21 months plus 28 days after the end of study drug]

Measure Type	Secondary
Measure Title	Treatment-emergent Serious Adverse Events (SAE)
Measure Description	Number of participants with at least one SAE during the study.
Time Frame	up to 21 months plus 28 days after the end of study drug
Safety Issue	Yes

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.
Study population

Reporting Groups

	Description

Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Measured Values

	Bosentan Treatment
Number of Participants Analyzed [units: participants]	**128**
Treatment-emergent Serious Adverse Events (SAE) [units: participants]	**51**

No statistical analysis provided for Treatment-emergent Serious Adverse Events (SAE)

5. Secondary: Occurrence of Liver Function Test (LFT: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)) Abnormality. [Time Frame: up to 21 months, plus 24 hours after the end of study treatment]

Measure Type	Secondary
Measure Title	Occurrence of Liver Function Test (LFT: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)) Abnormality.
Measure Description	Number of participants with an increase in ALT and/or AST to > 3 times upper limit of normal during the study.
Time Frame	up to 21 months, plus 24 hours after the end of study treatment
Safety Issue	Yes

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.
Study population

Reporting Groups

	Description
Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Measured Values

	Bosentan Treatment
Number of Participants Analyzed [units: participants]	**128**
Occurrence of Liver Function Test (LFT: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)) Abnormality. [units: participants]	**3**

No statistical analysis provided for Occurrence of Liver Function Test (LFT: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)) Abnormality.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Up to 28 days after the end of study drug
Additional Description	Only adverse events leading to premature discontinuation of study treatment were reported during the study. All serious adverse events occurring during and up to 28 days after end-of-study treatment were reported. Events listed as idiopathic pulmonary fibrosis were reported as worsening of idiopathic pulmonary fibrosis.

Reporting Groups

	Description

Bosentan Treatment	Oral bosentan 62.5 mg twice daily (b.i d.) for the first 4 weeks, and oral bosentan 125 mg b.i.d. (62.5 mg b.i.d. if </= 40 kg) thereafter

Serious Adverse Events

	Bosentan Treatment
Total, serious adverse events	
# participants affected / at risk	51/128 (39.84%)
Cardiac disorders	
Coronary artery disease [†1]	
# participants affected / at risk	2/128 (1.56%)
Arrhythmia [†1]	
# participants affected / at risk	1/128 (0.78%)
Atrial flutter [†1]	
# participants affected / at risk	1/128 (0.78%)
Cardiac arrest [†1]	
# participants affected / at risk	1/128 (0.78%)
Cardiopulmonary failure [†1]	
# participants affected / at risk	1/128 (0.78%)
Right ventricular failure [†1]	
# participants affected / at risk	1/128 (0.78%)
Gastrointestinal disorders	
Abdominal pain [†1]	
# participants affected / at risk	1/128 (0.78%)
Lower gastrointestinal haemorrhage [†1]	
# participants affected / at risk	1/128 (0.78%)
General disorders	
General physical health deterioration [†1]	
# participants affected / at risk	1/128 (0.78%)
Pyrexia [†1]	
# participants affected / at risk	1/128 (0.78%)
Hepatobiliary disorders	
Cholecystitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Hepatic failure [†1]	
# participants affected / at risk	1/128 (0.78%)
Ischaemic hepatitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Infections and infestations	
Lower respiratory tract infection [†1]	
# participants affected / at risk	4/128 (3.13%)
Pneumonia [†1]	
# participants affected / at risk	4/128 (3.13%)
Bronchitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Chronic sinusitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Diverticulitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Lobar pneumonia [†1]	
# participants affected / at risk	1/128 (0.78%)

Respiratory tract infection viral [†1]	
# participants affected / at risk	1/128 (0.78%)
Septic shock [†1]	
# participants affected / at risk	1/128 (0.78%)
Sinusitis [†1]	
# participants affected / at risk	1/128 (0.78%)
Viral infection [†1]	
# participants affected / at risk	1/128 (0.78%)
Injury, poisoning and procedural complications	
Anastomotic stenosis [†1]	
# participants affected / at risk	1/128 (0.78%)
Rib fracture [†1]	
# participants affected / at risk	1/128 (0.78%)
Investigations	
Blood iron decreased [†1]	
# participants affected / at risk	1/128 (0.78%)
Hepatic enzyme increased [†1]	
# participants affected / at risk	1/128 (0.78%)
Liver function test abnormal [†1]	
# participants affected / at risk	1/128 (0.78%)
Nervous system disorders	
Cerebrovascular accident [†1]	
# participants affected / at risk	1/128 (0.78%)
Psychiatric disorders	
Suicide attempt [†1]	
# participants affected / at risk	1/128 (0.78%)
Renal and urinary disorders	
Renal colic [†1]	
# participants affected / at risk	1/128 (0.78%)
Renal failure acute [†1]	
# participants affected / at risk	1/128 (0.78%)
Respiratory, thoracic and mediastinal disorders	
Idiopathic pulmonary fibrosis [†1]	
# participants affected / at risk	23/128 (17.97%)
Respiratory failure [†1]	
# participants affected / at risk	4/128 (3.13%)
Dyspnoea [†1]	
# participants affected / at risk	3/128 (2.34%)
Acute respiratory failure [†1]	
# participants affected / at risk	1/128 (0.78%)
Pleuritic pain [†1]	
# participants affected / at risk	1/128 (0.78%)
Pneumothorax [†1]	
# participants affected / at risk	1/128 (0.78%)
Pulmonary oedema [†1]	
# participants affected / at risk	1/128 (0.78%)
Respiratory disorder [†1]	
# participants affected / at risk	1/128 (0.78%)
Surgical and medical procedures	

Lung transplant †1	
# participants affected / at risk	3/128 (2.34%)
Vascular disorders	
Deep vein thrombosis †1	
# participants affected / at risk	1/128 (0.78%)
Hypotension †1	
# participants affected / at risk	1/128 (0.78%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (13.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	Up to 28 days after the end of study drug
Additional Description	Only adverse events leading to premature discontinuation of study treatment were reported during the study. All serious adverse events occurring during and up to 28 days after end-of-study treatment were reported. Events listed as idiopathic pulmonary fibrosis were reported as worsening of idiopathic pulmonary fibrosis.

Frequency Threshold

Threshold above which other adverse events are reported	0

Reporting Groups

	Description
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Other Adverse Events

	Bosentan Treatment
Total, other (not including serious) adverse events	
# participants affected / at risk	5/128 (3.91%)
General disorders	
OEDEMA PERIPHERAL †1	
# participants affected / at risk	1/128 (0.78%)
Investigations	
LIVER FUNCTION TEST ABNORMAL †1	
# participants affected / at risk	2/128 (1.56%)
Respiratory, thoracic and mediastinal disorders	
DYSPNOEA †1	
# participants affected / at risk	1/128 (0.78%)
IDIOPATHIC PULMONARY FIBROSIS †1	
# participants affected / at risk	1/128 (0.78%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (13.0)

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** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts he PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Actelion, wi h steering committee, shall complete the review and provide any modifications required to protect Actelion's patent rights and confidential information within sixty (60) days of receipt of the proposed publication. During this period, Investigator shall not permit publication. If Actelion reasonably anticipates filing a patent application claiming an invention arising out of the Study, such publication shall be delayed until after the application is filed.

Results Point of Contact:

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Other Study ID Numbers:	AC-052-322
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