Open-label extension study in patients with Idiopathic Pulmonary Fibrosis who completed protocol AC-052-321 BUILD-3

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To assess long-term safety and tolerability of bosentan in patients with IPF.

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON32143

Source
ToetsingOnline

Brief title
BUILD-3-OL: Bosentan Use in Interstitial Lung Diseases

Condition

- Respiratory disorders NEC

Synonym
cryptogenic fibrosing alveolitis, idiopathic pulmonary fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Bosentan, Idiopathic Pulmonary Fibrosis, open-label, Phase III

Outcome measures

Primary outcome

* AEs leading to premature discontinuation of study drug.

* Treatment-emergent SAEs and SAEs up to 28 days after the end of study drug

treatment.

* Occurrence of liver function test (ALT and AST) abnormality:

> 3 and * 5 times ULN; > 5 and * 8 times ULN; > 8 times ULN up to 24 hours

after the end of study treatment.

Secondary outcome

not applicable

Study description

Background summary

Idiopathic pulmonary fibrosis (IPF), also known as cryptogenic fibrosing alveolitis, is a distinct clinical disorder belonging to the spectrum of interstitial lung diseases (ILD). IPF is a progressive disease characterized by the presence of a histological pattern of usual interstitial pneumonia (UIP) on surgical lung biopsy.
IPF was considered a chronic inflammatory disease resulting in parenchymal fibrosis. However, recent evidence suggests a mechanism of abnormal wound healing, with progressive extracellular matrix accumulation, decreased fibroblast-myoblast cell death, continuous epithelial cell apoptosis and abnormal re-epithelialization. Progressive fibrotic tissue deposition in the interstitial areas of the lung leads to decreased lung compliance and reduced gas exchanges.
The onset of symptoms is usually gradual and patients complain of non-productive cough, shortness of breath occurring first on exercise and then at rest. Cyanosis, cor pulmonale, and peripheral edema may be observed in the late phase of the disease.

No therapies have been shown to improve the survival or quality of life for patients with IPF and none is registered. Current treatment is still based on the former assumption that IPF is an inflammatory process with concurrent remodeling of the lung by fibrosis. Consequently, it involves anti-inflammatory therapy, including corticosteroids (e.g., prednisone, prednisolone), immunosuppressive/cytotoxic agents (e.g., azathioprine, cyclophosphamide) or a combination of both. However, because of the marginal benefit and serious side effects of the current therapies, along with newer insights into the pathogenesis of IPF, there is an important need for novel therapeutic approaches.

Study objective

To assess long-term safety and tolerability of bosentan in patients with IPF.

Study design

The trial is an open-label, prospective, non-comparative (single-arm), multicenter study. It is an extension of the previous double-blind placebo-controlled study (AC-052-321 / BUILD-3).
The Build-3-OL study is designed to assess the long-term safety and tolerability of bosentan 125mg twice daily in IPF patients that have participated in the Build-3 study.

Currently no treatment (medicine) for IPF is registered. About 600 patients will participate. The treatment period is variable, and is dependent on the time the patient ends the previous Build-3 study and on the time the Build-3-OL studie will end.
After the study medication has been stoppen, the patient will be followed for 28 days for safety.

Intervention

Oral bosentan
* For patients who enter BUILD 3-OL before the release of BUILD 3 study results (i.e., study treatment in BUILD 3 unknown and must remain blinded):
* Initial dose: 62.5 mg b.i.d. for 4 weeks for all patients.
* Maintenance dose: 125 mg b.i.d. (62.5 mg b.i.d. if patient weighs < 40 kg/90 lbs).
* For patients who enter BUILD 3-OL after the release of the BUILD 3 study results (i.e., study treatment in BUILD 3 is known):
1. For patients administered bosentan during BUILD 3:
* Patients should continue bosentan treatment at the dose they were receiving at the end of BUILD 3.
2. For patients administered placebo during BUILD 3:
* Initial dose: 62.5 mg b.i.d. for 4 weeks.

* Maintenance dose: 125 mg b.i.d. (62.5 mg b.i.d. if patient weighs < 40 kg/90 lbs)

Study burden and risks

Visit 1= day of inclusion: there are three possibilities:
- If this visit is scheduled on the same day as the End of Study Visit of the the preceding Build-3 study, the extra burden to the patient consists of the informed consent procedure. The other assessments will then be carried out in the scope of the Build-3 study.
- Visit 1 within 4 weeks of the End of Study Visit of Build-3: The following assessments will be done: Informed Consent procedure, documenting of IPF-specific treatment, full physical exam, bloodpressure, heart rate, weight.
-Visit 1 more than 4 weeks after End of Study Visit of Build-3:In that case pulmonary function tests (FVC and DLco) will be performed in addition.

Every 6 months a visit to the site will be scheduled: full physical exam, bloodpressure, heart rate and weight will be assessed. Furthermore bloodsampling will be done to assess the liverfunction and the hemoglobine level, and if applicalbe a pregnancy test will be performed.

Monthly in city where patient lives: Bloodsampling to assess liverfunction and hemoglobin level. A Pregnancy test for women of childbearing potential will be performed monthly and up to 3 months after End Of Treatment..

Risks associated with participation i.e. the use of bosentan are abnormal liver function tests, and transient low hemoglobin levels. Therefore, all patients will have monthly blood samples taken for LFT monitoring. Hemoglobin will be monitored monthly up to Month 3, every 3 months thereafter up to End Of Treatment. There is a risk of bruising or pain, at the site from where the blood was drawn.

Every 6 months, patients will be seen at the outpatient*s department, for a physical examination, and to take some blood samples.
See also protocol page 12, Visit and Assessment Schedule.

There is no guarantee that patients will benefit directly from this research. Information obtained during the course of this clinical research study may contribute to a better understanding of the disease and may be useful in selecting medicines for future treatment. Regardless of any individual benefit, the knowledge gained from this study may contribute to information that would allow the use of this drug or similar drugs in later treatment for patients suffering from IPF.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Before the release of the BUILD 3 results: Patients who have experienced a BUILD 3 protocol-defined event of IPF worsening and have had at least 1 year of double-blind treatment in BUILD 3.
* If BUILD 3 shows positive results: all patients who have completed BUILD 3 have the option of entering this OL study within 2 months after the last visit in BUILD 3.
* Signed informed consent prior to initiation of any study-related procedures.
* Women of childbearing potential must have a negative serum pregnancy test and use reliable methods of contraception during study treatment and for 3 months after study treatment termination.
* Patients should have completed all the assessments from the BUILD 3 EOS visit.

Exclusion criteria

* Any major violation of protocol AC-052-321 / BUILD 3.
* Pregnancy or breast-feeding.
* AST and/or ALT > 3 times the upper limit of the normal range.
* Any known factor or disease that might interfere with treatment compliance, study conduct or interpretation of the results, such as drug or alcohol dependence or psychiatric disease.
Known hypersensitivity to bosentan or any of the excipients.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2008
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tracleer
Generic name:	bosentan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	04-07-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-04-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-001741-18-NL
CCMO	NL21448.018.08