# AN OPEN-LABEL BOSUTINIB TREATMENT EXTENSION STUDY FOR SUBJECTS WITH CHRONIC MYELOID LEUKEMIA (CML) WHO HAVE PREVIOUSLY PARTICIPATED IN BOSUTINIB STUDIES B1871006 OR B1871008

Published: 04-06-2013
Last updated: 24-04-2024

The objectives of the current study are:1. To allow long term bosutinib treatment in patients with chronic or advanced phases of Ph+ CML who received bosutinib in a previous Pfizer sponsored CML study (i.e., studies B1871006 and B1871008) and who...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Leukaemias |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON47755

**Source**
ToetsingOnline

**Brief title**
9002/0187 (B1871040)

### Condition

- Leukaemias

**Synonym**
cancer of the blood, malignant neoplasm of blood-forming tissues

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Pfizer
**Source(s) of monetary or material Support:** by the Sponsor (Pfizer Inc.)

## Intervention

**Keyword:** Leukemia, Open-label, Phase III

## Outcome measures

### Primary outcome

The objective of the study is to provide long term access to bosutinib treatment and assess long term safety, tolerability and duration of clinical benefit, without any formal hypothesis testing; therefore, there is no formal primary endpoint. In addition, data to be collected are planned to be different in the first line CP patients relative to the later line and advanced subjects.

For all patients regardless of the line of treatment:

- Long term safety of bosutinib, including type, incidence, severity, timing, seriousness and relatedness of adverse events (AEs) and laboratory abnormalities as well as reason of treatment discontinuation. A special focus will be made on diarrhea in order to satisfy the EMA post-commitment request;

- BCR -ABL mutations present at the time patients discontinue Bosutinib. (For all patients except those enrolled at sites in China)

- Overall survival (OS).

- Fulfill the EMA post-approval requirement to compare the pharmacokinetic analysis of Ctrough of bosutinib in this study to Ctrough of previous studies.

For 2nd or later line patients coming from study B1871006 who are still on

treatment with bosutinib, the following efficacy endpoints will be assessed:

- Duration of hematologic and cytogenetic responses;

- Progression-free survival;

- Time to transformation to accelerated or blast phase.

**Secondary outcome**

N/A

# Study description

**Background summary**

Bosutinib (Bosulif®) is an orally bioavailable, potent, selective, dual Src-Abl tyrosine kinase inhibitor (TKI) that has been developed as a tablet formulation for the treatment of adult patients with Philadephia positive (Ph+) chronic phase chronic myelogenous leukemia (CML) previously treated with other tyrosine kinase therapy.

CML is the fourth most commonly occurring adult leukemia and accounts for nearly 5,000 new cases annually in the United States.1 CML classically follows a tri-phasic course with most patients being diagnosed in an initial, chronic phase (CP) which eventually progresses into a more advanced accelerated phase (AP) and culminates in a blast phase (BP), a highly treatment-refractory form of acute leukemia that shows either a myeloid or a lymphoid phenotype. The transformation of CML from a fatal disease to a chronic illness that took place over the last decade has been due to the development of TKIs, small-molecule inhibitors of the kinase activity of BCR-ABL1(2).

Bosutinib is being developed for the treatment of Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) and to delay disease progression in patients with autosomal dominant polycystic kidney disease (ADPKD). Human experience with bosutinib is based on preliminary information obtained from subjects in clinical studies, including subjects with Ph+ leukemias; subjects with solid tumors, including advanced or metastatic breast cancer; subjects with autosomal dominant polycystic kidney disease; and healthy subjects. As presented in the May 2016 Bosutinib Investigator Brochure,

approximately 2478 patients, including 2141 patients with cancer, have received at least 1 dose of bosutinib in 24 clinical studies.

Bosutinib has shown an acceptable safety profile in the phase 1, phase 2, and phase 3 studies to date. In general, AEs with bosutinib have included predominantly low-grade GI toxicities and general symptoms such as fatigue and asthenia. Other frequent AEs include rash and increases in plasma levels of hepatic transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). Following continuous daily dose administration in cancer subjects, most GI AEs resolved with therapy, treatment interruption, and/or dose reduction and less frequently discontinuation of bosutinib in the case of dose-limiting toxicities (DLTs).

On 04 September 2012 bosutinib was approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy. More recently, on 17 January 2013, the CHMP issued a positive opinion recommending that bosutinib be granted conditional marketing authorization in the European Union (EU), for the treatment of adult patients with CP, AP and BP Ph+ CML previously treated with one or more tyrosine kinase inhibitor(s) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. Those approvals have been granted mainly based on the results obtained from the phase 1/2 study (B1871006) in adult patients with Ph+ leukemias who had failed prior TKI therapy, with the support of the results obtained as part of the phase 3 study (B1871008) comparing bosutinib with imatinib in newly diagnosed chronic phase Ph+ CML patients

This study is a treatment extension protocol aimed to allow long term bosutinib treatment in patients with chronic or advanced phases Ph+ CML who received bosutinib in a previous Pfizer sponsored CML study (i.e., Studies B1871006 and B1871008) and who are thought to have the potential, as judged by the investigator, to derive clinical benefit from continued treatment with bosutinib. It will also enable the collection of subsequent TKI therapy and long-term survival data for these patients, including those who have already discontinued treatment and are in the long term follow-up phase or who have completed the parent study. Finally, this study will fulfill the European Medicines Agency (EMA) post approval requirement for the collection and analysis of safety data about diarrhea incidence after switch from clinical study to commercial bosutinib formulation. Every effort should be made to enroll qualified patients into this extension study. The patients enrolled in China, due to a lack of local resources, are excluded from the requirements for pharmacokinetic (PK) and mutational analyses of the BCR ABL kinase domain testing.

**Study objective**

The objectives of the current study are:

1. To allow long term bosutinib treatment in patients with chronic or advanced phases of Ph+ CML who received bosutinib in a previous Pfizer sponsored CML study (i.e., studies B1871006 and B1871008) and who have the potential, as judged by the investigator, to derive clinical benefit from continued reatment with bosutinib;
2. To collect long term safety and efficacy data for bosutinib;
3. To assess the duration of clinical benefit for Ph+ CML patients treated with bosutinib;
4. To fulfill the EMA post-approval requirement for the collection and analysis of safety data about diarrhea incidence after switch from clinical study to commercial bosutinib formulation.

**Study design**

This is an open-label bosutinib treatment extension protocol. This protocol will be offered to those bosutinib patients who were previously enrolled in one of the two parent CML bosutinib studies (B1871006 or B1871008).

Patients to be enrolled will include those who at the time of this protocol amendment approval, are still receiving bosutinib in either one of the parent studies and are benefiting from bosutinib treatment as judged by the investigator, as well as those patients who have already discontinued bosutinib as part of the parent studies and are in follow up for survival. The former group will continue to receive bosutinib as part of the extension study; the latter group will only enter into the long term survival follow up part of the extension study.

In order to have the most accurate and unbiased statistical analysis of long term survival, the maximum number of patients who have received bosutinib should be enrolled in the extension study including those who have completed the 2 years of follow-up as planned in the study B1871006 and then discontinued the study. For this purpose every effort should be made to re-contact the patients who have completed the parent study B1871006 and offer themthe opportunity to participate in the extension study.

Each patient will remain in the extension study, either on bosutinib treatment or in long term survival follow-up phase, until the last patient has reached 10 years of follow-up, as calculated from the date of his/her first dose of bosutinib administered in the parent study. When this milestone is reached, the present study will be closed. At that time, patients still benefiting from bosutinib will switch to the most appropriate therapy available at that time.

**Intervention**

This is an open-label bosutinib treatment extension protocol. This protocol will be offered to those bosutinib patients who were previously enrolled in one

of the two parent CML bosutinib studies (B1871006 or B1871008).

In this extension study, patients who are still on treatment will receive open-label bosutinib. The commercial formulation of bosutinib will be used in this study. Dosing will be continuous and at the dose currently administered in the respective parent study. Each patient will receive daily bosutinib until such time as the last patient reaches 10 years of follow-up, unless disease progression, unacceptable toxicity, death, withdrawal of consent or Sponsor study discontinuation occurs.

**Study burden and risks**

For a list of the associated side effects and risks, please see section E9 of this form.

Benefits:
It is possible that the patient's condition or health may improve because of taking part in this study. However, there is no guarantee that the patient will benefit in any way. Information from this study may help other people in the future.

# Contacts

**Public**
Pfizer

East 42nd Street 235
New York NY 10017
US
**Scientific**
Pfizer

East 42nd Street 235
New York NY 10017
US

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Patients must meet all of the following inclusion criteria to be eligible for enrollment into the study:
1. Evidence of a personally signed and dated informed consent document indicating that the patient (or a legal representative) has been informed of all pertinent aspects of the study.
1. Previous enrollment in the bosutinib arm of one of the two Pfizer parent Studies
: B1871006 or B1871008. This includes:
a. Patients still receiving bosutinib in either Study B1871006 or Study B1871008;
b. Patients who have discontinued bosutinib but are still in the long term follow-up phase of the Study B1871006 or B1871008;
c. Patients from study B1871006 who have discontinued bosutinib and have already completed the long term follow-up period.
3. Patients who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.
4. Male and female patients of childbearing potential must agree to use a highly effective method of contraception throughout the study and for at least 30 days after the last dose of assigned treatment. A patient is of childbearing potential if, in the opinion of the investigator, he/she is biologically capable of having children and is sexually active.
In order to be considered a female of non-childbearing potential the patient must meet at least 1 of the following criteria:
a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause or a serum follicle-stimulating hormone (FSH) level confirming the postmenopausal state;
b. Have undergone a documented hysterectomy and/or bilateral oophorectomy;
c. Have medically confirmed and documented ovarian failure.
All other female subjects (including female subjects with tubal ligations) are considered to be of childbearing potential.

## Exclusion criteria

Patients presenting with any of the following will not be included in the study:

1. Participation in other studies involving investigational drug(s) (Phases 1-4) while patient in the active treatment phase of the current study.
2. Patients who are investigational site staff members directly involved in the conduct of the trial and their family members, site staff members otherwise supervised by the Investigator, or patients who are Pfizer employees directly involved in the conduct of the trial.
3. Other severe acute or chronic medical or psychiatric condition including recent (within the past year) or active suicidal ideation or behavior or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patients inappropriate for entry into this study.
4. Pregnant female subjects; breastfeeding female subjects; fertile male subjects and female subjects of childbearing potential who are unwilling or unable to use 2 highly effective methods of contraception as outlined in this protocol for the duration of the study and for at least 28 days after the last dose of investigational product

# Study design

## Design

| | |
|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 12-02-2014 |
| Enrollment: | 14 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Bosulif |

| | |
|---|---|
| Generic name: | Bosutinib |
| Registration: | Yes - NL intended use |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 04-06-2013 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 29-07-2013 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 08-04-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-04-2014 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 22-04-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 05-01-2017 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-03-2017 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 17-05-2017 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-06-2017 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-04-2018 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 31-08-2018 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 15-11-2018 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 27-03-2019 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 12-07-2019 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

| | |
|---|---|
| Approved WMO Date: | 29-07-2019 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# 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 | EUCTR2013-000691-15-NL |
| CCMO | NL44626.056.13 |