BI 811283 in Combination With Cytarabine in Previously Untreated AML Ineligible for Intensive Treatment

This study is ongoing, but not recruiting participants.

First Received on March 4, 2008. Last Updated on June 28, 2012

Sponsor: Boehringer Ingelheim Pharmaceuticals

Information provided by (Responsible Party): Boehringer Ingelheim Pharmaceuticals

ClinicalTrials.gov Identifier: NCT00632749

Purpose

The trial will be performed in two parts, a phase I part and a phase IIa part. In the phase I part of the trial, two schedules of BI 811283 in combination with LD-Ara-C will be investigated. In the phase I part, the dose of BI 811283 will be escalated to determine the maximum tolerated dose (MTD) of the two dosing schedules of BI 811283 in combination with LD-Ara-C.

In the phase IIa part, the two combination schedules of BI 811283 at MTD with LD-Ara-C and one LD-Ara-C monotherapy schedule will be investigated to determine the efficacy of the two combination schedules in comparison to LD-Ara-C monotherapy in previously untreated AML patients ineligible for intensive treatment.

Condition | Intervention | Phase
---|---|---
Leukemia, Myeloid, Acute | Drug: BI 811285 (d1 and 15)  
Drug: Cytarabine  
Drug: BI 811283 (d1) | Phase 2

Study Type: Interventional

Study Design: Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Intervention Model: Parallel Assignment

Masking: Open Label

Primary Purpose: Treatment

Official Title: An Open Phase I/IIa Trial to Investigate the Maximum Tolerated Dose, Safety, Efficacy and Pharmacokinetics of BI 811283 in Combination With Cytarabine in Patients With Previously Untreated Acute Myeloid Leukaemia Ineligible for Intensive Treatment

Resource links provided by NLM:

- Genetics Home Reference related topics: familial acute myeloid leukemia with mutated CEBPA
- MedlinePlus related topics: Acute Myeloid Leukemia Leukemia
- Drug Information available for: Cytarabine
- U.S. FDA Resources

Further study details as provided by Boehringer Ingelheim Pharmaceuticals:

Primary Outcome Measures:
Phase I part: maximum tolerated dose (MTD) of two schedules of BI 811283 in combination with low-dose cytarabine (LD-Ara-C). [Time Frame: 4 weeks]  
[Designated as safety issue: No]

Phase IIa part: Response (complete remission, CR; complete remission with incomplete blood count recovery, CRi) [Time Frame: minimum 4 weeks, maximum n/a]  
[Designated as safety issue: No]

Secondary Outcome Measures:

- Pharmacokinetics of BI 811283 BS in the presence of cytarabine [Time Frame: during the first 4-week treatment cycle]  
  [Designated as safety issue: No]
- Incidence and intensity of adverse events graded according to CTCAE (version 3.0) [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Incidence of dose limiting toxicity. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Partial remission. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Event free survival. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Relapse free survival. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Remission duration. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Overall Survival. [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Supportive care requirements (blood products, antibiotic usage, hospitalisation). [Time Frame: minimum 4 weeks, maximum n/a]  
  [Designated as safety issue: No]
- Pharmacodynamic monitoring: drug effect on leukaemia cells (e.g. polyploidy, histone H3 phosphorylation, morphologic changes). [Time Frame: during the first 4-week treatment cycle]  
  [Designated as safety issue: No]
- Pharmacokinetics of cytarabine after a single dose and at steady state when given alone and in combination with BI 811283 BS (free base of BI 811283) [Time Frame: during the first 4-week treatment cycle]  
  [Designated as safety issue: No]

Estimated Enrollment: 169  
Study Start Date: May 2008  
Estimated Primary Completion Date: December 2012 (Final data collection date for primary outcome measure)

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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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<td><strong>Experimental: Schedule A</strong></td>
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BI 811283 on days 1 and 15 in combination with LD-Ara-C  
Drug: BI 811285 (d 1 and 15)  
BI 811283 (24 hours i.v.c.i.) on day 1 and 15 of a 4-week treatment cycle  
Drug: Cytarabine  
Cytarabine 2 x 20 mg/d s.c. on days 1-10 of a 4-week treatment cycle |
| **Experimental: Schedule B** |  
BI 811283 on day 1 only in combination with LD-Ara-C  
Drug: Cytarabine  
Cytarabine 2 x 20 mg/d s.c. on days 1-10 of a 4-week treatment cycle  
Drug: BI 811283 (d1)  
BI 811283 (24 hours i.v.c.i.) on day 1 of a 4-week treatment cycle |
| **Active Comparator: Schedule C** |  
Control arm in phase IIa: LD-Ara-C (2x20 mg/d on days 1-10)  
Drug: Cytarabine  
Cytarabine 2 x 20 mg/d s.c. on days 1-10 of a 4-week treatment cycle |

**Eligibility**

Ages Eligible for Study: 18 Years and older  
Genders Eligible for Study: Both  
Accepts Healthy Volunteers: No
Criteria

Inclusion criteria:

- Male or female adult with previously untreated acute myeloid leukaemia (AML)
- Confirmed diagnosis of AML according to the WHO definition (except for acute promyelocytic leukaemia, APL)
- Patient is considered ineligible for intensive treatment
- Patient is eligible for low-dose cytarabine (LD-Ara-C) treatment
- Life expectancy > 3 months
- Eastern co-operative oncology group (ECOG, R01-0787) performance score <=2 at screening
- Signed written informed consent consistent with international conference on harmonisation good clinical practice (ICH-GCP) and local legislation

Exclusion criteria:

- Patient with APL (AML subtype M3 according to the French-American-British (FAB) classification).
- Relapsed or treatment refractory AML.
- Hypersensitivity to one of the trial drugs or the excipients.
- Other malignancy requiring treatment.
- Known central nervous system involvement.
- Aspartate amino transferase (AST) or alanine amino transferase (ALT) greater than 2.5 times the upper limit of normal (ULN).
- INR > 1.5 x ULN for subjects not on therapeutic vitamin K antagonists (phenprocoumon, warfarin).
- Bilirubin greater than 1.5 mg/dl.
- Serum creatinine greater than 2.0 mg/dl.
- LVEF (Left ventricular ejection fraction) < 50% in echocardiography or clinical congestive heart failure New York Heart Association (NYHA) grade III or IV.
- Concomitant intercurrent illness, which would compromise the evaluation of efficacy or safety of the trial drug, e.g. active severe infection, unstable angina pectoris or cardiac arrhythmia.
- Psychiatric illness or social situation that would limit compliance with trial requirements.
- Contraindication for cytarabine treatment according to the summary of product characteristics (SPC).
- Patients who are sexually active and unwilling to use a medically acceptable method of contraception during the trial (hormonal contraception, intrauterine device, condom with spermicide, etc.).
- Pregnant or nursing female patients.
- Patient unable to comply with the protocol.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00632749

Locations

Germany

1247.3.49007 Boehringer Ingelheim Investigational Site
Berlin, Germany

1247.3.49005 Boehringer Ingelheim Investigational Site
Frankfurt/Main, Germany

1247.3.49004 Boehringer Ingelheim Investigational Site
Freiburg, Germany

1247.3.49006 Boehringer Ingelheim Investigational Site
Hamburg, Germany

1247.3.49003 Boehringer Ingelheim Investigational Site
Heidelberg, Germany

1247.3.49002 Boehringer Ingelheim Investigational Site

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