BL-8040 Addition to Consolidation Therapy in AML Patients (BLAST)

This study is currently recruiting participants. (see Contacts and Locations)

Verified September 2015 by Martin-Luther-Universität Halle-Wittenberg

Sponsor:
Dr. Petra Tschanter

Collaborator:
BioLineRx, Ltd.

Information provided by (Responsible Party):
Dr. Petra Tschanter, Martin-Luther-Universität Halle-Wittenberg

ClinicalTrials.gov Identifier:
NCT02502968

First received: July 6, 2015
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History of Changes

Purpose

This study evaluates the addition of BL-8040 to the standard consolidation therapy with cytarabine in the treatment of acute myeloid leukemia (AML) in adults. Half of participants will receive BL-8040 and cytarabine in combination, while the other half will receive placebo and cytarabine.

Condition	Intervention	Phase
Acute Myeloid Leukemia	Drug: Cytarabine Drug: BL-8040 Drug: Placebo (for BL-8040)	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: **A Double- Blind, Placebo Controlled, Randomized, Multicenter, Phase II Study to Assess the Efficacy of BL-8040 Addition to Consolidation Therapy in AML Patients**

Resource links provided by NLM:

Genetics Home Reference related topics: core binding factor acute myeloid leukemia cytogenetically normal acute myeloid leukemia familial acute myeloid leukemia with mutated CEBPA

MedlinePlus related topics: Leukemia

Drug Information available for: Cytarabine

Genetic and Rare Diseases Information Center resources: Myeloid Leukemia Acute Myeloid Leukemia Acute Non Lymphoblastic Leukemia

U.S. FDA Resources

Further study details as provided by Martin-Luther-Universität Halle-Wittenberg:

Primary Outcome Measures:

- Relapse Free Survival time [Time Frame: 18 months] [Designated as safety issue: No]

  Relapse is defined as recurrence of leukemic blasts (more than 5%) in the bone marrow after confirmed complete remission

Secondary Outcome Measures:

- Overall Survival [Time Frame: 18 months] [Designated as safety issue: No]
- Time to relapse [Time Frame: 18 months] [Designated as safety issue: No]

- Relapse free survival [Time Frame: 6, 9, 12 and 18 months] [Designated as safety issue: No]
- Relapse [Time Frame: 6, 9, 12 and 18 months] [Designated as safety issue: No]

  Defined as recurrence of leukemic blasts (more than 5%) in the bone marrow after confirmed complete remission

- Minimal residual disease [Time Frame: 6, 9, 12 and 18 months] [Designated as safety issue: No]

  Immunophenotypic characterization of human bone marrow cells will be done to determine MRD

- Toxicity [Time Frame: enitire study course until 18 months] [Designated as safety issue: Yes]

  Number and CTC grade of all adverse events related to study treatment analyzed in an descriptive way

Estimated Enrollment: 194
Study Start Date: September 2015
Estimated Primary Completion Date: July 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Cytarabine & BL8040 Subjects ≥60 years: cytarabine 1g/m2 intravenously twice a day over 3 hours on day 1, 3 and 5 on 2 cycles and BL-8040 (1.25 mg/kg) subcutaneously on days 1 to 5 of each cycle Subjects <60 years: cytarabine 3g/m2 intravenously twice a day over 3 hours on day 1, 3 and 5 on 3 cycles and BL-8040 (1.25 mg/kg) subcutaneously on days 1 to 5 of each cycle	Drug: Cytarabine Drug: BL-8040
Active Comparator: Cytarabine & Placebo Subjects ≥60 years: cytarabine 1g/m2 intravenously twice a day over 3 hours on day 1, 3 and 5 on 2 cycles and Placebo (for BL-8040) subcutaneously on days 1 to 5 of each cycle Subjects <60 years: cytarabine 3g/m2 intravenously twice a day over 3 hours on day 1, 3 and 5 on 3 cycles and Placebo (for BL-8040) subcutaneously on days 1 to 5 of each cycle	Drug: Cytarabine Drug: Placebo (for BL-8040) Powder for solution for injection manufactured to mimic BL-8040

Detailed Description:
The majority of AML patients in first complete Remission (CR) do relapse despite the current consolidation therapy. Leukemic stem cells that are dormant in the bone marrow are presumed to be a major reason for AML relapse. Allogenic stem cell transplantation is an option only for a minority of AML patients in 1st CR. BL-8040 is a novel CXCR4 inhibitor that has a dual mechanism of action: inducing mobilization of leukemic blasts from the bone marrow which enhances cytotoxic effects of chemotherapy and has direct antileukemic, pro-apoptotic properties. The treatment with BL-8040 in combination with consolidation therapy (standard consolidation with high-dose cytarabine) should improve the efficacy of the consolidation therapy resulting in longer lasting remissions.

Eligibility

Ages Eligible for Study: 18 Years to 75 Years (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Histologically or morphologically confirmed diagnosis of AML except for AML M3 (acute promyelocytic leukemia)
- AML who achieved complete remission (CR), including CRi and CRp after a maximum number of 2 cycles of induction chemotherapy.
- AML subjects younger than 60 years at the time of diagnosis with intermediate or high-risk cytogenetics
- ECOG performance status ≤2
- Laboratory values as follows (at time of randomization): WBC < 30.000/µl and > 1000/µl, Platelets count > 70.000/µl, Creatinine < 1.0 mg/dl. If creatinine is between 1.0mg/dl and 1.3mg/dl, creatinine clearance should be > 30ml/min as calculated using the Cockroft-Gault formula
- Women of child-bearing potential must practice an acceptable method of birth control until 6 month after the last dose of treatment. Female subjects who are lactating must discontinue nursing prior to the first dose of study drug and should refrain from nursing throughout the treatment period and for 14 days following the last dose of study drug.
- Male with a female partner of childbearing potential using a barrier method of contraception
- Written informed consent
- Subject is able and willing to comply with the requirements of the protocol.

Exclusion Criteria:

- Relapsed or refractory AML
- Start of induction cycle > 90 days before randomization.
- Subjects who have received >2 cycles of induction chemotherapy for AML therapy.
- Subjects younger than 60 years at the time of diagnosis with favorable cytogenetics (t(8;21) or inv(16) or t(16;16) or t(15;17)) or the confirmed presence of the resulting fusion protein AML1-ETO, CBFB-MYH11 or PML-RARA.
- Subjects for which allogeneic HSCT is planned in CR1.
- Planned further maintenance therapy after the end of the protocol defined consolidation therapy.

- Known allergic or hypersensitivity to BL8040- or cytarabine or to any of the test compounds, materials
- Use of investigational device or agents within 2 weeks or less than 5 half lifes for each investigational product /device at the time of enrolment. Registry studies are permissible.
- Abnormal liver function tests: Serum AST/ GOT or ALT/ GPT > 3x upper limit of normal (ULN), Serum bilirubin: Total bilirubin > 2.0mg/dl, conjugated bilirubin > 0.8mg/dl
- O2 saturation < 92% (on room air)
- Concurrent, uncontrolled medical condition, laboratory abnormality, or psychiatric illness which could place the subject at unacceptable risk
- Another malignancy within 3 years of enrolment, except in situ malignancy, or low-risk prostate, skin or cervical cancer after curative therapy. History of other cancer that according to the Investigator might confound the assessment of the endpoints of the study.
- A co-morbid condition which, in the view of the Investigators, renders the subject at high risk from treatment complications.
- History of any or more of the following cardiovascular conditions: cardiac angioplasty (within 6 months) or stenting (within 6 months) and/or myocardial infarction (MI) (within 6 months) or cerebro-vascular event within the past 6 months, unstable angina, vascular disease, class III or IV, congestive heart failure (as defined by the New York Heart Association (NYHA))
- Known central nervous system disease that may jeopardize the subject's study participation according to the investigator judgement
- Active, uncontrolled infection.
- Prior clinically significant grade 3-4 non-hematological toxicity to high-dose cytarabine or grade ≥ 2 of neurological toxicity
- Positive serology for HIV, active Hepatitis C and Hepatitis B (HBsAG pos.) at baseline
- Left ventricular ejection fraction (LVEF) of <40% by multiple gated acquisition (MUGA) scan or echocardiogram (ECHO) at baseline
- Subjects with psychological, psychiatric, neurological, familial, sociological, or geographical conditions that do not permit compliance with the protocol

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02502968

Contacts

Contact: Simone Kowoll, MSc +49-345-5574908 blast@kks-halle.de

Locations

Germany

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Sponsors and Collaborators

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Investigators

Principal Investigator: Carsten Müller-Tidow, MD University Hospital Halle, Germany

More Information

Responsible Party:	Dr. Petra Tschanter, Dr. med., Martin-Luther-Universität Halle-Wittenberg
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Additional relevant MeSH terms:

Leukemia, Myeloid, Acute
Leukemia, Myeloid
Leukemia
Neoplasms by Histologic Type
Neoplasms
Cytarabine
Antimetabolites, Antineoplastic
Antimetabolites

Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents
Antiviral Agents
Anti-Infective Agents
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs

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