Study of Palbociclib in MLL-rearranged Acute Leukemias

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

Verified July 2016 by University of Ulm

Sponsor:
University of Ulm

Collaborators:
Pfizer
Nationales Centrum für Tumorerkrankungen Heidelberg

Information provided by (Responsible Party):
Prof. Dr. Richard Schlenk, University of Ulm

ClinicalTrials.gov Identifier:
NCT02310243

First received: December 1, 2014
Last updated: July 22, 2016
Last verified: July 2016
History of Changes

Purpose

Diagnosis: Acute myeloid leukemia; Acute lymphoblastic leukemia Age ≥ 18 years, no upper age limit Study drug: Palbociclib Phase Ib/IIa, open-label

- Phase Ib: Based on previous experience with 125 mg palbociclib once daily for 21 days followed by 7 days of rest in patients with breast cancer, liposarcoma, non-small cell lung cancer, hepatocellular carcinoma, ovarian cancer, mantle-cell lymphoma, and glioblastoma, this regimen will be chosen for the first dose to be evaluated in the phase Ib. Based on a 3 + 3 modified Fibonacci design, the tolerable dose of palbociclib for the phase IIa is defined.
- Phase IIa: single-agent palbociclib using the tolerable dose defined in the phase Ib part of the study is administered once daily for 21 days followed by 7 days of rest. Based on the optimal two-stage design of Simon, 21 patients are treated in the first stage. If results are positive, 29 additional patients will be recruited into the second stage of the study. An efficacy of the investigational therapy will be rejected in the first stage of 21 treated patients if two or less patients achieve complete remission (CR), CR with incomplete blood count recovery (CRi), partial remission (PR), or anti-leukemic effect (ALE). If three or more patients achieve CR, CRi, PR, or ALE during this first stage, the trial is intended to be continued in the second stage with a total sample size of 50 patients.

Start of recruitment: Febuary 2015 End of recruitment: Febuary 2017 End of study (last patient out): Febuary 2018 The treatment duration of an individual patient is estimated to be 2-6 months, but may be unlimited in patients with sustained response ("case-by-case decision").

Observation time per patient after entry into the study (incl. treatment) is at least 12 months.

Condition	Intervention	Phase
Acute Myeloid Leukemia Acute Lymphoblastic Leukemia	Drug: Palbociclib	Phase 1 Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Phase Ib/IIa Study of Palbociclib in MLL-rearranged Acute Leukemias **AMLSG 23-14**/Palbo-AL-1

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: Acute Myeloid Leukemia Chronic Lymphocytic Leukemia Leukemia

Drug Information available for: Palbociclib

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

U.S. FDA Resources

Further study details as provided by University of Ulm:

Primary Outcome Measures:

- Number of Participants with Adverse Events [Time Frame: 12 months] [Designated as safety issue: Yes]

  Safety assessments

- Maximum tolerated dose of palbociclib [Time Frame: 12 months] [Designated as safety issue: Yes]
- overall response rate [Time Frame: 12 months] [Designated as safety issue: No]

Secondary Outcome Measures:

- Relapse-free survival [Time Frame: three years] [Designated as safety issue: No]
- Overall survival [Time Frame: three years] [Designated as safety issue: No]
- Evaluation of target (CDK6) inhibition by palbociclib [Time Frame: three years] [Designated as safety issue: No]
- Assessment of Quality of life [Time Frame: 6 months] [Designated as safety issue: No]

Estimated Enrollment:	50
Study Start Date:	July 2015
Estimated Study Completion Date:	July 2018
Estimated Primary Completion Date:	July 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Palbociclib Phase1b: 125 mg palbociclib once daily for 21 days followed by 7 days of rest; this regimen will be chosen for the first dose to be evaluated. phase IIa: single-agent palbociclib using the tolerable dose defined in the phase Ib part of the study is administered once daily for 21 days followed by 7 days of rest.	Drug: Palbociclib oral, once daily (125mg, 100mg or 75mg) for 21 days Other Name: PD-0332991-00

Eligibility

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

Criteria

Inclusion Criteria:

- Patients with confirmed diagnosis of acute leukemia with MLL rearrangement according to the 2008 WHO Classification
- Patients with MLL-rearranged leukemia who are refractory to standard induction therapy and not immediate candidates for allogeneic HSCT (bridge to transplant is allowed)
- Patients with MLL-rearranged leukemia who relapsed after standard first-line treatment and are not immediate candidates for allogeneic HSCT (bridge to transplant is allowed)
- Patients with newly diagnosed MLL-rearranged leukemia who are not eligible for intensive first-line therapy
- Genetic assessment in the AMLSG central laboratory
- Age ≥ 18 years, no upper age limit
- WHO performance status of ≤ 2
- No prior chemotherapy two weeks before study entry except hydroxyurea to control hyperleukocytosis
- Non-pregnant and non-nursing. Women of child-bearing potential must have a negative serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL within 72 hours prior to registration (WOCBP is defined as a sexually active mature woman who has not undergone a hysterectomy or who has had menses at any time in the preceding 24 months).
- Female patients in the reproductive age and male patients must agree to avoid getting pregnant or to father a child while on therapy and for three months after the last dose of therapy.
- Women of child-bearing potential must either commit to continued abstinence from heterosexual intercourse or begin one acceptable method of birth control (IUD, tubal ligation, or partner's vasectomy). Hormonal contraception is an inadequate method of birth control.
- Men must agree not to father a child and must use a latex condom during any sexual contact with WOCBP while receiving therapy and for three months after therapy is stopped, even if they have undergone successful vasectomy.
- Signed written informed consent

Exclusion Criteria:

- Prior treatment with palbociclib
- Performance status > 2 according to WHO criteria
- Organ insufficiency: creatinine > 1.5 x upper normal serum level; bilirubin, AST, or AP > 2.5 x upper normal serum level; heart failure NYHA III/IV; uncontrolled hypertension; unstable angina; serious cardiac arrhythmia; severe obstructive or restrictive ventilation disorder
- Uncontrolled infection

- Patients with a "currently active" second malignancy other than non-melanoma skin cancer. Patients are not considered to have a "currently active" malignancy if they have completed therapy and are considered by their physician to be at less than 30% risk of relapse within one year.
- Severe neurologic or psychiatric disorder interfering with ability of giving informed consent
- Known or suspected active alcohol or drug abuse
- Known positivity for HIV, active HAV, HBV, or HCV infection
- Bleeding disorder unrelated to leukemia
- Uncontrolled CNS involvement (treatment for CNS-involvement prior to inclusion is allowed)
- QTc > 470 msec (based on the mean value of triplicate ECGs), family or personal history of long or short QT syndrome, Brugada syndrome, or known history of QTc prolongation or Torsade de Pointes
- Uncontrolled electrolyte disorders that can aggravate the effects of a QTc-prolonging drug (e.g., hypocalcemia, hypokalemia, hypomagnesemia)
- No consent for registration, storage, and processing of individual disease characteristics, information on the course of the disease, and information obtained from the family physician and/or other physicians involved in the treatment of the patient about study participation
- No consent for biobanking

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: NCT02310243

Locations

Germany

Klinikum Augsburg — **Recruiting**
Augsburg, Germany, 86156
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Helios Klinikum Bad Saarow — **Recruiting**
Bad Saarow, Germany, 15526
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Charité Campus Benjamin Franklin — **Recruiting**
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Vivantes Klinikum Neukölln — **Recruiting**
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Charité Campus Virchow-Klinikum — **Recruiting**
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Universitätsklinikum Bonn — **Recruiting**
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Kliniken Essen Süd, Ev. Krankenhaus Essen-Werden gGmbH — **Recruiting**
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Sponsors and Collaborators

University of Ulm

Pfizer

Nationales Centrum für Tumorerkrankungen Heidelberg

More Information

Responsible Party:	Prof. Dr. Richard Schlenk, Prof. Dr. med., University of Ulm
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Study First Received:	December 1, 2014
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Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

Keywords provided by University of Ulm:
Acute myeloid leukemia
Acute lymphoblastic leukemia
MLL-rearranged leukemia
Palbociclib (PD-0332991-0054)

Additional relevant MeSH terms:

Leukemia	Lymphatic Diseases
Leukemia, Myeloid	Immunoproliferative Disorders
Leukemia, Myeloid, Acute	Immune System Diseases
Precursor Cell Lymphoblastic Leukemia-Lymphoma	Palbociclib
Leukemia, Lymphoid	Antineoplastic Agents
Neoplasms by Histologic Type	Protein Kinase Inhibitors
Neoplasms	Enzyme Inhibitors
Lymphoproliferative Disorders	Molecular Mechanisms of Pharmacological Action

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