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Protocol in Acute Myeloid Leukemia With FLT3-ITD

This study is currently recruiting participants.

Verified July 2012 by University of Ulm

Sponsor:
University of Ulm

Collaborator:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT01477606

First received: November 17, 2011
Last updated: July 10, 2012
Last verified: July 2012
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

This is a phase II, single-arm, open-label, multi-center study in adult patients with Acute Myeloid Leukemia (AML) and FLT3-ITD as defined in inclusion/exclusion criteria.

The primary efficacy object is to evaluate the impact of midostaurin given in combination with intensive induction, consolidation including allogeneic hematopoietic stem cell transplantation and single agent maintenance therapy on event-free survival (EFS) in adult patients with AML exhibiting a FLT3-ITD.

Sample size: 142 patients

The treatment duration of an individual patient is between 18 and 24 months. Duration of the study for an individual patient including treatment (induction, consolidation [chemotherapy or allogeneic SCT], maintenance and follow-up period: 48 months

Condition	Intervention	Phase
Acute Myeloid Leukemia	Drug: Midostaurin Drug: Cytarabine Drug: Daunorubicin	Phase 2

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

Official Title: Phase-II Study Evaluating Midostaurin in Induction, Consolidation and Maintenance Therapy Also After Allogeneic Blood Stem Cell Transplantation in Patients With Newly Diagnosed Acute Myeloid Leukemia Exhibiting a FLT3 Internal Tandem Duplication

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 Daunorubicin Daunorubicin hydrochloride

U.S. FDA Resources

Further study details as provided by University of Ulm:

Primary Outcome Measures:

- Event-free Survival [Time Frame: Two years] [Designated as safety issue: Yes]

  To evaluate the impact of midostaurin given in combination with intensive induction, consolidation including allogeneic hematopoietic stem cell transplantation and single agent maintenance therapy on event-free survival (EFS) in adult patients with AML exhibiting a FLT3-ITD.

Secondary Outcome Measures:

- Rate of complete remission (CR) [Time Frame: Two months] [Designated as safety issue: No]

- Relapse-free survival [Time Frame: four years] [Designated as safety issue: No]
- overall survival [Time Frame: four years] [Designated as safety issue: Yes]
- Cumulative incidence of relapse [Time Frame: four years] [Designated as safety issue: No]
- cumulative incidence of death in CR [Time Frame: four years] [Designated as safety issue: Yes]
- Target (FLT3) inhibition by measuring the FLT3 plasma inhibitory activity [Time Frame: four years] [Designated as safety issue: No]

  Evaluation of target (FLT3) inhibition by continuous dosing of midostaurin

- Quality of life [Time Frame: 5 years] [Designated as safety issue: No]

  Quality of life assessed by the EORTC Quality of Life Core Questionnaire (QLQ-C30), supplemented by information on self-assessed concomitant diseases, late treatment effects, and demographics initially, in first CR, after one year,3 and 5 years after initial diagnosis.

- Rate of early deaths and hypoplastic deaths (ED/HD) [Time Frame: two months] [Designated as safety issue: Yes]
- Death in CR [Time Frame: four years] [Designated as safety issue: Yes]
- Toxicities [Time Frame: between 18 and 24 months] [Designated as safety issue: Yes]

  Type, frequency, severity (graded using the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] Version 3.0), timing and relatedness of hematological and non-hematological toxicities observed during the different treatment cycles

Estimated Enrollment:	142
Study Start Date:	May 2012
Estimated Study Completion Date:	September 2017
Estimated Primary Completion Date:	September 2015 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Midostaurin	Drug: Midostaurin Induction therapy: 50 mg, oral, twice daily, starting on day 8, thereafter continuous dosing until 48h before start of subsequent chemotherapy cycle. Consolidation therapy: 50 mg, oral twice daily, starting on day 6, thereafter continuous dosing until 48h before start of conditioning therapy for allogeneic HSCT or 48h before start of subsequent consolidation chemotherapy. Maintenance therapy: 50 mg oral twice daily over one year. Other Name: PKC412 Drug: Cytarabine Induction therapy: 200 mg/m2/day by continuous i.v. infusion on days 1-7 (total dose 1400 mg/m²) Consolidation therapy: Younger adult patients (18 to 65 yrs): 3 g/m2 by i.v infusion over 3 hours every 12 hours on days 1, 3, and 5 (total dose 18 g/m2). Older patients (>65 yrs): 1 g/m2 by i.v. infusion over 3 hours every 12 hours on days 1, 3, and 5 (total dose 6 g/m2). Drug: Daunorubicin Induction therapy: 60 mg/m², by 1-hour i.v. infusion, day 1-3 (total dose 180 mg/m²)

Eligibility

Ages Eligible for Study:	18 Years to 70 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Patients with suspected diagnosis of AML or related precursor neoplasm, or acute leukemia of ambiguous lineage (classified according to the World Health Organization (WHO) 2008 classification)
- Presence of FLT3-ITD assessed in the central AMLSG reference laboratories
- Patients considered eligible for intensive chemotherapy
- WHO performance status of ≤ 2
- Age ≥ 18 years and ≤ 70 years
- No prior chemotherapy for leukemia except hydroxyurea to control hyperleukocytosis (≤ 7 days)
- Non-pregnant and non-nursing. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test within a sensitivity of at least 25 mIU/mL within 72 hours prior to registration ("Women of childbearing potential" 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 consecutive 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 3 month after the last dose of chemotherapy
- 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 use a latex condom during any sexual contact with women of childbearing potential, even if they have undergone a successful vasectomy (while on therapy and for 3 month after the last dose of chemotherapy)
- Signed written informed consent.

Exclusion Criteria:

•AML with the following recurrent genetic abnormalities (according to WHO 2008): AML with t(8;21)(q22;q22); RUNX1-RUNX1T1 AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11 AML with t(15;17)(q22;q12); PML-RARA (or variant translocations with other RARA gene fusions)

- Performance status WHO >2
- Patients with ejection fraction < 50% by MUGA or ECHO scan within 14 days of day 1
- Organ insufficiency (creatinine >1.5x upper normal serum level; bilirubin, AST or ALP >2.5x upper normal serum level, not attributable to AML; heart failure NYHA III/IV; severe obstructive or restrictive ventilation disorder)
- Uncontrolled infection
- Severe neurological or psychiatric disorder interfering with ability of giving an informed consent
- Patients with a "currently active" second malignancy other than non-melanoma skin cancers. 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
- Known positive for HIV; active HBV, HCV, or Hepatitis A infection
- Bleeding disorder independent of leukemia
- No consent for registration, storage and processing of the individual disease-characteristics and course as well as information of the family physician and/or other physicians involved in the treatment of the patient about study participation.
- No consent for biobanking.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01477606

Contacts

Contact: Sabine Kayser, MD +49-731-500-45714 sabine.kayser@uniklinik-ulm.de

Show 50 Study Locations

Sponsors and Collaborators

University of Ulm

Novartis Pharmaceuticals

Investigators

Principal Investigator: Richard F Schlenk, MD University Hospital of Ulm

More Information

No publications provided

Responsible Party:	Dr. Richard Schlenk, PD Dr. Richard Schlenk, University of Ulm
ClinicalTrials.gov Identifier:	NCT01477606 History of Changes
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Study First Received:	November 17, 2011
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Keywords provided by University of Ulm:
Acute myeloid leukemia
FLT3-ITD
midostaurin (PKC412)

Additional relevant MeSH terms:

Leukemia	Molecular Mechanisms of Pharmacological Action
Leukemia, Myeloid, Acute	Pharmacologic Actions
Leukemia, Myeloid	Antineoplastic Agents
Neoplasms by Histologic Type	Therapeutic Uses
Neoplasms	Antiviral Agents
Cytarabine	Anti-Infective Agents
4'-N-benzoylstaurosporine	Immunosuppressive Agents

Daunorubicin
Staurosporine
Antimetabolites, Antineoplastic
Antimetabolites
Immunologic Factors
Physiological Effects of Drugs
Antibiotics, Antineoplastic
Enzyme Inhibitors

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