Randomized Phase III Study of Intensive Chemotherapy With or Without Dasatinib (Sprycel™)

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

Verified December 2015 by University of Ulm

Sponsor:
University of Ulm

Information provided by (Responsible Party):
Prof. Dr. Hartmut Doehner, University of Ulm

ClinicalTrials.gov Identifier:
NCT02013648

First received: December 11, 2013
Last updated: December 1, 2015
Last verified: December 2015
History of Changes

Purpose

This is a randomized phase III open-label, multicenter trial evaluating standard induction therapy (daunorubicin [DNR] and cytarabine [Ara-C]) and consolidation therapy (high-dose cytarabine [HDAC]) with or without dasatinib in adult patients with newly diagnosed CBF-AML

Condition	Intervention	Phase
Acute Myeloid Leukemia (AML)	Drug: Dasatinib Drug: Cytarabine Drug: Daunorubicin	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Randomized Phase III Study of Intensive Chemotherapy With or Without Dasatinib (Sprycel™) in Adult Patients With Newly Diagnosed Core-Binding Factor Acute Myeloid Leukemia (CBF-AML)

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 Leukemia

Drug Information available for: Cytarabine Daunorubicin Daunorubicin hydrochloride Dasatinib Daunorubicin citrate

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

U.S. FDA Resources

Further study details as provided by University of Ulm:

Primary Outcome Measures:

- Event-free Survival [Time Frame: 4 years] [Designated as safety issue: No]

  To assess event-free survival (EFS) after intensive induction (daunorubicin and cytarabine) and consolidation (high-dose cytarabine) chemotherapy with or without dasatinib in patients with CBF-AML

Secondary Outcome Measures:

- Cumulative incidence of relapse (CIR) [Time Frame: 4 years] [Designated as safety issue: No]
- Cumulative incidence of death (CID) [Time Frame: 4 years] [Designated as safety issue: Yes]
- overall survival [Time Frame: 4 years] [Designated as safety issue: No]
- relapse-free survival [Time Frame: 4 years] [Designated as safety issue: No]
- PIA analysis [Time Frame: 4 years] [Designated as safety issue: No]

  Pharmacodynamic inhibition of KIT as assessed by the KIT plasma inhibitory assay (PIA)

- toxicity [Time Frame: 7 months (standard arm) / 19 months (investigational arm)] [Designated as safety issue: Yes]

  Type, frequency, severity (graded using the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] version 4.03), timing and relatedness of non-hematologic toxicity observed during different treatment cycles.

Estimated Enrollment:	277
Study Start Date:	July 2014
Estimated Study Completion Date:	July 2022
Estimated Primary Completion Date:	December 2020 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: Standard arm Induction therapy: Patients will receive induction therapy (one or two cycles) with daunorubicin 60 mg/m2/day administered on days 1-3 and cytarabine 200 mg/m2/day administered by continuous IV infusion on days 1-7. No dose reduction is planned in elderly (>60 years) patients. Optional second induction cycle: Patients achieving PR only at the end of cycle 1 will receive a second induction cycle with daunorubicin 50 mg/m2/day administered on days 1-3 and cytarabine 200 mg/m2/day administered by cont. IV infusion daily on days 1-5. Consolidation therapy: Patients will receive 4 cycles of consolidation therapy. Consolidation therapy consists of high-dose cytarabine 3 g/m2 (>60 years: 1 g/m2) q12h, days 1-3 administered intravenously over three hours. Follow-up period: There is no maintenance therapy in the standard arm. Patients will be closely followed, in particular for molecular disease persistence or molecular relapse.	Drug: Cytarabine Other Name: ARA-cell Drug: Daunorubicin Other Name: Daunoblastin
Experimental: Investigational arm Induction therapy: Patients will receive induction therapy (one or two cycles) with daunorubicin 60 mg/m2/day administered on days 1-3 and cytarabine 200 mg/m2/day administered by continuous IV infusion on days 1-7. Patients will receive dasatinib 100 mg once daily (QD) on days 8-21. Opt. 2nd induction cycle: Patients achieving PR only at the end of cycle 1 will receive a 2nd induction cycle with daunorubicin 50 mg/m2/day administered on days 1-3 and cytarabine 200 mg/m2/day administered by cont. IV infusion on days 1-5. Patients will receive dasatinib 100 mg QD on days 6-21. Consolidation therapy: Patients will receive 4 consolidation cycles. Treatment consists of high-dose cytarabine 3 g/m2 (>60 years: 1 g/m2) q12h, days 1-3 administered IV over 3 hours. Patients will receive dasatinib 100 mg QD on days 4-21. Maintenance therapy: Patients completing consolidation therapy will continue to receive single agent dasatinib 100 mg QD for one year (or until relapse).	Drug: Dasatinib Other Name: Sprycel Drug: Cytarabine Other Name: ARA-cell Drug: Daunorubicin Other Name: Daunoblastin

Detailed Description:

This is a randomized phase III open-label, multicenter trial evaluating standard induction therapy (daunorubicin [DNR] and cytarabine [Ara-C]) and consolidation therapy (high-dose cytarabine [HDAC]) with or without dasatinib in adult patients with newly diagnosed CBF-AML; in the investigational arm, consolidation therapy is followed by a one-year maintenance therapy with dasatinib. Patients with molecular disease persistence or molecular relapse as assessed by quantitative RQ-PCR for the CBF fusion transcripts will be eligible for hematopoietic stem cell

transplantation before overt hematologic relapse occurs. Primary endpoint is event-free survival.

AML patients will be assessed for the CBF fusion genes in one of two AMLSG central laboratories within 48 hours of diagnosis, and only patients with CBF-AML will be enrolled.

Eligibility

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

Criteria

Inclusion Criteria:

- Core-binding factor (CBF) AML with molecular diagnosis of RUNX1-RUNX1T1 fusion transcript resulting from t(8;21)(q22;q22) (or a variant form) or of CBFB-MYH11 fusion transcript resulting from inv(16)(p13.1q22)/t(16;16)(p13.1;q22) as assessed in one of the central AMLSG reference laboratories (Ulm, Hannover)
- Age ≥ 18; there is no upper age limit
- No prior chemotherapy for leukemia except hydroxyurea for up to 5 days during the diagnostic screening phase
- Non-pregnant and non-nursing. Due to the unknown teratogenic potential of dasatinib in humans, pregnant or nursing patients may not be enrolled. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test within a sensitivity of at least 25 mIU/mL with-in 72 hours prior to registration. Women of child-bearing potential must either commit to continued abstinence from heterosexual intercourse or begin TWO acceptable methods of birth control - one highly effective method (e.g., IUD, hormonal, tubal ligation, or partner's vasectomy), and one additional effective method (e.g., latex condom, diaphragm, or cervical cap) - AT THE SAME TIME, at least four weeks before she begins dasatinib therapy. "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.
- Men must agree not to father a child and must use a latex condom during any sexual contact with women of childbearing potential while taking dasatinib and for 3 months after therapy is stopped, even if they have undergone a successful vasectomy.
- Signed written informed consent.

Exclusion Criteria:

- Performance status WHO >2
- Pulmonary edema and/or pleural/pericardial effusion within 14 days of day 1. If edema/effusion resolves to CTC Grade ≤1, patients can be treated with dasatinib.
- Patients with ejection fraction <50% by echocardiography within 14 days of day 1
- Organ insufficiency (creatinine >1.5x upper normal serum level; bilirubin, AST or AP >2.5x upper normal serum level; heart failure NYHA III/IV; severe obstructive or restrictive ventilation disorder)
- Uncontrolled infection
- 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.
- Severe neurological or psychiatric disorder interfering with ability of giving an informed consent
- 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

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: NCT02013648

Contacts

Contact: Hartmut Doehner, Prof. Dr.	0049-731-500- ext 45501	hartmut.doehner@uniklinik-ulm.de
Contact: Peter Paschka, Dr.	0049-731-500 ext 45746	peter.paschka@uniklinik-ulm.de

Show 49 Study Locations

Sponsors and Collaborators

University of Ulm

Investigators

Principal Investigator: Hartmut Doehner, Prof. Dr. University of Ulm

More Information

No publications provided

Responsible Party:	Prof. Dr. Hartmut Doehner, Prof. Dr., University of Ulm
ClinicalTrials.gov Identifier:	NCT02013648 History of Changes
Other Study ID Numbers:	AMLSG 21-13
Study First Received:	December 11, 2013
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Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

Keywords provided by University of Ulm:
AML
Dasatinib
Core Binding Factor (CBF)

Additional relevant MeSH terms:

Leukemia, Myeloid
Leukemia, Myeloid, Acute
Leukemia
Neoplasms
Neoplasms by Histologic Type
Cytarabine
Dasatinib
Daunorubicin
Anti-Infective Agents
Antibiotics, Antineoplastic
Antimetabolites
Antimetabolites, Antineoplastic
Antineoplastic Agents
Antiviral Agents
Enzyme Inhibitors
Immunologic Factors
Immunosuppressive Agents
Molecular Mechanisms of Pharmacological Action
Pharmacologic Actions
Physiological Effects of Drugs
Protein Kinase Inhibitors
Therapeutic Uses
Topoisomerase II Inhibitors
Topoisomerase Inhibitors

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