Comparison Between Two Dose Levels of Daunorubicin and Between One vs. Two Induction Cycles for Adult Patients With AML (DaunoDouble)

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

Verified May 2014 by Technische Universität Dresden

Sponsor:
Technische Universität Dresden

Collaborator:
Universitäts KrebsCentrum an der TU Dresden

Information provided by (Responsible Party):
Technische Universität Dresden

ClinicalTrials.gov Identifier:
NCT02140242

First received: May 9, 2014
Last updated: May 14, 2014
Last verified: May 2014
History of Changes

Purpose

The proposed trial will address two clinically important questions for younger patients with newly diagnosed acute myeloid leukemia (AML): the optimal dose of daunorubicin in induction therapy and the necessity of a second induction cycle in patients with a good response after the first induction. In the first part of the trial, patients will be randomly assigned to receive either 90 mg/m**2** or 60 mg/m**2** daunorubicin in the first induction cycle in addition to standard dosed cytarabine. The primary endpoint is the rate of good responders. Assuming a superiority of 90 mg/m**2**, 436 patients will be recruited. In the second part of the trial, good responders will be randomized to receive either a second or no further induction cycle. Assuming a non-inferiority of the single induction regarding the rate of complete remissions, a number of 360 patients will be included in the second part. Secondary outcomes will be relapse-free survival, overall survival and minimal residual disease kinetics. Patients will be recruited in about 40 treatment centers of the Study Alliance Leukemia study group over a period of 40 months. The results will be of great clinical relevance: First, the study could facilitate the establishment or confirmation of the optimal daunorubicin dose. Furthermore, in case of a non-inferiority of single versus double induction in good responders, about half of all younger AML patients could be spared a second induction cycle, leading to a reduction in treatment-related mortality, fewer days spent in hospital and improved quality of life.

Condition	Intervention	Phase
Leukemia, Myelocytic, Acute	Drug: study part 1 - dose daunorubicin Procedure: induction cycles	Phase 3

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

Official Title: Randomized Comparison Between Two Dose Levels of Daunorubicin and Between One Versus Two Cycles of Induction Therapy for Adult Patients With Acute Myeloid Leukemia ≤60 Years

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: Daunorubicin Daunorubicin hydrochloride Daunorubicin citrate

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

U.S. FDA Resources

Further study details as provided by Technische Universität Dresden:

Primary Outcome Measures:

- response rate after first induction [Time Frame: day 15] [Designated as safety issue: No]

  To investigate whether a higher dose of daunorubicin in induction chemotherapy leads to an increase in hematological good responders defined as having <5% myeloid blasts on day 15 after start of induction therapy.

- Rate complete remissions [Time Frame: day 35 after final induction] [Designated as safety issue: No]

  To investigate whether the rate of complete remissions (CR) after single induction is similar to that after double induction in patients with good response to induction I.

Secondary Outcome Measures:

- rate cytogenetic and molecular complete remissions [Time Frame: day 35] [Designated as safety issue: No]

  To investigate whether a higher dose of daunorubicin in induction chemotherapy will lead to an increase in cytogenetic and molecular complete remissions.

- event-free survival (EFS) [Time Frame: 5 years] [Designated as safety issue: No]

  To investigate whether a higher dose of daunorubicin will lead to improved event-free survival (EFS), relapse-free survival (RFS) and overall survival (OS). To investigate whether EFS, RFS and OS are similar after single versus double induction in patients with good response to induction I.

- relapse-free survival (RFS) [Time Frame: 5 years] [Designated as safety issue: No]

  To investigate whether a higher dose of daunorubicin will lead to improved event-free survival (EFS), relapse-free survival (RFS) and overall survival (OS). To investigate whether EFS, RFS and OS are similar after single versus double induction in patients with good response to induction I.

- overall survival (OS) [Time Frame: 5 years] [Designated as safety issue: No]

  To investigate whether a higher dose of daunorubicin will lead to improved event-free survival (EFS), relapse-free survival (RFS) and overall survival (OS). To investigate whether EFS, RFS and OS are similar after single versus double induction in patients with good response to induction I.

- Correlation between Minimal Residual Disease (MRD) and EFS, RFS, OS [Time Frame: day 35] [Designated as safety issue: No]

  To correlate the level of cytogenetic and molecular minimal residual disease after induction treatment with survival outcomes EFS, RFS and OS.

- Rate of induction deaths [Time Frame: day 60] [Designated as safety issue: Yes]

  Rate of induction deaths (until day 60 or beginning of consolidation treatment - whichever occurs first)

- Incidence of serious infectious complications [Time Frame: day 35] [Designated as safety issue: Yes]

  Incidence of serious infectious complications Grades 3-4 (Common Toxicity Criteria for Adverse Effects (CTCAE) V4.0

- Sonographic cardiac left ventricular ejection fraction [Time Frame: day 35] [Designated as safety issue: Yes]

  Sonographic cardiac left ventricular ejection fraction

- Serum levels of pro-brain natriuretic peptide (por-BNP) and Troponin-T [Time Frame: day 35] [Designated as safety issue: Yes]

  Serum levels of pro-BNP and Trop-T

- Incidence of CTCAE grade ≥3 cardiac complications [Time Frame: day 35] [Designated as safety issue: Yes]

  Incidence of CTCAE grade ≥3 cardiac complications

- Rate of early deaths [Time Frame: week 2] [Designated as safety issue: Yes]

  Rate of early deaths (2 weeks)

Estimated Enrollment: 600
Study Start Date: April 2014
Estimated Study Completion Date: August 2018
Estimated Primary Completion Date: May 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: daunorubicin 60 mg/m2 study part 1 - dose daunorubicin standard dose daunorubicin in induction 1 (60 mg/m2) on days 3-5	Drug: study part 1 - dose daunorubicin standard induction dose of daunorubicin 60 mg/m2 on days 3-5 versus 90 mg/m2
Active Comparator: Double induction study part 2: induction cycles double induction (only patients with good response)	Procedure: induction cycles single induction cycle versus double induction cycles (only patients with good response after first induction) Allocation is randomized for cytogenetic risk.
Experimental: daunorubicin 90 mg/m2 study part 1 - dose daunorubicin experimental dose daunorubicin in induction 1 (90 mg/m2) on days 3-5	Drug: study part 1 - dose daunorubicin standard induction dose of daunorubicin 60 mg/m2 on days 3-5 versus 90 mg/m2
Experimental: Single induction study part 2: induction cycles single induction (only patients with good response)	Procedure: induction cycles single induction cycle versus double induction cycles (only patients with good response after first induction) Allocation is randomized for cytogenetic risk.

Eligibility

Ages Eligible for Study: 18 Years to 60 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:

- Newly diagnosed AML other than acute promyelocytic leukemia (APL) according to WHO criteria, i.e. bone marrow aspirate or biopsy must contain ≥20% blasts of all nucleated cells or differential blood count must contain ≥20% blasts. In acute erythroid leukemia, ≥20% blasts in all non-erythroid bone marrow cells. In AML defined by cytogenetic aberrations, the rate of blasts may be <20%. Secondary AMLs are eligible for inclusion.
- Age 18-60 years
- Eastern Cooperative Oncology Group (ECOG) performance status 0-2
- Adequate liver and renal function as assessed by the following laboratory requirements to be conducted within 7 days prior to screening:
  - Total bilirubin ≤ 1.5 times the upper limit of normal
  - alanine transaminase (ALT) and aspartate transaminase (AST) ≤ 2.5 times upper limit of normal
  - Creatinine ≤ 1.5 times upper limit of normalExclusion Criteria:
- Adequate cardiac function, i.e. left ventricular ejection fraction (LVEF) of ≥ 50% as assessed by transthoracic two-dimensional echocardiography ("M Mode") or multiple gated acquisition scan (MUGA scan)
- Signed informed consent
- Women must fulfill at least one of the following criteria in order to be eligible for trial inclusion:
  - Post-menopausal (12 months of natural amenorrhea or 6 months of amenorrhea with Serum follicle stimulating hormone (FSH) > 40 U/ml)
  - Postoperative (i.e. 6 weeks) after bilateral ovariectomy with or without hysterectomy
  - Continuous and correct application of a contraception method with a Pearl Index of <1% (e.g. implants, depots, oral contraceptives, intrauterine device - IUD).
  - Sexual abstinence
  - Vasectomy of the sexual partner

Exclusion criteria:

- Patients w ho are not eligible for standard chemotherapy as assessed by the treating physician
- Central nervous system manifestation of AML
- Cardiac disease: i.e. heart failure New York Heart Association (NYHA) III or IV; unstable coronary artery disease (MI more than 6 months prior to study entry is permitted); serious cardiac ventricular arrhythmias requiring anti-arrhythmic therapy
- Patients undergoing renal dialysis
- Chronic pulmonary disease w ith clinical relevant hypoxia
- Know n HIV or Hepatitis infection
- Uncontrolled active infection
- Medical conditions other than AML w ith an estimated life expectancy below 6 months
- Previous treatment of AML except hydroxyurea up to 5 days
- Relapsed or primary refractory AML
- Acute promyelocytic leukemia
- Previous anthracycline-containing chemotherapy
- Treatment w ith any know n non-marketed drug substance or experimental therapy w ithin 4 w eeks prior to enrollment
- Incapability of understanding purpose and possible consequences of the trial
- Pregnant or breastfeeding w omen
- Evidence suggesting that the patient is not likely to follow the study protocol (e.g. lacking compliance)

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith 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: NCT02140242

Contacts

Contact: Frank Staps +049 - 0351 458 5198 frank.staps@uniklinikum-dresden.de

Contact: Kerstin Wirth +049 - 0351 458 4671 kerstin.w irth@uniklinikum-dresden.de

Locations

Germany

PD Dr. med. Matthias Hänel **Not yet recruiting**
Chemnitz, Germany
Principal Investigator: Matthias Hänel, MD

PD Dr. Christoph Röllig **Recruiting**
Dresden, Germany
Principal Investigator: Christoph Röllig, MD

Sponsors and Collaborators

Technische Universität Dresden

Universitäts KrebsCentrum an der TU Dresden

Investigators

Principal Investigator: Christoph Röllig, PD Dr. med. Universitätsklinikum Dresden Carl Gustav Carus

More Information

Additional Information:

study alliance EXIT

University Hospital EXIT

No publications provided

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ClinicalTrials.gov Identifier:	NCT02140242 History of Changes
Other Study ID Numbers:	TUD-**2DAUNO**-058
Study First Received:	May 9, 2014
Last Updated:	May 14, 2014
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

Keyw ords provided by Technische Universität Dresden:
AML
leukemia
induction treatment
daunorubicin
7+3

Additional relevant MeSH terms:

Leukemia	Antineoplastic Agents
Leukemia, Myeloid	Enzyme Inhibitors
Leukemia, Myeloid, Acute	Molecular Mechanisms of Pharmacological Action
Neoplasms	Pharmacologic Actions
Neoplasms by Histologic Type	Therapeutic Uses
Daunorubicin	Topoisomerase II Inhibitors
Antibiotics, Antineoplastic	Topoisomerase Inhibitors

ClinicalTrials.gov processed this record on November 16, 2014