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AML-BFM 2012: clinical trial for the treatment of acute myeloid leukemia in children and adolescents

Submission date 05/01/2013	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 25/03/2013	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 17/07/2020	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute myeloid leukaemia (AML) is an aggressive cancer of the myeloid cells (a type of white blood cell). Without treatment patients die within a short time after diagnosis. Treatment involves intensive chemotherapy to kill the cancerous cells in the blood and bone marrow. During the chemotherapy different drugs are given in cycles of treatment: treatment for a few days and then a rest period. The number of cycles of treatment depends on the treatment plan and how well the treatment works. The aim of this study is to find out whether adding a new drug called clofarabine improves survival in children and adolescents with AML.

Who can participate?
Patients aged under 18 with newly diagnosed AML

What does the study involve?
The chemotherapy is divided into induction, consolidation and maintenance therapy. The induction treatment aims to get rid of AML, so that there are no leukemia cells in the blood or bone marrow. Participants are randomly allocated to one of two groups. One group is treated with clofarabine in combination with cytarabine and liposomal daunorubicin as induction therapy. The other group is treated with the standard induction therapy of liposomal daunorubicin, cytarabine and etoposide. Most of the drugs are given into a vein, directly into the bloodstream. Sometimes a long tube called central line that helps to give the drugs directly into a large vein in the chest is needed. The second phase of treatment is called consolidation and can be given as courses with chemotherapy drugs similar to induction treatment. The last is maintenance therapy, which is given to stop the cancer coming back. Participants are randomly allocated to be treated with either 1 year or 8 weeks of maintenance therapy using Cytarabin und 6-Thioguanin to find out whether treatment side effects can be reduced and quality of life improved without worsening their chance of survival (prognosis).

What are the possible benefits and risks of participating?
The possible benefits are improved survival through the use of clofarabine in induction therapy and reduction of treatment toxicity and improvement in quality of life by shortening the

maintenance therapy without worsening the prognosis. As chemotherapy for AML is one of the most aggressive treatments severe toxic side effects are possible. Some of them can be life threatening, particularly infections. There are different methods to reduce the side effects, for example antibiotics and blood transfusions. Because of the high risk of illness and death the treatment is carried out by experienced professionals.

Where is the study run from?
The study has been set by the Hannover Medical School (Germany) in collaboration with other big national and international hemato/oncology centers from Germany, Austria, Czech Republic, Slovakia and Switzerland

When is the study starting and how long is it expected to run for?
July 2013 to June 2018

Who is funding the study?
German Cancer Aid

Who is the main contact?
Prof. Dr Dirk Reinhardt, dirk.reinhardt@uk-essen.de

Study website
http://www.aml-bfm.de

Contact information

Type(s)
Scientific

Contact name
Prof Dirk Reinhardt

Contact details
Universitätsklinikum Essen
Hufelandstr. 55
Essen
Germany
45147
+49 (0)201 723 3784
dirk.reinhardt@uk-essen.de

Additional identifiers

EudraCT/CTIS number
2013-000018-39

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

AML-BFM2012

Study information

Scientific Title
AML-BFM 2012: clinical trial for the treatment of acute myeloid leukemia in children and adolescents - an open prospective randomized phase III trial

Acronym
AML-BFM 2012

Study objectives
1. Improvement in the event-free and overall survival of children and adolescents with acute myeloid leukemia (AML) through the introduction of Clofarabine in induction therapy.
2. Minimization of treatment toxicity and improvement in quality of life by shortening the maintenance therapy without worsening the prognosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Open prospective randomized phase III trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Pediatric acute myeloid leukemia

Interventions
In total 500 patients will be recruited with study duration of 5 years and estimated 100 patients randomised per year. Randomisation 1: 448 Patients till the end 2017, randomisation 2: 380 Patients till the end 2017.

Randomisation 1
Arm A: CDxA (Clofarabine; 40mg/m2; 5 days)
Arm B: ADxE (Etoposide; 150 mg/m2/d; 3 days)

Randomisation 2:
Arm A: long maintenance therapy, 1 year
[6-Thioguanin 40 mg/ m2; daily
HD_Cytarabine 1g/m2; infusion, day: 1-3, 6x
Cytarabine, 20-40mg/m2, i.th.; day: 1
Cytarabine, Methotraxate, Prednisolone i.th.; day1; week: 5, 7, 9)

Arm B: short maintenance therapy, 8 weeks
(6-Thioguanine: 40 mg/ m2; daily; week: 4-8
Cytarabine: 40mg/m2; day: 1-4, each 4 weeks
Cytarabine, Methotraxate, Prednisolone i.th.; day: 1, 14, 28, 42)

The early treatment response (% blasts before the second treatment block; days 21-28) and treatment response after the second treatment block (% blasts day 42), event-free, disease-free and overall survival and AML toxicity rates will be evaluated.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
lofarabine, Cytarabine, liposomal Daunorubicin, Etoposide, Idarubicine, Methotrexat, Mitoxantrone, Sorafenib, 6-Thioguanin

Primary outcome measure
1. Event-Free Survival (EFS) of the randomized patients. The EFS will be calculated from day 0 (date of diagnosis) to the first event (non-response, relapse, second malignancy or death for any reason) or the last follow-up.
2. Disease-Free Survival (DFS). The DFS will be calculated from date of randomization to the first event (relapse, second malignancy or death for any reason) or the last follow-up.

Secondary outcome measures
1. Overall survival
2. Detection of molecular relapse
3. Response kinetics for minimal residual disease.
The minimal Rest Disease (MRD) will be monitored at the start of each treatment element in the peripheral blood (PB) and bone marrow samples (BM). In all patients with molecular or cytogenetic markers for MDR (Fusion genes AML1/ETO, CBL/MYH11, MLL/X, OTT/MAL; Mutations: NPM1, FLT3-ITD, WT1, c-kit, GATA1, CEPBα, RAS)
4. Relapse incidence
5. Quality of life through toxicity monitoring
6. Assessment of safety: Serious Adverse Events (SAE), long-term follow-up of late adverse effects

Overall study start date

01/07/2013

Completion date
30/06/2018

Reason abandoned (if study stopped)
Lack of staff/facilities/resources

Eligibility

Key inclusion criteria
1. Diagnosis of an AML (It. WHO classification 2008)
2. Ages 0 to 18 years, either sex
3. Informed Consent of the guardians

Participant type(s)
Patient

Age group
Child

Lower age limit
0 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
448

Key exclusion criteria
1. Existing illnesses / syndromes which exclude treatment
2. Patients with trisomy 21 and ML-DS and/or transient myeloproliferative syndrome (referred to TMD-prevention study or the ML-DS 2006 study)
3. Refusal of treatment/missing consent to treatment or protocol
4. Pregnancy/breastfeeding
5. Patients of child-bearing age who decline a pregnancy test
6. Previous-therapy with cytostatic medicines of more than 14 days

Date of first enrolment
01/07/2013

Date of final enrolment
30/06/2018

Locations

Countries of recruitment
Austria

Czech Republic

Germany

Slovakia

Switzerland

Study participating centre
Carl-Neuberg-Str. 1
Hannover
Germany
30625

Sponsor information

Organisation
Medical School of Hannover (MHH) (Germany)

Sponsor details
Carl-Neuberg-str. 1
Hannover
Germany
30625

Sponsor type
University/education

Website
http://www.mh-hannover.de

ROR
https://ror.org/00f2yqf98

Funder(s)

Funder type
Charity

Funder Name

Deutsche Krebshilfe

Alternative Name(s)
Stiftung Deutsche Krebshilfe, German Cancer Aid

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Germany

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration