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International study on the treatment of pediatric relapsed acute myeloid leukemia

Submission date
15/01/2014

Recruitment status
No longer recruiting

Registration date
20/02/2014

Overall study status
Completed

Last Edited
21/05/2021

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] 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 white blood cells. AML can be resistant to treatment (refractory AML) and can return after a period of improvement (relapsed AML). Therefore, there is a need for new treatment options to treat relapsed/refractory AML. Improved knowledge about the mechanisms and mutations involved in AML and the development of new drugs targeting these mechanisms has led to the concept of targeted treatments which might further improve patient outcome when added to conventional chemotherapy. For example, the drug gemtuzumab ozogamicin (Mylotarg®) is designed to attach to and kill leukemia cells. Mylotarg has been found to be effective in studies of relapsed AML with moderate toxicity (side effects). The aim of this study is to find out whether adding Mylotarg to standard chemotherapy improves the elimination of leukemia cells.

Who can participate?
Children and adolescents with refractory or relapsed AML, aged under 18 at the start of the initial chemotherapy and aged under 21 at the start of this relapsed AML treatment.

What does the study involve?
Participants are randomly allocated to be treated with chemotherapy either with or without Mylotarg. This treatment is followed by either further chemotherapy of high or low intensity or by stem cell transplantation.

What are the possible benefits and risks of participating?
Mylotarg may improve the elimination of leukaemia cells and cause less damage to the heart (cardiotoxicity) than other drugs, improving survival rates. As the chemotherapy used in this study is one of the most aggressive, severe toxic adverse 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.

Where is the study run from?
The study has been set up by the Hannover Medical School (Germany) in collaboration with other

national and international hemato/oncology centers from Germany, Austria, Belgium, Czech Republic, Denmark, Hungary, Finland, France, Ireland, Italy, Netherlands, Slovakia, Spain, Sweden, Switzerland and the UK.

When is the study starting and how long is it expected to run for?
June 2013 to March 2023

Who is funding the study?
1. Pfizer Pharma (Germany)
2. Deutsche José Carreras Leukämie-Stiftung e.V (Germany)

Who is the main contact?
Prof. Dr Dirk Reinhardt
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2010-018980-41

Protocol serial number
Pediatric Relapsed AML 2010/01

Study information

Scientific Title
International randomized phase III study on the treatment of children and adolescents with refractory or relapsed acute myeloid leukemia: Pediatric Relapsed 2010/01

Acronym
Pediatric Relapsed AML 2010/01

Study objectives
The response to treatment of patients with relapsed or refractory pediatric AML can be improved by the addition of Gemtuzumab ozogamicin - GO (Mylotarg®) to the standard DX-FLA based reinduction chemotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee (Ethik-Kommission der MHH, Carl-Neuberg-Str. 1, Hannover, 30625, Germany), 16/01/2014

Study design
International prospective randomized multicenter two arm phase III optimization study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
The aim of this study is to answer a randomized study question: can the response to the first reinduction chemotherapy block be improved by the addition of GO to the standard therapy?

Standard Arm: DX-FLA (Triple IT: Cytarabine, Methotraxate, Prednisolone i.th in age related dosis on day 0, liposomal daunorubicine dosis: 60 mg/m2/day, day 1,3,5; Fludarabine dosis: 30 mg/m2 /day, day 1-5; Cytarabine dosis: 2000 mg/m2/day, day 1-5)

Experimental Arm: DX-FLA + GO (Triple IT: Cytarabine, Methotraxate, Prednisolone i.th in age related dosis on day 0, liposomal daunorubicine dosis: 60 mg/m2/day, day 1,3,5; Fludarabine dosis: 30 mg/m2/day, day 1-5; Cytarabine dosis: 2000 mg/m2/day, day 1-5; Gemtuzumab ozogomicin dosis: 4.5 mg/m2, day 6)

Subsequent therapy depends on the response to the first block:

>20% blasts off protocol

≤20% blasts
Second Reinduction: FLA (Triple IT: Cytarabine, Methotraxate, Prednisolone i.th in age related dosis on day 1, Fludarabine dosis: 30mg/m2/day, day 1-5; Cytarabine dosis: 2000mg/m2/day, day 1-5)

Consolidation high intensity (Triple IT: Cytarabine, Methotraxate, Prednisolone i.th in age related dosis on day 1; Cytarabine dosis: 500 mg/m2/day, day 1-4; Etoposide dosis: 100 mg/m2/day, day 1-5)
or

Consolidation low intensity (Triple IT: Cytarabine, Methotraxate, Prednisolone i.th in age related dosis on day 1; Cytarabine dosis: 75 mg/m2/day, day 1-4 and 15-18 s.c.; Thioguanine dosis: 100 mg /m2/day, max. 4 weeks oral dose)

Stem cell transplantation (SCT)

Total duration of therapy will be up to three months. Follow-up duration will be five years.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Gemtuzumab ozogamicin

Primary outcome(s)
The early treatment response will be determined by morphological and flow cytometric examination of the BM sampled at day 28 (in practice anytime between day 28 and 42 after start of first reinduction chemotherapy). If the BM shows 20% of leukemic blasts or less, the response is good. If the BM shows > 20% leukemic blasts, the response is poor. Event-free, disease-free and overall survival and AML toxicity rates will be evaluated.

Key secondary outcome(s))
1. Determination of the incidence of refractory disease, CR/CRi rates after two courses and long-term efficacy (cumulative incidence of relapse, event-free survival, and overall survival) in the different study arms
2. Determination of the toxicity of GO (Mylotarg®) when added to DX-FLA in terms of BM aplasia, liver toxicity including VOD, cardiotoxicity, mucosal toxicity and other adverse reactions according to CTCAEv4 which are considered to be relevant in relapsed AML and the proposed therapy when compared to treatment with DX-FLA only
3. Identification of additional prognostic factors in pediatric relapsed AML, other than early treatment response, cytogenetics and duration of first remission
4. Providing of individual biological characterization of leukemia (morphology, immunophenotype, cytogenetics, molecular genetics and activated signalling pathways), for future individualized stratification to targeted therapy

Completion date
31/03/2023

Eligibility

Key inclusion criteria
1. Children and adolescents < 18 years of age at start of initial chemotherapy and < 21 years of age at start of this relapsed AML treatment
2. Patients with first relapsed (including relapse after SCT) or primary refractory AML
3. Signed written informed consent from patients and/or from parents or legal guardians for minor patients, according to local law and regulations
4. In female patients of childbearing potential pregnancy must be excluded
5. Sexually active patients must be using two reliable contraception methods from the time of

screening/baseline and during the study for a minimum of 3 months after the last administration of study medication. This includes every combination of a hormonal contraceptive (such as injection, transdermal patch, implant, cervical ring) or of an intrauterine device (IUD) with a barrier method (e.g. diaphragm, cervical cap, or condom) or with a spermicide.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Upper age limit
21 years

Sex
All

Key exclusion criteria
1. Acute promyeloblastic leukemia (AML FAB type M3; please refer to your local group for the appropriate treatment protocol)
2. Myeloid Leukemia of Down syndrome (please refer to your local group for treatment alternatives)
3. Symptomatic cardiac dysfunction (CTCAEv4 grade 3 or 4) and/or a Fractional Shortening at echocardiography below 29%
4. A Karnofsky performance status < 40% (children ≥ 16 years) or an Lansky performance status of < 40% (children < 16 years) before start of chemotherapy
5. Any other organ dysfunction (CTCAEv4 grade 4) that will interfere with the administration of the therapy according to this protocol
6. Impaired liver function defined as > 3.0 x UNL for transaminases and for bilirubin
7. History of VOD
8. History of hepatitis C positivity
9. Renal impairment with creatinine < 30 ml/min
10. Decompensated hemolytic anemia
11. Hypersensitivity to GO and/or other chemotherapeutic drugs
12. Inability to potentially complete the treatment protocol for any other reason
13. Pregnant or breastfeeding patients
14. Current participation in another clinical trial for the time of first course of reinduction chemotherapy.

Date of first enrolment
30/06/2013

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
United Kingdom

Austria

Belgium

Czech Republic

Denmark

Finland

France

Germany

Hungary

Ireland

Italy

Netherlands

Slovakia

Slovenia

Spain

Sweden

Switzerland

Study participating centre
Hannover Medical School
Hannover
Germany
D-30625

Sponsor information

Organisation
Hannover Medical School represented by Hannover Clinical Trial Center (HCTC)

ROR

https://ror.org/00f2yqf98

Funder(s)

Funder type
Industry

Funder Name
Pfizer Pharma (Germany)

Funder Name
Deutsche José Carreras Leukämie-Stiftung e.V (Germany) DJCLS R 10/08

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes