# International study on the treatment of pediatric relapsed acute myeloid leukemia

Submission date	Recruitment status	Prospectively registered
15/01/2014	No longer recruiting	Protocol
Registration date	Overall study status	Statistical analysis plan
20/02/2014	Completed	Results
Last Edited	Condition category	[] Individual participant data
21/05/2021	Cancer	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 reinhardt.dirk@mh-hannover.de

#### Study website

http://www.aml-bfm.de

#### Contact information

#### Type(s)

Scientific

#### Contact name

Prof Dirk Reinhardt

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### Additional identifiers

#### EudraCT/CTIS number

2010-018980-41

IRAS number

ClinicalTrials.gov number

#### Secondary identifying numbers

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

#### 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 below to request a patient information sheet (study sites only).

#### 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)

ОΓ

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 measure

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.

#### Secondary outcome measures

- 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

#### Overall study start date

30/06/2013

#### 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

#### Age group

Child

#### Upper age limit

21 Years

#### Sex

Both

#### Target number of participants

252

#### 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  $\geq$  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

Hungary

Ireland

Netherlands

Slovakia

Slovenia

Spain

Sweden

Italy

- 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 Austria Belgium Czech Republic Denmark **Finland** France Germany

#### Switzerland

**United Kingdom** 

#### Study participating centre Hannover Medical School Hannover Germany D-30625

# Sponsor information

#### Organisation

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

#### Sponsor details

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#### Sponsor type

University/education

#### Website

http://www.clinical-trial-center.de/

#### 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**

**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