International randomized phase III study on the treatment of children and adolescents with refractory or relapsed acute myeloid leukemia

Published: 29-01-2014
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The main objective of this treatment protocol is to study the efficacy on the treatment response after adding a single gift of Mylotarg. Furthermore, monitoring of toxicity and long term efficacy is also important.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON47169

Source
ToetsingOnline

Brief title
Pediatric relapsed AML 2010/01

Condition

- Leukaemias

Synonym
relapsed acute myeloid leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Kinderoncologie Nederland

Source(s) of monetary or material Support: Ministerie van OC&W,Free drug + vergoeding tbv apotheekkosten van Pfizer,Pfizer

Intervention

Keyword: AML, pediatric, relapse, treatment

Outcome measures

Primary outcome

Bone marrow blasts on *day 28* (before the start of the second reinduction

course) given as * 20% or >20%.

Secondary outcome

1. overall survival

2. event-free survival

3. Percentage of patients that achieve CR after two courses of reinduction

chemotherapy

4. Incidence of treatment related mortality and toxicity according to NCI-CTC

criteria

Study description

Background summary

Pediatric relapsed AML still has a poor prognosis. The probability of survival at 4 years is 36% in the most recent study Relapsed AML 2001/01, which is better than reported before, but not good enough. Further improvements of current treatment are thus required. Gemtuzumab ozogamicin (GO, Mylotarg®) consists of a calicheamicin conjugated to the monoclonal CD33 antibody and has proven to be effective in terms of CR achievement and better overall survival in adult AML studies and in pediatric AML relapse and salvage therapy studies with moderate toxicity. The best arm of the current study, which is the reinduction course including liposomal daunorubicin (DaunoXome®), fludarabine, cytarabine and G-CSF (DX-FLA) will constitute the standard first reinduction course of chemotherapy. This regimen will be compared with DX-FLA plus GO at

4.5 mg/m2 as single dose in combination chemotherapy. In case of too much toxicity with GO at 4.5 mg/m2, the dose will be reduced permanently to 3.0 mg/m2. Patients who do respond poorly to this first course of chemotherapy with >20% BM blasts on before the start of the second course become eligible for phase I/II studies. All other patients proceed to the second reinduction course.

Study objective

The main objective of this treatment protocol is to study the efficacy on the treatment response after adding a single gift of Mylotarg. Furthermore, monitoring of toxicity and long term efficacy is also important.

Study design

Intergroup, international, multicenter open label comparative and randomised phase III study on the efficacy of Mylotarg added to standard reinduction chemotherapy in children and adolescents with refractory and relapsed AML.

Intervention

All patients eligible for this study will be randomised in a 1:1 fashion for the addition or not of GO (Mylotarg®) at 4.5 mg/m2 to DX-FLA in the first course of reinduction chemotherapy. If GO at 4.5 mg/m2 proves to be too toxic, the dose will be reduced permanently to 3.0 mg/m2. Patients who do respond poorly to this first course of chemotherapy with >20% BM blasts on *day 28* (before the start of the second course) become eligible for phase I/II studies. All other patients proceed to the second reinduction course. Patients who do not achieve a CR after these two courses become eligible for phase I/II studies. In CR, all patients are eligible for allo-SCT. If more time is needed to perform that SCT, guidelines for intensive and low-intensity consolidation are provided in the protocol. The choice for either the intensive or non-intensive regimen must be based on the anticipated time until SCT and on the condition of the patient.

Study burden and risks

To get cured, children with relapse AML must be treated. The extent of burden and risks associated with this treatment are not different than other treatments used untill now in the Netherlands. This treatment protocol has strict stopping rules and safety guidelines.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

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 or primary refractory AML
3. Patients with a second or subsequent relapsed AML that were not previously treated according to this particular protocol
4. Signed written informed consent from patients or from parents or legal guardians for minor patients, according to local law and regulations
5. In women of childbearing potential pregnancy must be excluded.
6. Sexually active patients must be using an adequate method of contraception to avoid

pregnancy throughout the study and for up to 3 months after the study in such a manner that the risk of pregnancy is minimized.

Exclusion criteria

1. 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 (CTC grade 3 or 4) and/or a Fractional Shortening at echocardiography below 29%
4. A Karnofsky performance status <40% (children * 16 years) or an Lanksy performance status of <40% (children < 16 years) before start of chemotherapy
5. Any other organ dysfunction (CTC grade 4) that will interfere with the administration of the therapy according to this protocol
6. Impaired liver function defined as > than NCI-CTC grade 1 (max 2.0 x ULN for transaminases and bilirubin)
7. History of veno-occlusive disease (VOD)
8. Hypersensitivity to gemtuzumab ozogamicin
9. Inability to potentially complete the treatment protocol for any other reason
10. Pregnant women

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	cytarabine injection solution 20mg/ml and 100 mg/ml
Generic name:	cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	DaunoXome injection
Generic name:	liposomal daunorubicin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Fludara 50mg powder for solution for injection or infusion
Generic name:	Fludarabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Methotrexate 100 mg/ml Injection
Generic name:	Methotrexate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Mylotarg
Generic name:	gemtuzumab ozogamicin for Injection

Ethics review

Approved WMO Date:	29-01-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-04-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-11-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-018980-41-NL
CCMO	NL34473.078.13