Protocol for treatment of children and adolescents with acute myeloid leukemia 0-18 years

Published: 15-07-2013
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This study has been transitioned to CTIS with ID 2024-518254-16-00 check the CTIS register for the current data. The primary aim of the NOPHO-DBH AML 2012 study is to improve EFS and OS in children with AML. To improve outcome, an intensified…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON55459

Source
ToetsingOnline

Brief title
NOPHO-DBH AML 2012 Protocol

Condition

- Leukaemias

Synonym
bloodcancer, leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Västra Götalandregionen, Queen Silvias Childrens and Adolescents Hospital
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: adolescents, AML, children, treatment

Outcome measures

Primary outcome

The primary endpoint is the MRD level at day 22 from start of the course.

Secondary outcome

Secondary outcome measures in both studies include EFS, OS, remission rate and

toxicity.

Study description

Background summary

The outcome of paediatric acute myeloid leukaemia is still unsatisfactory with an overall survival around 70% and a relapse rate of 30-40% after primary treatment.

Study objective

This study has been transitioned to CTIS with ID 2024-518254-16-00 check the CTIS register for the current data.

The primary aim of the NOPHO-DBH AML 2012 study is to improve EFS and OS in children with AML. To improve outcome, an intensified induction regimen will be given and a response guided risk-group stratification using flow cytometric minimal residual disease measurements to evaluate therapy response will be used. Patients with a poor response to the two induction courses will be assigned to the high-risk group and receive consolidation therapy including stem cell transplantation whereas those with a good response will be given three chemotherapy courses as consolidation therapy. An exception are patients with good response and inv(16), who will not be given HAM and thus receive two consolidation courses only. The only other cytogenetic feature that will affect risk stratification is the presence of an FLT3-ITD mutation which, when not associated with concomitant nucleophosmin (NPM1) mutation, will stratify patients to the high-risk group.
Effective induction therapy is crucial for outcome in AML and MRD levels

following induction are highly predictive of outcome.

Study design

randomised clinical trial

Intervention

NOPHO-DBH AML 2012 includes two randomised studies that both address the efficacy of induction therapy.
The first study is based on the induction course from the Japanese AML99 trial and compares the efficacy of mitoxantrone and DaunoXome in the first treatment course. The primary outcome measure is the MRD level on day 22 from start of the course.
The second study compares ADxE (low-dose cytarabine, DaunoXome and etoposide) with FLADx (fludarabine, high-dose cytarabine and DaunoXome) as the second induction course.

Per the amendment dated 13-12-2018 the 1st randomisation is closed, and all patients will receive MEC as 1st induction course. In the 2nd induction course DaunoXome can be replaced by Daunorubicine, in case DaunoXome is not available.

Per 09-08-2021 the 2nd randomisation is also closed. All patients will receive standard ADxE as 2nd induction course. DaunoXome can be replaced by Daunorubicin in case DaunoXome is not available.

Study burden and risks

Children and adolescents with AML need to be treated. With respect to burden and risks this protocol does not differ from other treatments for AML as has been used in the past in the Netherlands. This protocol has safety guidelines to monitor the outcome.

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)
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

Patients are eligible for the study if they fulfil all three criteria below, 1)
AML as defined by the diagnostic criteria in section 16
2) Age < 19 years at time of diagnosis
3) Written informed consent

Exclusion criteria

Patients are excluded if any of the criteria below are present
1) Previous chemotherapy or radiotherapy.
2) AML secondary to previous bone marrow failure syndrome.
3) Down syndrome (DS).
4) Acute promyelocytic leukaemia (APL).
5) Myelodysplastic syndrome (MDS).
6) Juvenile Myelomonocytic Leukaemia (JMML).
7) Known intolerance to any of the chemotherapeutic drugs in the protocol.
8) Fanconi anaemia.
9) Major organ failure precluding administration of planned chemotherapy.

10) Positive pregnancy test.

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-01-2014
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cytarabine Sandoz 50mg/ml
Generic name:	Cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	DaunoXome® 2 mg/ml,
Generic name:	Liposomal Daunorubicin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Etoposide Sandoz 20 mg/ml,
Generic name:	Etoposide
Registration:	Yes - NL outside intended use

Product type:	Medicine
Brand name:	Fludarabine Fresenius Kabi 50 mg
Generic name:	Fludarabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Mitoxantron PCH 2 mg/ml
Generic name:	Mitoxantrone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-10-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	17-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-518254-16-00
EudraCT	EUCTR2012-002934-35-NL
ClinicalTrials.gov	NCT01828489
CCMO	NL41711.029.13