CHIP-AML22 Master protocol: An open label complex clinical trial in newly diagnosed pediatric de novo AML patients - a study by the NOPHO-DBSHIP consortium

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This study has been transitioned to CTIS with ID 2023-504999-25-00 check the CTIS register for the current data. To investigate wether the treatment of children and adolescents with AML can be improvedby means of:1) improved risk-group adapted…

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

Summary

ID

NL-OMON53580

Source
ToetsingOnline

Brief title
CHIP-AML22/Master

Condition

- Leukaemias

Synonym
Acute Myeloid Leukemia (AML), blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Ministerie van OC&W,Een deel van het onderzoek wordt gefinancierd vanuit een EU-grant.

Intervention

Keyword: Acute Myeloid Leukemia (AML), Adolescents, Children, Initial / newly diagnosed

Outcome measures

Primary outcome

Overarching Primary Objective:

• To improve the overall EFS for children and adolescents with newly diagnosed

AML, compared to NOPHO-DBH AML-2012.

* Endpoint: EFS

Primary objective Randomisation Consolidation:

• To demonstrate non-inferiority in disease-free survival of two courses of

consolidation therapy, by omitting HA3E, as compared to three courses, in the

entire standard-risk group eligible for this randomization

* Endpoint: DFS

Secondary outcome

Entire study population:

To improve short-term efficacy by different endpoints, overall survival (OS),

disease-free survival (DFS) and the cumulative incidence of relapse (CIR).

Endpoints:

• Bone marrow blast counts by morphology and multi-color flow cytometry (MFCM)

after course #1 and #2 and before allo-SCT; ORR (CR, CRp, and CRi) and

morphologic leukemia-free state (MLFS) rates after course #1 and #2; MRD negativity after course #1 and #2 and before allo-SCT; absolute MRD levels after course #1 and #2 and before allo-SCT.

• OS

• DFS,

• CIR.

Entire study population:

To decrease treatment-related toxicity.

Endpoints:

• Cumulative toxicity, defined as the total of all grades AEs over time, which are graded by NCI CTCAE version 5.0.

• Non-relapse mortality (NRM).

Randomisation Consolidation:

To improve safety of consolidation treatment.

Endpoints:

• Cumulative toxicity, defined as the total of all grade >=3 AESIs over time, which are graded by NCI CTCAE version 5.0.

• Non-relapse mortality (NRM).

Study description

Background summary

The treatment of children with AML comprises intensive chemotherapy, and sometimes also stem cell transplantation. To determine the exact treatment, patients are divided in several risk groups. These are based on characteristics of AML-cells at diagnosis, and the treatment response at the start of treatment. The protocol that was used until now for treatment of children and adolescents with AML showed good results: 70-80% of children survives AML with this treatment.
When treatment response is poor, or in case of relapse, the prognosis is worse. It is therefore important to prevent bad response or relapse.
In this new study, the treatment will overall be similar to the previous protocol. By using data from previous research it is now possible to better look at characteristics that determine the risk groups for treatment. In addition, extra treatment options for specific groups were added to the standard treatment. The overall aim is to improve the treatment of children and adolescents with AML.

Study objective

This study has been transitioned to CTIS with ID 2023-504999-25-00 check the CTIS register for the current data.

To investigate wether the treatment of children and adolescents with AML can be improved
by means of:
1) improved risk-group adapted treatment
2) reduced treatment toxicity through shortened consolidation therapy.

Study design

This is a master protocol comprising a complex clinical trial with a stratification approach to allocate patients to randomized studies described in the master protocol or linked trials

Intervention

The aim of the randomisation study is to investigate whether treatment with 2 consolidation courses is as effective as treatment with 3 consolidation courses.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness (if applicable):
The treatment according to this protocol is considered the standard treatment

for children and adolescents with AML.
In the randomisation study is being investigated whether treatment with 2 consolidation courses of children and adolescents with standard risk AML, is as good as treatment with 3 consolidation courses.
The additional burden compared to standard treatment consists of completing some questionnaires. Parents / patients will be asked 4 times in total during the study to complete questionnaires related to Quality of Life. This takes approximately 10 minutes each time.
The most important risks are standard for pediatric oncology treatment. A risk related to participation in the consolidation randomization is that by leaving out on consolidation course, the treatment will be less effective. However, based on previous research this is not expected, and additionally it is expected that adverse events will be decreased. The latter is a significant advantage, since there is even the risk of dying because of the last course of chemotherapy.

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

1) Newly diagnosed AML as defined by the diagnostic criteria in the study protocol. Note that different blast thresholds may apply for different genetic abnormalities in case of low blast percentages. The origin of AML must be de novo (not secondary to bone marrow failure or therapy-related).
2) Age >=1 day and <= 18 years old at initial diagnosis.
3) Written informed consent/assent from patients and/or from parents or legal guardians for minor patients, according to local law and regulations. Informed consent should ideally be obtained before day 7 of induction course 1, as patients that are eligible for the linked quizartinib trial should be enrolled before the end of induction course 1, and in view of the planned Mylotarg® randomisation. Thus, standard of care induction treatment may be started before informed consent has been obtained.
4) Able to comply with scheduled follow-up and with management of toxicity.

Additional inclusion criteria for the Rc randomization
1) Patients included in the CHIP-AML22 protocol and stratified to Standard Risk Group according to the stratification algorithm of the protocol
2) Informed consent for participation in randomization Rc

Exclusion criteria

1) Previous chemotherapy or radiotherapy. This includes patients with therapy-related AML after previous cancer therapy. These patients may be treated according to the master protocol but will not be part of the formal study population, and data of these patients will not be collected.
2) Patients with a (known) germline predisposition for bone marrow failure, like Fanconi anemia. 3) Myeloid Leukemia of Down syndrome (ML-DS). Patients with ML-DS are recommended to be treated according to the international ML-DS protocol. Patients with AML and DS older than 5 years who often lack GATA1 mutation and do not have typical myeloid leukemia of DS may be treated according to the master protocol but will not be part of the formal study population, hence data of these patients will not be collected.
4) Acute promyelocytic leukemia (APL).
5) Myelodysplastic syndrome (MDS).

6) Juvenile Myelomonocytic Leukemia (JMML).
7) Known intolerance to any of the chemotherapeutic drugs in the protocol.
8) Evidence of cardiac dysfunction (shortening fraction below 28%).
9) Pregnant or lactating patients, or sexually active female patients of childbearing potential not willing to use an highly effective method of contraception for the duration of study therapy and up to 7 months after the completion of all study therapy.
10) Sexually active, fertile male patients, not willing to use an effective method of contraception, for the duration of study therapy, and up to 6 months after the completion of all study therapy.
11) Concomitant administration of any other experimental drug under investigation, or concurrent treatment with any other anti-cancer therapy other than specified in this protocol or in one of the linked trials linked to this Master protocol is not allowed.
12) Patients who in the opinion of the investigator, may not be able to comply with the study requirements of the study.
13) Patients with known active hepatitis B, hepatitis C, or HIV infection.
14) Patients for whom informed consent was not obtained.
Additional information on contraception measures
Females:
A female participant is considered of childbearing potential i.e., fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. As contraception, we suggest the use of one of the highly effective methods of contraception, as described below.
Highly effective methods of contraception according to the CTFG-2020 guidelines are those that, alone or in combination, result in a failure rate of less than 1% per year when used consistently and correctly (i.e., perfect use).
Contraception is indicated at least 4 months after last dose of mitoxantrone, at least 6 months after last dose of cytarabine, etoposide, fludarabine or methotrexate, and at least 7 months after last dose of quizartinib, whichever is longer.
Males:
A male patient is considered fertile after puberty unless permanently sterile by bilateral orchidectomy. If the male is sexually active, he must use a condom during intercourse, and agree not to father a child or donate sperm during therapy. Contraception recommendations should also be considered for a non-pregnant female partner of childbearing potential (see above).
Contraception is indicated at least 6 months after last dose of mitoxantrone, cytarabine, etoposide, daunorubicin, fludarabine, and at least 4 months after last dose of quizartinib, whichever is longer.

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:	Recruiting
Start date (anticipated):	18-09-2023
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cytarabine
Generic name:	Cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Etoposide
Generic name:	Etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	10-01-2023

Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-03-2023
Application type:	First submission
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 19921
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2023-504999-25-00
EudraCT	EUCTR2022-002885-34-NL
CCMO	NL82495.041.22