# Dutch- Belgian pediatric acute myeloid leukemia (AML) protocol.

No registrations found.

| | |
|---|---|
| **Ethical review** | Not applicable |
| **Status** | Pending |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON28546

**Source**
NTR

**Brief title**
DB-AML-01

**Health condition**

Newly diagnosed acute myeloid leukaemia in children and adolescents.

### Sponsors and support

**Primary sponsor:** Stichting Kinderoncologie Nederland (SKION)
**Source(s) of monetary or material Support:** Stichting Kinderoncologie Nederland (SKION)

### Intervention

### Outcome measures

**Primary outcome**

1. To conduct an international pediatric study for AML based on the NOPHO-AML 2004 protocol with optimal outcome and less toxicity;

2. To reduce cumulative anthracycline dosage

to reduce the number of intensive courses to 5.

### Secondary outcome

To monitor cardiotoxicity by echocardiography.

## Study description

### Background summary

Acute myeloid leukemia (AML) is a sporadic disease in children. In the Netherlands and Belgium approximately 25-30 children each year will be diagnosed with AML (age 0-18 years). A complete remission (CR) can be reached in 85-90% of the children. However, the 5-yr overall survival (OS) is 50-60% due to high relapse frequency especially during the first and second year after diagnosis. The results of the latest NOPHO protocol 1993 were for 5-yr OS 65% and EFS 48%, combined with a CR rate of 92%. These results are amongst the best from europe. The first remission rates of the NOPHO are comparable to the remission rates of the Berlin- Frankfurt- Münster (BFM) and Medical research council (MRC) pediatric study groups. A special characteristic of the NOPHO strategy is the timing of the second course. There is an intensive timing, e.g. at day 15 after the first course when the bone marrow reveals more then 5% blasts. The NOPHO demonstrated the feasibility of this attitude in their latest two trials. With this CR rate a major therapeutic issue is to prevent relapses. There is evidence that increasing the total dose of ARA-C reduces the relapse rate, whereas the complete remission rate is not increased anymore. The NOPHO backbone consists of high total dosages of ARA-C during consolidation. This might be related to their success.
In general, over the past 20 years there has been an important increase in therapeutic outcome due to intensification of treatment based upon high dosages of cytarabine-arabinoside and anthracyclins during induction and consolidation.

Early studies established the cardiotoxic threshold dose of 550 mg/m2 in adults. In children even lower dosages of anthracyclines are at risk of exhibiting subclinical cardiovascular dysfunction and clinically significant cardiomyopathy. Relatively limited data are available concerning studies including the cardiovascular status of survivors more than 10-15 years after completion of therapy. Currently available studies show a progressive cardiovascular dysfunction over time when treated with anthracycline dosages over 300 mg/m2. Altogether, these results anno 2009 have made us aware of possible cardiac damage in the upcoming long term survivors after AML treatment. The NOPHO-AML 2004 trial still uses anthracycline dosages of 450 mg/m2. In this study protocol we limited the cumulative dose of anthracyclines to 330 mg/m2.

In international studies two collaborative groups (e.g. BFM and MRC) showed identical good results when the number of courses is reduced to 4 or 5. The original NOPHO-AML 2004 protocol is designed with 6 intensive courses. To limit the cumulative anthracycline dose while remaining high cumulative dosages of ARA-C we decided to skip the most toxic course

which frequently resulted in a delay of treatment and propose a study protocol with 5 intensive chemotherapeutic courses.

The role of allogeneic stem cell transplantation (SCT) is controversial. For several years it has been accepted practice to offer allogeneic transplantation to all AML patients with an HLA-identical sibling donor. The updates of the larger international collaborative study groups show no significant benefit with sibling-SCT in standard-risk or high risk groups. While the outcome has improved with more effective chemotherapy, a more restricted attitude towards allogeneic SCT in AML patients has been adopted in several study groups and also by us. In this protocol allogeneic SCT in 1st CR is not recommended.

Belgium is the other participating country.

**Study objective**

To assess whether the NOPHO- AML 2004 protocol can be used for the treatment of Dutch and Belgian children with newly diagnosed AML, whereby the cumulative dose of the possible cardiotoxic cytostatic antracyclines is lowered without increasing the relapse rate and without changing the outcome (overall survival) unfavourably.

**Study design**

Complete remission (CR) rates after induction, rates of relapse and deaths in first CR and reasons for failure, 1-, 3- and 5- year overall survival rates, several blood and bone marrow evaluations as described in the protocol as well as cardiac evaluation with echocardiography.

**Intervention**

Patients will be treated with two induction courses and depending on the riskgroup, one to three consolidation courses. Cytarabine- arabinoside, etoposide and anthracyclines are the backbone chemotherapeutics in this protocol.

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# Eligibility criteria

## Inclusion criteria

1. Primary diagnosed AML as defined by the diagnostic criteria;

2. Age lower than 19 years at time of study entry;

3. Written informed consent.

## Exclusion criteria

1. Previous chemo- or radiotherapy;

2. AML secondary to previous bone marrow failure syndrome;

3. Down syndrome (DS) with age <5 years and DS =>5 yrs with GATA1 mutation;

4. Acute promyelocytic leukemia (APL);

5. Juvenile myelomonocytic leukemia (JMML);

6. Myelodysplastic syndrome (MDS);

7. Fanconi anemia;

8. Positive pregnancy test.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Non controlled trial |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-02-2010 |
| Enrollment: | 110 |
| Type: | Anticipated |

# Ethics review

Not applicable

| | |
|---|---|
| Application type: | Not applicable |

# 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 |
|---|---|
| NTR-new | NL2003 |
| NTR-old | NTR2120 |
| Other | EudraCTnr : 2009-014462-26 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Study results

**Summary results**
N/A