Randomized induction and post induction therapy in adult patients (= 1.5.

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The 3 hypotheses to be tested are that the outcome in: 1. The high dose arm B is better than in the low dose arm A; 2. The G-CSF arm is better than in the non-G-CSF arm; 3. The PBSCT arm 2 is better than the chemotherapy cycle III arm 1.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25506

Bron
NTR

Verkorte titel
HOVON/SAKK 42 AML

Aandoening

Acute myelocytic leukemia, RAEB, RAEB-t.

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Endpoint for the comparison of induction treatment arm B with arm A and for the comparison yes or no G-CSF priming:
1. Event-free survival (i.e., time from registration to induction failure, death or relapse whichever occurs first); the time to failure of patients with induction failure is set at one day.

Endpoint for the comparison of PBSCT with cycle III:
1. Disease-free survival measured from the date of second randomization to relapse or death from any cause.

Endpoint for the evaluation of Allo SCT:
1. Disease-free survival measured from the date of Allo SCT to relapse or death from any cause.

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase:

phase III.

Study objectives:

Evaluation of the effect of escalated doses of Ara-C in induction cycles I and II. Evaluation of G-CSF priming in induction cycles I and II. Evaluation of the effect of marrow ablative chemotherapy followed by autologous peripheral blood stem cell transplantation in patients with intermediate or poor risk in CR in comparison to conventional consolidation chemotherapy.

Evaluation of the effect of allogeneic sibling or unrelated donor SCT in subgroups of patients with AML of intermediate or poor risk.

Patient population:

patients with AML (except FAB M3 or t(15;17)), RAEB or RAEB-t with IPSS >= 1.5, previously untreated, age 18-60 years (incl.)

Study design:

prospective, multicenter, randomized with randomization up front for induction treatment with conventional dose or high dose Ara-C, and randomization between yes or no G-CSF priming, and randomization of patients in CR with intermediate or poor risk without a suitable donor between auto PBSCT and consolidation chemotherapy.

Duration of treatment:

expected duration of induction cycles I and II inclusive evaluation is about 3 months. Consolidation treatment will take an additional 1-3 months.

Doel van het onderzoek

The 3 hypotheses to be tested are that the outcome in:

1. The high dose arm B is better than in the low dose arm A;

2. The G-CSF arm is better than in the non-G-CSF arm;

3. The PBSCT arm 2 is better than the chemotherapy cycle III arm 1.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

Patients will be randomized on entry for induction between:

Arm A:

1. Cycle I: idarubicin and conventional dose cytarabine;

2. Cycle II: amsacrine and intermediate dose cytarabine;

Arm B:

1. Cycle I: idarubicin and intermediate dose cytarabine;

2. Cycle II: amsacrine and high dose cytarabine;

A second randomization for induction will involve yes or no priming with G-CSF during chemotherapy of induction cycles I and II.

All CR patients will be distinguished according to good risk, intermediate risk, and poor risk features:

1. Good risk patients will receive a third cycle of chemotherapy (cycle III: mitoxantrone plus etoposide) and will not be randomized.

2. Intermediate or poor risk patients with age below 55 yrs and with a HLA matched family donor will proceed to allogeneic stem cell transplantation.

3. Poor risk patients with age below 50 yrs without a HLA matched sibling donor, but with a phenotypically matched unrelated donor may proceed to marrow ablative treatment and allogeneic stem cell transplantation as soon as they have entered CR. If patients are already distinguished as poor risk following cycle I and logistically there are no impediments the patient may proceed to Allo SCT as soon as possible after cycle I.

4. All other patients in CR, including patients who refuse stem cell transplantation, will undergo stem cell mobilization with G-CSF and stem cell collection.

Patients with an adequate harvest and meeting the eligibility criteria will be randomized between:

1. Arm 1: chemotherapy cycle III: mitoxantrone and etoposide;

2. Arm 2: busulfan-cyclophosphamide ablation + autologous PBSCT.

Patients who are not eligible for Allo SCT or who do not meet the eligibilty criteria for randomization will receive cycle III as consolidation treatment.

Poor risk patients in PR after cycle II with a HLA matched family donor (and patient’s age

below 55 yrs) or with a phenotypically matched unrelated donor (and patient’s age below 50 yrs) may proceed to allogeneic stem cell transplantation.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age 18-60 years (incl.);

2. Subjects with a cytopathologically.

confirmed diagnosis of (a)AML (M0-M2 and M4-M7, FAB classification), or (b) with refractory anemia with excess of blasts (RAEB) or refractory anemia with excess of blasts in transformation (RAEB-t) with an IPSS score of >=1.5;

3. Patients with therapy-related AML/RAEB/RAEB-t are eligible provided they have not received chemotherapy during the past 6 months. Also patients with biphenotypic leukemia may be included;

4. Subjects with a secondary AML progressing from antecedent myelodysplasia are eligible.

Antecedent MDS refers to a condition of at least 4 month duration;

5. WHO performance status <= 2;

6. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Prior chemotherapy within 6 months of study entry;

2. Relapse of AML or MDS after induction chemotherapy;

3. Prior stem cell transplant;

4. Previous polycythemia rubra vera;

5. Primary myelofibrosis;

6. Blast crisis of chronic myeloid leukemia;

7. AML-FAB type M3 or AML with cytogenetic abnormality t(15;17) or AML with a PML/RAR alpha or a variant RAR alpha fusion gene;

8. Impaired hepatic or renal function as defined by: ALT and/or AST > 3 x normal value, Bilirubin > 3 x normal value, Serum creatinine > 3 x normal value (after adequate hydration), (unless these are most likely caused by AML organ infiltration);

9. Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, etc.);

10. Cardiac dysfunction as defined by: myocardial infarction within the last 6 months of study entry, or reduced left ventricular function with an ejection fraction <=50% as measured by MUGA scan or echocardiogram (another method for measuring cardiac function is acceptable), unstable angina, unstable cardiac arrhythmias;

11. Pregnancy.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	02-01-2001
Aantal proefpersonen:	800
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	06-09-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL193

Register	ID
NTR-old	NTR230
Ander register	: Ho42
ISRCTN	ISRCTN38648181

Resultaten

Samenvatting resultaten

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