Randomized study with a run-in feasibility phase to assess the added value of Clofarabine in combination with standard remission-induction chemotherapy in patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or myelodysplasia (MDS) (RAEB with IPSS =>1.5).

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22750

Source
NTR

Brief title
HOVON 102 AML

Health condition

Acute Myeloid leukemia (AML), RAEB

Sponsors and support

Primary sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)

P/a HOVON Data Center
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Source(s) of monetary or material Support: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Koningin Wilhelmina Fonds (KWF)
Genzyme

Intervention

Outcome measures

Primary outcome

Part A:

To determine the feasibility of Clofarabine when given at three possible dose levels together with standard induction cycles I and II in patients with AML/ RAEB with IPSS=>1.5 in a prospective comparison to standard induction cycles I and II without Clofarabine.

Part B:

To evaluate the effect of Clofarabine at the selected feasible dose level when combined with remission induction chemotherapy cycles I and II as regards clinical outcome ("event-free survival") in comparison to remission induction cycles I and II with no addition of Clofarabine in a phase III study.

Secondary outcome

Part A:

To investigate the clinical efficacy of Clofarabine in combination with remission induction chemotherapy cycles I and II with regard to complete remission rate at different dose levels of Clofarabine.

Part B:

1. To investigate the clinical efficacy of Clofarabine with regard to the complete remission

rate, disease free survival (DFS), risk of relapse and overall survival (OS) when combined with remission induction chemotherapy cycles I and II in all patients;

2. To investigate the clinical efficacy of Clofarabine when combined with remission induction chemotherapy cycles I and II in molecularly and cytogenetically distinguishable subsets with regard to the complete remission rate, disease free survival (DFS), risk of relapse and overall survival (OS);

3. To investigate the tolerance and toxicity of Clofarabine in combination with remission induction chemotherapy cycles I and II;

4. To assess the effect of Clofarabine on peripheral CD34 cell numbers for autologous peripheral blood transplantation;

5. To determine the prognostic value of molecular markers and gene expression profiles of the leukemia assessed at diagnosis;

6. To evaluate the treatment effects according minimal residual disease (MRD) measurements following therapy by standardized sampling of marrow/blood;

7. To evaluate the outcome of allogeneic sibling or unrelated donor SCT and autologous SCT in cytogenetically and molecularly defined and prognostic subgroups of patients.

Study description

Background summary

Study phase:

Phase III.

Study objective:

Part A:
To determine the feasibility of Clofarabine when given at three possible dose levels together with standard induction cycles I and II in patients with AML/ RAEB with IPSS=>1.5 in a prospective comparison to standard induction cycles I and II without Clofarabine.

Part B:
To evaluate the effect of Clofarabine at the selected feasible dose level when combined with remission induction chemotherapy cycles I and II as regards clinical outcome ("event-free survival") in comparison to remission induction cycles I and II with no addition of Clofarabine in a phase III study.

Patient population:

Patients with previously untreated AML (except acute promyelocytic leukemia) or MDS RAEB with IPSS => 1.5, age 18-65 years.

Study design:

Part A: Comparative, randomized feasibility study of remission induction chemotherapy combined with Clofarabine at three possible dose levels 10, 15, 20 mg/m2 given intravenously for 5 days.

Part B: Multicenter, phase III study at the selected feasible dose level of Clofarabine in a prospective randomized approach between Clofarabine combined with two induction cycles of chemotherapy versus the same chemotherapy with no addition of Clofarabine.

Duration of treatment:

Expected duration of 2 induction cycles inclusive evaluation is approximately 3 months.
Consolidation treatment will take an additional 1-3 months.
All patients will be followed until 10 years after randomization.

Study objective

The hypothesis to be tested is that arm B is tolerable and that the outcome in arm B is better than in arm A.

Study design

1. At entry;

2. After each induction cycle;

3. After cycle III, autoSCT or alloSCT;

4. During follow up: every 6 months.

Intervention

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, conventional dose cytarabine and assigned dose of Clofarabine;

2. Cycle II: amsacrine, conventional dose cytarabine and assigned dose Clofarabine.

Contacts

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Eligibility criteria

Inclusion criteria

1. Age 18-65 years, inclusive;

2. Subjects with:

A. A cytopathologically confirmed diagnosis of AML according WHO classification (excluding acute promyelocytic leukaemia) or;

B. A diagnosis of refractory anemia with excess of blasts (RAEB) and IPSS score =>1.5 or;

C. Patients with therapy-related AML/RAEB or;

D. Patients with biphenotypic leukemia (Appendices A1 and A2).

3. Adequate renal and hepatic function tests as indicated by the following laboratory values:

A. Serum creatinine =<1.0 mg/dl (=< 88.7 micromol/L); if serum creatinine >1.0 mg/dl (>88.7 micromol/L), then the glomerular filtration rate (GFR) must be >60 ml/min/1.73 m2 as calculated by the Modification of Diet in Renal Disease equation where the predicted GFR (ml/min/1.73 m2) = 186 x (Serum Creatinine in mg/dl)^-1.154 x (age in years)^-0.203 x (0.742 if patient is female) x (1.212 if patient is black).
NOTE: if serum creatinine is measured in micromol/L, recalculate it in mg/dl according to the equation: 1 mg/dl = 88.7 micromol/L) and used above mentioned formula;

B. Serum bilirubin =<1.5 x upper limit of normal (ULN);

C. Aspartate transaminase (AST)/alanine transaminase (ALT) =<2.5 x ULN;

D. Alkaline phosphatase =<2.5 x ULN.

4. WHO performance status 0, 1 or 2 (see Appendix I);

5. Written informed consent.

Exclusion criteria

1. Acute promyelocytic leukaemia;

2. Previous treatment for AML or RAEB, except hydroxyurea;

3. Concurrent history active malignancy in two past years prior to diagnosis except for:

A. Basal and squamous cell carcinoma of the skin;

B. In situ carcinoma of the cervix.

4. Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, pulmonary disease etcetera);

5. Cardiac dysfunction as defined by:

A. Myocardial infarction within the last 6 months of study entry, or;

B. Reduced left ventricular function with an ejection fraction < 50% as measured by MUGA scan or echocardiogram (another method for measuring cardiac function is acceptable), or;

C. Unstable angina, or;

D. Unstable cardiac arrhythmias.

6. Pregnant or lactating females;

7. Unwilling or not capable to use effective means of birth control.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	25-01-2010
Enrollment:	800
Type:	Anticipated

Ethics review

Positive opinion

Date:	29-01-2010
Application type:	First submission

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	NL2070
NTR-old	NTR2187
Other	HOVON : HO102
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A