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).

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22750

Bron
NTR

Verkorte titel
HOVON 102 AML

Aandoening

Acute Myeloid leukemia (AML), RAEB

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
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Overige ondersteuning: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Koningin Wilhelmina Fonds (KWF)
Genzyme

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

1. At entry;

2. After each induction cycle;

3. After cycle III, autoSCT or alloSCT;

4. During follow up: every 6 months.

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, conventional dose cytarabine and assigned dose of Clofarabine;

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	25-01-2010
Aantal proefpersonen:	800
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	29-01-2010
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	NL2070
NTR-old	NTR2187
Ander register	HOVON : HO102
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A