Randomized study to assess the added value of Laromustine 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)

Gepubliceerd: 15-09-2008 Laatst bijgewerkt: 18-08-2022

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-OMON26145

Bron
NTR

Verkorte titel
HOVON 92 AML

Aandoening

Acute Myeloid leukemia (AML), RAEB

Ondersteuning

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

Overige ondersteuning: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Koningin Wilhelmina Fonds (KWF)
VION pharmaceuticals, Inc.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Part A:
The assessment of DLT and duration of myelosuppression of the combination of Laromustine at three selected dose levels.
Part B:
Event-free survival (EFS) in relation to the induction treatment arms with and without Laromustine (i.e., time from registration to induction failure, death or relapse whichever occurs first).

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase:

phase III

Study objective:

Part A:

To determine the feasibility of Laromustine 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 Laromustine

Part B:

To evaluate the effect of Laromustine 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 Laromustine 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 Laromustine at three possible dose levels 200, 300, 400 mg/m2.

Part B:

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

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

-At entry

-After each induction cycle

-After cycle III, autoSCT or alloSCT

-During follow up: every 6 months

Onderzoeksproduct en/of interventie

Patients will be randomized on entry for induction between:

Arm A:

Cycle I: idarubicin and conventional dose cytarabine

Cycle II: amsacrine and intermediate dose cytarabine

Arm B:

Cycle I: idarubicin, conventional dose cytarabine and assigned dose of Laromustine

Cycle II: amsacrine, conventional dose cytarabine and assigned dose Laromustine

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

- Good risk patients will receive a third cycle of chemotherapy (cycle III: mitoxantrone plus etoposide).

- Intermediate or poor risk patients with a HLA matched family donor will proceed to allogeneic stem cell transplantation.

- Poor risk patients 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.

- 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 who are not eligible for Allo SCT or auto SCT will receive cycle III as consolidation treatment.

Poor risk patients in PR after cycle II with a HLA matched family donor or with a phenotypically matched unrelated donor may proceed to allogeneic stem cell transplantation.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age 18-65 years, inclusive

2. Subjects with

- a cytopathologically confirmed diagnosis of AML according WHO classification (excluding acute promyelocytic leukaemia) or

- a diagnosis of refractory anemia with excess of blasts (RAEB) and IPSS score >= 1.5 or

- patients with therapy-related AML/RAEB or

- patients with biphenotypic leukemia (Appendices A1 and A2).

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

4. Written informed consent

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1. During part A of the study patients with a good risk AML, if already known at randomisation. These patients will be treated outside the study according to the control arm.

2. Acute promyelocytic leukaemia

3. Previous treatment for AML or RAEB, except hydroxyurea

4. Impaired hepatic or renal function as defined by:

- ALT and/or AST > 3 x Upper Limit of Normal (ULN), or

- Bilirubin > 3 x ULN, or

- Serum creatinine> 3 x ULN (after adequate hydration), unless these are most likely caused by AML organ infiltration,

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

6. 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), or

- Unstable angina, or

- Unstable cardiac arrhythmias

7. Pregnant or lactating females

8. Impossibility to stop Disulfiram (Antabuse) and metronidazol (Flagyl) 24 hours prior to study treatment. (Please note that this medication must be stopped 24 hours prior to study treatment.)

9. 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:	01-10-2008
Aantal proefpersonen:	800
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	15-09-2008
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	NL1386

Register	ID
NTR-old	NTR1446
Ander register	: MEC-2008-216
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A