Randomized study with a run-in dose-selection phase to assess the added value of lenalidomide in combination with standard remission-induction chemotherapy and post-remission treatment in patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or high risk myelodysplasia (MDS) (IPSS-R risk score > 4.5)

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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 gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20903

Bron
Nationaal Trial Register

Verkorte titel
HOVON 132 AML

Aandoening

Acute Myeloid Leukemia (AML), myelodysplasia (MDS), Lenalidomide

Ondersteuning

Primaire sponsor: HOVON Data Center
Overige ondersteuning: Genzyme Corporation, KWF kanker bestrijding, HOVON

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Part A-run-in: Lenalidomide dose level selection
DLT and duration of myelosuppression of induction treatment with or without lenalidomide for each of the distinct predefined dose levels

Part A: Induction - Efficacy
EFS after induction treatment with or without lenalidomide (i.e., time from registration to induction failure, death from any cause or relapse whichever occurs first)

Part B: Maintenance - Efficacy
Cumulative incidence of relapse (CIR) after second randomization (maintenance treatment with lenalidomide or observation only)

Toelichting onderzoek

Achtergrond van het onderzoek

Study design
Phase III randomized trial for remission
induction as well as for the maintenance starting with a dose selection run-in phase.

Patient population
Patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or myelodysplasia (MDS) with IPSS-R > 4.5.

Intervention
First, we will establish in a randomized run-in study the dose level of lenalidomide in addition to the standard induction treatment of idarubicin/cytarabine (cycle I) and daunorubicine/cytarabine (cycle II) (part A-run-in).
Following the dose-selection phase the study will continue as a randomized study for induction therapy (part A).
Subsequently, we will also investigate the effect of lenalidomide maintenance treatment (10 mg/day) by randomization to be administered in first CR.

Duration of treatment
Patients will receive an induction treatment of 2-3 months. If eligible for the second part of the study, patients in the maintenance arm will receive maintenance therapy for 7 to 8 months.
Subsequently, patients will be followed until 10 years after registration for the phase III trial.

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 of alloSCT
4. Before start each maintenance cycle or every 5 weeks
5. During follow up: every 6 months

Onderzoeksproduct en/of interventie

1. A randomized run-in study to establish the dose level of lenalidomide in addition to the standard induction treatment of idarubicin/cytarabine (cycle I) and daunorubicine/cytarabine (cycle II) (part A-run-in).
2. Following the dose-selection phase the study will continue as a randomized study for induction therapy (part A).
3. Subsequently, the effect of lenalidomide maintenance treatment (10 mg/day) by randomization to be administered in first CR will be investigated.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

First randomization:
1. Age 18-65 years, inclusive
2. Patients with
a. A diagnosis of AML and related precursor neoplasms according to WHO 2008 classification (excluding acute promyelocytic leukemia) including secondary AML (after an antecedent hematological disease (e.g. MDS) and therapy-related AML), or
b. Acute leukemia's of ambiguous lineage according to WHO 2008 or
c. A diagnosis of refractory anemia with excess of blasts (MDS) and IPSS-R score > 4.5
3. WHO performance status 0, 1 or 2
4. Sampled bone marrow and/ blood cells at diagnosis for centralized molecular analysis, MRD evaluation and biobanking, unless in case of a dry marrow tap with no possibility to collect marrow cells. In cases of marrow tap failure only blood cells will be sampled.
5. Adequate renal and hepatic functions unless clearly disease related as indicated by the following laboratory values:
a. Serum creatinine ≤1.0 mg/dL (≤88.7 µmol/L); if serum creatinine >1.0 mg/dL (>88.7 µmol/L), then the estimated glomerular filtration rate (GFR) must be >60 mL/min/1.73 m2 as calculated by the Modification of Diet in Renal Disease equation where 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 umol/L, recalculate it in mg/dL according to the equation: 1 mg/dL = 88.7 umol/L) and use above mentioned formula.
b. Serum bilirubin ≤2.5 x upper limit of normal (ULN)
c. Aspartate transaminase (AST) ≤ 2.5 x ULN
d. Alanine transaminase (ALT) ≤ 2.5 x ULN
e. Alkaline phosphatase ≤ 2.5 x ULN
6. Written informed consent
7. Ability and willingess to adhere to the lenalidomide Pregnancy Prevention Program

Second randomization:
1. CR or CRi
2. Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L
3. Platelet count ≥ 75 x 10^9/L
4. Serum creatinine clearance ≥ 30 ml/min or estimated glomerular filtration rate (GFR)

>60mL/min/1.73 m2
5. Total bilirubin ≤ 2.5 x ULN
6. AST ≤ 2.5 x ULN
7. ALT ≤ 2.5 x ULN

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

First randomization:
1. Previous therapy with lenalidomide
2. Acute promyelocytic leukemia
3. Myeloproliferative neoplasia
4. Previous treatment for AML or high risk MDS (IPSS-R > 4.5), except hydroxyurea
5. Concurrent history of 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
6. Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, pulmonary disease etcetera)
7. 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 MUG scan or echocardiogram or
c. Unstable angina, or
d. Unstable cardiac arrhythmias
8. Pregnant or lactating females
9. Unwilling or not capable to use effective means of birth control
10. Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule

Second randomization:
1. Severe cardiac dysfunction (NYHA classification II-IV, see appendix G)
2. Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix F)
3. Severe neurological or psychiatric disease
4. Serious active infections
5. Previous serious toxicities related to the use of lenalidomide
6. CMV reactivation, which is not responsive to first line valganciclovir

Onderzoeksopzet

Opzet

Type: Interventie onderzoek

Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-03-2014
Aantal proefpersonen:	972
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	14-01-2014
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	NL4231

Register	ID
NTR-old	NTR4376
Ander register	2013-002843-26 : HO132 AML

Resultaten

Samenvatting resultaten
N/A