A randomized phase II multicenter study with a safety run-in to assess the tolerability and efficacy of the addition of oral lenalidomide to standard induction therapy in AML and RAEB ≥ 66 years and very poor risk AML ≥ 18 years.

No registrations found.

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

Summary

ID

NL-OMON25046

Source
NTR

Brief title
HOVON 103 AML Lenalidomide

Health condition

Acute Myeloid leukemia (AML), RAEB

Sponsors and support

Primary sponsor: HOVON foundation
Source(s) of monetary or material Support: Cellgene, Koningin Wilhelmina Fonds (KWF), HOVON

Intervention

Outcome measures

Primary outcome

Part A of the study (if applicable):

1. To assess the safety and tolerability of lenalidomide added to standard induction chemotherapy for AML (frequency and severity of toxicities and the durations of neutropenia and thrombocytopenia) and select the feasible dose level for part B of the study;

2. To assess in a randomized comparison the effect of lenalidomide on the CR rate.

Part B of the study:

1. To assess the safety and tolerability of lenalidomide added to standard induction chemotherapy for AML (frequency and severity of toxicities and the durations of neutropenia and thrombocytopenia) as regards the selected dose level of lenalidomide;

2. To assess in a randomized comparison the effect of the in Part A selected dose of lenalidomide on the CR rate.

Secondary outcome

For part B:

1. To determine the efficacy profile (event free survival (EFS), disease free survival (DFS) and overall survival (OS)) associated with the two therapy regimens;

2. To measure MRD by immunophenotyping in relation to clinical response parameters;

3. To identify potential biomarkers predictive of response, EFS, DFS and OS by exploratory genomic analysis (microarray, gene mutations).

Study description

Background summary

Randomized phase II study.

Primary objectives:

Part A of the study (if applicable):

1. To assess the safety and tolerability of lenalidomide added to standard induction chemotherapy for AML (frequency and severity of toxicities and the durations of neutropenia and thrombocytopenia) and select the feasible dose level for part B of the study;

2. To assess in a randomized comparison the effect of lenalidomide on the CR rate.

Part B of the study:

1. To assess the safety and tolerability of lenalidomide added to standard induction chemotherapy for AML (frequency and severity of toxicities and the durations of neutropenia and thrombocytopenia) as regards the selected dose level of lenalidomide;

2. To assess in a randomized comparison the effect of the in Part A selected dose of lenalidomide on the CR rate.

Secondary objectives:

Part B of the study:

1. To determine the efficacy profile (event free survival
(EFS), disease free survival (DFS) and overall survival (OS)) associated with the two therapy regimens;

2. To measure MRD by immunophenotyping in relation to clinical response parameters;

3. To identify potential biomarkers predictive of response, EFS, DFS and OS by exploratory genomic analysis (microarray, gene mutations).

Patient population:

Patients with AML (except FAB M3) or RAEB with IPSS ≥ 1.5, previously untreated, age ≥ 66 yrs and very poor risk AML, age ≥ 18 yrs.

Study design:

This is a prospective, open label, multicenter study that is conducted in the frame of a masterprotocol with multiple parallel randomized phase II studies. The scheme of this design

consists of one arm with the standard treatment for AML as compared to various arms with experimental treatments.

Patients in this study are treated with standard induction chemotherapy with or without lenalidomide. During part A of the study the feasibility of combining lenalidomide with DNR/Cytarabine will be evaluated and the dose of lenalidomide will be selected. Decisions regarding dose escalation, continuation with starting dose level or stopping, are based on the incidence of DLT (dose limiting toxicity: death within 31 days of start cycle I and before start cycle II).

During part B of the study that will be conducted with the selected dose of lenalidomide, the CR rate (primary endpoint) and secondary endpoints (EFS, DFS, OS, as well as MRD and genomic profiling) will be assessed.

Duration of treatment:

Expected duration of 2 cycles of induction chemotherapy with or without lenalidomide including evaluation is about 3 months.

Study objective

To assess the tolerability and efficacy of the addition of oral lenalidomide to standard induction therapy.

Study design

Clinical and laboratory evaluations:

1. At entry;

2. After each induction cycle;

3. During Follow Up, every 6 months.

Intervention

1. Arm A: Cycle I: Dauno/Cytarabine, cycle II: Cytarabine;

2. Arm B: Cycle I: Dauno/Cytarabine/Lenalidomide, cycle II: Cytarabine/Lenalidomide.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients eligible for standard chemotherapy;

2. Patients ≥ 66 years with a cytopathologically confirmed diagnosis according WHO classification of:

A. AML (not APL) or;

B. Refractory anemia with excess of blasts (RAEB) with an IPSS score ≥ 1.5.

OR

3. Patients of any age ≥ 18 years with a cytopathologically confirmed diagnosis according WHO classification of very poor risk AML;

4. Subjects with secondary AML progressing from antecedent (at least 4 months duration) myelodysplasia are also eligible;

5. SGOT (AST) and SGPT (ALT) ≤ 1.5 x the upper limit of the normal range (ULN) at the laboratory where the analyses were performed;

6. Total serum bilirubin level ≤ 1.5 x the ULN at the laboratory where the analysis was performed;

7. Serum creatinine concentration ≤ 1.5 x ULN at the laboratory where the analysis was performed;

8. WHO performance status ≤ 2;

9. Written informed consent;

10. Female patients of childbearing potential must have a negative serum pregnancy test within 2 weeks prior to enrollment;

11. Male and female patients must use an effective contraceptive method during the study and for a minimum of 6 months after study treatment.

Exclusion criteria

1. Acute promyelocytic leukemia;

2. Patients previously treated for AML (any antileukemic therapy including investigational agents)- a short treatment period (< 2 weeks) with Hydroxyurea is allowed;

3. Past or current history (within the last 2 years prior to randomization) of malignancies except for the indication under this study and curatively treated:

A. Basal and squamous cell carcinoma of the skin;

B. In situ carcinoma of the cervix.

4. Blast crisis of chronic myeloid leukemia;

5. Clinically significant (i.e. active) cardiovascular disease, for example cerebrovascular accidents (≤ 6 months prior to randomization), myocardial infarction (≤ 6 months prior to randomization), unstable angina, New York Heart Association (NYHA) grade II or greater congestive heart failure;

6. Patients with a history of non-compliance to medical regimens or who are considered unreliable with respect to compliance;

7. Patients with any serious concomitant medical condition which could, in the opinion of the investigator, compromise participation in the study;

8. Patients who have senile dementia, mental impairment or any other psychiatric disorder that prohibits the patient from understanding and giving informed consent;

9. Pregnant or lactating patients;

10. Current concomitant chemotherapy, radiation therapy, or immunotherapy other than as specified in the protocol.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-04-2010
Enrollment:	200
Type:	Anticipated

Ethics review

Positive opinion

Date:	19-04-2010
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	NL2170
NTR-old	NTR2294
Other	Hovon : HO103LEN
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A