A randomized phase II multicenter study with a safety run-in to assess the tolerability and efficacy of the addition of oral selinexor (KPT-330) to standard induction chemotherapy in AML and high risk myelodysplasia (MDS) (IPSS-R > 4.5) in patients aged >66 years .

Gepubliceerd: 15-06-2016 Laatst bijgewerkt: 18-08-2022

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

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

Samenvatting

ID

NL-OMON25024

Bron
NTR

Verkorte titel
HOVON 103 AML Selinexor

Aandoening

Acute Myeloid Leukemia (AML), MDS

Ondersteuning

Primaire sponsor: HOVON Data Center
Overige ondersteuning: KWF, HOVON, Karyopharm Therapeutics inc.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

• Incidence of DLT (part A)
• The effect of selinexor on the CR rate (part B of study)

Toelichting onderzoek

Achtergrond van het onderzoek

Randomized phase II study.

Primary objectives:

For part A of the study (if applicable):

1. To assess the safety and tolerability of selinexor 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

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

For part B:

1. To assess the safety and tolerability of selinexor 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 selinexor

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

Secondary objectives:

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)

Patient population:

Patients with AML or high risk MDS with IPSS-R > 4.5, previously untreated, age ≥ 66 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 selinexor. During part A of the study the feasibility of combining selinexor with DNR/Cytarabine will be evaluated and the dose of selinexor 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 selinexor, 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 selinexor including evaluation is about 3 months.

Doel van het onderzoek

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

Onderzoeksopzet

Clinical and laboratory evaluations:

1. At entry;

2. After each induction cycle;

3. During Follow Up, every 6 months.

Onderzoeksproduct en/of interventie

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

2. Arm C: Cycle I: Dauno/Cytarabine/Selinexor, cycle II: Cytarabine/Selinexor.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• Patients eligible for standard chemotherapy.

• Patients 66 years and older

• Patients with:

o 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

o acute leukemia's of ambiguous lineage according to WHO 2008 or

o a diagnosis of refractory anemia with excess of blasts (MDS) and IPSS-R > 4.5

• Adequate renal and hepatic functions unless clearly disease related as indicated by the following laboratory values:

o 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 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 µmol/L, recalculate it in mg/dL according to the equation: 1 mg/dL = 88.7 µmol/L and use the above mentioned formula.

o Serum bilirubin ≤ 2.5 x upper limit of normal (ULN)

o Aspartate transaminase (AST) ≤ 2.5 x ULN

o Alanine transaminase (ALT) ≤ 2.5 x ULN

o Alkaline phosphatase ≤ 2.5 x ULN

• WHO performance status 0, 1 or 2

• Written informed consent.

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Acute promyelocytic leukemia

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

• Concurrent history of active malignancy in the two past years prior to diagnosis except for:

o Basal and squamous cell carcinoma of the skin

o in situ carcinoma of the cervix

• Blast crisis of chronic myeloid leukemia

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

• Cardiac dysfunction as defined by:

o Myocardial infarction within the last 6 months of study entry, or

o Reduced left ventricular function with an ejection fraction < 50% ad measured by MUG scan or echocardiogram or

o Unstable angina or

o New York Heart Association (NYHA) grade II or greater congestive heart failure (see Appendix I) or

o Unstable cardiac arrthythmias

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

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

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

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

• Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel

Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-07-2016
Aantal proefpersonen:	230
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	15-06-2016
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	NL5748
NTR-old	NTR5902
Ander register	2014-001876-75 : HO103SEL

Resultaten

Samenvatting resultaten
N/A