A phase I/II feasibility study of panobinostat alone and the combination of panobinostat and decitabine prior to donor lymphocyte infusion in recipients of allogeneic stem cell transplantation with poor and very poor risk AML

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Primary objective:Part I- To asses the feasibility of addition of post-transplant panobinostat combined with decitabine to a regimen of T-cell replete RIC alloHSCT in patients with very poor risk AML/RAEB, and select the dose level for the phase II...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON50408

Source
ToetsingOnline

Brief title
HOVON 116 AML

Condition

- Leukaemias

Synonym
acute myeloid leukemia (AML), myelodysplastic syndrome

Research involving

Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: KWF;Novartis,Novartis

Intervention

Keyword: (very) poor risk AML, decitabine, panobinostat

Outcome measures

Primary outcome

Part I

• Feasibility of protocol treatment as defined by the number of DLTs during the

first cycle PNB/DAC

Part II

• Feasibility of protocol treatment as defined by percentage of patients

actually receiving treatment according to protocol up to eligibility for the

first DLI within 115 days.

Part III

• Feasibility of protocol treatment as defined by percentage of patients

actually receiving treatment according to protocol up to eligibility for the

first DLI within 115 days.

Secondary outcome

• Response to first cycle PNB/DAC

• Response to second cycle PNB/DAC

• Percentage of successful donor searches

• Percentage of patients who received alloHSCT

• Best response on protocol

• Engraftment after alloHSCT

• Incidence and severity of acute and chronic GvHD

• (Serious) adverse events

• Overall survival (OS) from registration and start of protocol treatment

• PFS from registration and from start of protocol treatment

Study description

Background summary

This study will explore the feasibility of post-transplant panobinostat combined with decitabine after reduced intensity conditioning (RIC) alloHSCT in patients with AMLor RAEB with IPSS >= 1.5 (AML/RAEB). While recent studies showed that the allogeneic graft-versus-leukemia (GVL) effect is clearly operational in (very) poor risk AML, relapse rates after alloHSCT in those patients are still unacceptably high, with no curative options left. Based on recent experience by others exploring the combination of panobinostat and decitabine in AML patients and by different groups exploring post-transplant chemotherapy including panobinostat, we here propose to study the combination of panobinostat and decitabine after alloHSCT to be followed by donor lymphocyte infusions to optimally profit from the allogeneic GVL-effect.
Feasibility in this study will be defined by the completion of protocol treatment up to eligibility for a first dose of DLI in at least 70% of patients starting protocol treatment, without dose limiting toxicity up to that point of time.
Given recent findings showing favorable results of PNB alone, also the feasibility and efficacy of PNB monotherapy will be investigated.

Study objective

Primary objective:
Part I
- To asses the feasibility of addition of post-transplant panobinostat combined with decitabine to a regimen of T-cell replete RIC alloHSCT in patients with very poor risk AML/RAEB, and select the dose level for the phase II part of the study.
Part II
-Assess the feasibility of addition of post-transplant panobinostat combined

with decitabine to a regimen of T-cell depleted RIC alloHSCT and DLI in patients with (very) poor-risk AML
Part III
-Assess the feasibility of addition of post-transplant panobinostat to a regimen of T-cell depleted RIC alloHSCT and DLI in patients with (very) poor-risk AML

Secondary objectives:
-Assess efficacy in terms of complete remission rate, overall and progression free survival.
-Assess toxicity

Study design

Multicenter, prospective phase I/II trial

Intervention

During part I of the trial the combination of panobinostart en decitabine will be tested at 4 dose levels, the first being panobinstat alone.

In part II, patients will be treated with T cell replete RIC alloHSCT, followed by 2 cycles of panobinostat and decitabine (PNB/DAC), followed by DLI at 3 months after alloHSCT, followed by another 2 cycles of PNB/DAC and if no GvHD a second DLI (and third DLI).

In part III, patients will be treated with T cell replete RIC alloHSCT, followed by 2 cycles of panobinostat (PNB) followed by DLI at 3 months after alloHSCT, followed by another 2 cycles of PNB and if no GvHD a second DLI (and third DLI).

Study burden and risks

Although alloHSCT is standard care in (very) poor-risk AML/RAEB, the incidence of relapse after alloHSCT is high, leaving patients without curative options.
In this protocol post-transplant panobinostat and azacitidine followed by donor lymphocyte infusions is evaluated. The aim is to prevent early relapse prior to DLI and to optimally profit from the allogeneic Graft versus Leukemia effect, to improve outcome.
The risks associated with this procedure are opportunistic infections associated with neutropenia and lymphopenia, that may occur after PNB/DAC, as compared to standard alloHSCT.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Patients with poor-risk or very poor-risk AML or RAEB with IPSS >= 1.5 ,
-Eligibility for continuation with intensive induction/consolidation chemotherapy
-Eligible for allogeneic donor search (related/unrelated)
-18-70 years, inclusive
-Written informed consent

Exclusion criteria

- History of active malignancy during the past 2 years with the exception of basal carcinoma of the skin or carcinoma *in situ* of the cervix or breast

- Known HIV-positivity
- Pregnant or breast-feeding female patients

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-01-2014
Enrollment:	115
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dacogen
Generic name:	decitabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	panobinostat

Ethics review

Approved WMO

Date:	19-09-2013
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-11-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	15-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2012-003344-74-NL
CCMO	NL41789.078.13