A phase I/II feasibility study of 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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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20360

Bron
NTR

Verkorte titel
HOVON 116 AML

Aandoening

(very) poor risk AML or RAEB with IPSS >= 1.5

Ondersteuning

Primaire sponsor: HOVON
Overige ondersteuning: KWF, HOVON, Novartis, Janssen-Cilag

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Part I
To asses the safety and feasibility of post-transplant panobinostat combined with decitabine to a regimen of Tcell replete RIC alloHSCT and DLI and select the dose
level for part II of the study.
Part II
Assess the feasibility and efficacy of post-transplant panobinostat combined with decitabine to a regimen of Tcell replete RIC alloHSCT and DLI in patients with (very)
poor-risk AML.

Toelichting onderzoek

Achtergrond van het onderzoek

N/A

Doel van het onderzoek

This study will explore the feasibility of post-transplant panobinostat combined with decitabine after reduced intensity conditioning (RIC) alloHSCT in patients with (very) poor-risk AMLor RAEB with IPSS >= 1.5 (AML/RAEB). While recent studies showed that the allogeneic graftversus-
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 (PNB) and decitabine (DAC) in AML patients and by different groups exploring posttransplant chemotherapy including panobinostat, we here propose to study the combination of panobinostat and decitabine after alloHSCT to be followed by DLI 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.

Onderzoeksopzet

Time of clinical evaluations:

- Within 2 weeks before alloHSCT

- After alloHSCT

- After PNB/DAC cycle 1

- After PNB/DAC cycle 2

- After PNB/DAC cycle 3

- After PNB/DAC cycle 4

- 9, 12 and 18 months after alloHSCT

- 24 months after alloHSCT, and once a year thereafter.

All patients will be followed until 5 years after registration.

Onderzoeksproduct en/of interventie

Panobinostat combined with decitabine in the setting of RIC-alloHSCT

The setting, framework of RIC-alloHSCT is detailed as follows:

- T cell replete RIC alloHSCT with a short-course posttransplant GvHD prophylaxis consisting of high-dose cyclophosphamide and short-term ciclosporin, 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, followed by

- a second DLI (and third DLI), if no GvHD has developed.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Eligibility for registration:

- Patients with poor-risk or very poor-risk AML or RAEB with IPSS ¡Ý 1.5 , (see appendix D). During the phase I part only very poor-risk patients will be included

- Eligibility for continuation with intensive induction/consolidation chemotherapy

- Eligible for allogeneic donor search (related/unrelated) 18-70 years, inclusive

- Written informed consent

Eligibility for start protocol treatment:

- Poor-risk or very poor-risk AML or RAEB with IPSS >= 1.5. During the phase I part only very poor-risk patients will be included.

- Responsive disease (< 10% blasts at 3 and/or 4 weeks after start of induction cycle II)

- Recovery of mucositis after preceding chemotherapy

- Absence of active opportunistic infections

- Absence of active CNS localisation

- HLA-compatible donor available (8/8 matched unrelated donor or fully matched sibling donor)

- WHO-performance status 0-2

- Written informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Eligibility for registration:

- 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

Eligibility for start protocol treatment:

- Severe cardiac dysfunction (NYHA classification II-IV, see appendix H)

- Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix G)

- Severe neurological or psychiatric disease

- Significant hepatic dysfunction (serum bilirubin or transaminases >= 5 times upper limit of normal)

- Significant renal dysfunction (creatinine clearance < 30 ml/min after rehydration)
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule

- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd

Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-12-2013
Aantal proefpersonen:	100
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	19-11-2013
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	NL4053
NTR-old	NTR4269
Ander register	2012-003344-74 / NL41789.078.13 : HOVON 116 AML
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A