Allogeneic Stem Cell Transplantation after Reduced Intensity Conditioning for High-risk Relapsed or Refractory CLL

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Evaluation of the effect of salvage therapy with R-DHAP followed by reduced-intensity conditioning and allogeneic stem cell transplantation from a sibling or unrelated donor

Ethical review	-
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON38321

Source
ToetsingOnline

Brief title
HOVON 88 CLL

Condition

- Leukaemias

Synonym
B-CLL

Research involving
Human

Sponsors and support

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

Intervention

Keyword: B-CLL, High Risk, R-DHAP, Reduced Intensity Conditioning Allogeneic stem cell transplatation

Outcome measures

Primary outcome

progression-free survival from registration with progression defined as time to:

a. death due to any cause, or

b. progression or relapse excluding progressive MRD triggering cessation of

immunosuppression or DLI whichever comes first

Secondary outcome

- incidence and severity of tumor lysis during first course of R-DHAP

- response to three courses of R-DHAP including SD;

- percentage of successful donor searches,

- percentage of patients who received alloSCT

- best response on protocol

- engraftment after alloSCT;

- incidence and severity of acute and chronic GVHD;

- toxicity;

- overall survival (OS) from registration;

- response of MRD to immunomodulation (either accelerated cessation of

immunosuppression or DLI)

- response of PD to recommended off-protocol immunomodulation (either

accelerated cessation of immunosuppression or DLI)

- disease status at two years after registration;

- PFS and OS after alloSCT

Study description

Background summary

B-Cell Chronic Lymphocytic Leukemia (CLL) is a heterogeneous disease entity. Survival from diagnosis varies from several years to more than 25 years. The most reliable prognostic factors, i.e. cytogenetic abnormalities and previous antigen-induced activation, only predict in main lines for survival. At the end a large proportion of patients can not be rescued by currently available therapies and die of their disease. These patients can be identified because of:
- refractoriness for fludarabine or relapse within 12 months after the last fludarabine treatment, or
- refractoriness or relapse within two years after combined therapy with fludarabine and an anti-B-cell antibody, or
- having relapsed in the presence of del 17p13.
Two years progression free survival (PFS) in these patients is 25%.
For these patients allogeneic stem cell transplantation (allo SCT) seems to improve survival considerably.

From the published series of patients it became clear that a high disease burden at transplant negatively influences outcome. We therefore aim during donor search at inducing remission or at least stabilization of the disease state. It*s of note that the incidence of severe or opportunistic infections in this phase should be as low as possible to avoid negative influence on the outcome of allo SCT. The R-DHAP regimen was chosen, to which all participating are familiar with for treatment of relapsed aggressive non-Hodgkin*s Lymphoma. The addition of Rituximab is expected to induce higher remission rates similarly as observed in first and second line treatment of B-CLL, while toxicity will not increase.

Study objective

Evaluation of the effect of salvage therapy with R-DHAP followed by reduced-intensity conditioning and allogeneic stem cell transplantation from a sibling or unrelated donor

Study design

Fase II, prospective, multicenter, non randomized
All patients will be treated with at least three courses of R-DHAP while a HLA-identical donor is being searched first among siblings and second, if negative, in the world donor bank. Patients with a donor and responsive or

stable disease (SD) after at least three courses R-DHAP proceed to 'reduced intensity conditioning' (RIC) alloSCT.

Intervention

All patients will be treated with at least three courses of R-DHAP while a HLA-identical donor is being searched first among siblings and second, if negative, in the world donor bank. Patients with a donor and responsive or stable disease (SD) after at least three courses R-DHAP proceed to 'reduced intensity conditioning' (RIC) alloSCT.

Study burden and risks

Known side effects of chemotherapy and alloSCT.
R- DHAP may cause tumor lysis in CLL; prophylaxis is strongly recommended and monitoring during the first week is demanded.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- B-CLL confirmed according to WHO Classification
- Fludarabine refractory, defined as no response or relapse within 12 months after the last administration of fludarabine monotherapy or fludarabine containing regimen, and needing treatment, or; refractory or relapsed and needing treatment and having deletion of 17p13 or; refractory or relapsed within 24 months after the last administration of fludarabine combined with a monoclonal antibody and needing treatment;
- Age 18-70 years inclusive;
- WHO performance status <= 2 (see appendix E);;- HCT-CI <= 2 (see appendix F);
- Written informed consent.

Exclusion criteria

- Intolerance to exogenous protein administration
- Previously treated with DHAP
- Richter*s transformation;
- Suspected or documented CNS involvement by CLL;
- Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease);
- Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix D);
- Severe neurological or psychiatric disease;
- Significant hepatic dysfunction (serum bilirubin or transaminases >= 3 times upper limit of normal) except when caused by leukemic infiltration;
- Significant renal dysfunction (creatinine clearance < 30 ml/min after rehydration);
- History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma;
- Active, uncontrolled infections;
- Patient known to be HIV-positive;
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule;

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):	18-11-2008
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cytarabine
Generic name:	Cytarabine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	Dexametasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Mabthera
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	25-11-2011

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-11-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-04-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-05-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-08-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-03-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2007-005487-28-NL
CCMO	NL23247.068.08