A phase I/ II study. Efficacy and safety of alpha / betaT- /CD19B-cell depleted allogeneic haematopoietic stem cells transplantation in high risk or relapsed acute leukaemia / MDS followed by an innate donor lymphocyte infusion (iDLI).

No registrations found.

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28903

Source
NTR

Brief title
iDLI

Health condition

High risk acute leukemia or MDS or relapse acute leukemia or MDS patients

Sponsors and support

Primary sponsor: UMC Utrecht
Heidelberglaan 100
3584 CX Utrecht

Intervention

Outcome measures

Primary outcome

Feasibility and safety of alpha/ betaT-/CD19 B-cell depleted allo-SCT in high risk or relapsed acute leukaemia / MDS followed by an innate donor lymphocyte infusion (iDLI)
by assessing:

1. Time to neutrophil engraftment;

2. Time to platelet engraftment;

3. Time to donor engraftment (chimerism >95%);

4. Time to red blood cell transfusion independence;

5. Incidence and grade of acute GvHD;

6. Incidence and grade of chronic GvHD;

7. Ability to generate and apply an iDLI;

8. Incidence of infections;

9. Transplant related mortality (TRM).

Secondary outcome

1. Immune reconstitution by counting total number of CD3+ T cells, CD4+ and CD8+ subtyping of T cells, CD3-CD16/56+ (NK cells), alpha / beta T-cells at 3, 6, 12 and 24 months after transplantation;

2. Progression free survival (PFS, i.e. time from transplantation until progression/relapse or death from any cause, whichever comes first);

3. Overall survival (OS) calculated from transplantation. Patients still alive or lost to follow up are censored at the date they were last known to be alive.

Study description

Background summary

Rationale:

Patients suffering from high risk or relapsed leukaemia or high risk MDS can only occasionally be cured with conventional chemotherapy. Allogeneic stem cell transplantation (allo-SCT) has substantially improved the outcome of such patients due to a potent graft versus leukaemia effect after transplantation, but still for the high price of severe and life-threatening GvHD. Also relapses are still observed after allo-SCT. This study aims therefore to improve the outcome of this potent treatment modality by combining T-cell depleted allo-SCT with reduced toxicity and post-allo-SCT immunomodulations in order to enhance the anti-tumor-effect.

Objective:

To test feasibility and safety of alphabetaT-/CD19 B-cell depleted allo-SCT in high risk or relapsed acute leukaemia / MDS followed by an innate donor lymphocyte infusion (iDLI).

Study design:

Phase I/II study.

Study population:

Patients with high risk or relapsed acute leukaemia after high dose chemotherapy in remission and high risk MDS disease with less than 10% blasts in the bone marrow.

Intervention:

Myeloablative or non-myeloablative conditioning regime, alphabetaT-/CD19 B-cell depleted stem cell graft, short immunosuppression with ciclosporin, immunomodulation with zoledronic acid and innate donor lymphocyte infusion (iDLI).

Main study parameters/endpoints:

Feasibility with respect to engraftment, toxicity in terms of incidence of GvHD and infectious complications.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The protocol comprises a different processing of the donor stem cells source followed by innate DLI (iDLI). All other acts, measurements, follow-up and level of care are similar to off-study patients undergoing allo-SCT. The burden of the therapy is associated with the allo-SCT itself which is a necessary therapeutic intervention in all subjects. Possible increased risks of acute (a) and chronic (c) GvHD exist due to the earlier application of immune cells. There is a possible increased risk engraftment failure due to T cell depletion. However, we expect a lower mortality, secure engraftment, and less relapse and infection due to NK- and γδT-cell activity as well as a lower risk of aGvHD and cGvHD.

Study objective

Patients suffering from high risk or relapsed leukaemia or high risk MDS can only occasionally be cured with conventional chemotherapy. Allogeneic stem cell transplantation (allo-SCT) has substantially improved the outcome of such patients due to a potent graft versus leukaemia effect after transplantation, but still for the high price of severe and life-threatening GvHD. Also relapses are still observed after allo-SCT. This study aims therefore to improve the outcome of this potent treatment modality by combining T-cell depleted allo-SCT with reduced toxicity and post-allo-SCT immunomodulations in order to enhance the anti-tumor-effect.

Study design

Date form allo-SCT till 1 year after allo-SCT.

Intervention

Selection of T cells and depletion of B-cell in the alloSCT. After that zolendronic acid administations and iDLI after immunosupressive medication is stopped.
Normally there is no selection of T oor B-cells or IDLI.

Contacts

Public
Heidelberglaan 100
L.C.J. Boome, te
Utrecht 3584 CX
The Netherlands
Scientific
Heidelberglaan 100
L.C.J. Boome, te
Utrecht 3584 CX

The Netherlands

Eligibility criteria

Inclusion criteria

1. Age 18-65 years;

2. Meeting the criteria for a allo-SCT and high risk disease * (see below);

3. WHO performance status ≤ 2;

4. Written informed consent.

*High risk disease as defined by:

1. AML with monosomal karyotype, abnormal 3q26, t(9;22) EVI-1-expression, or complex karyotype in first CR;

2. No CR after first induction cycle chemotherapy;

3. Relapsed AML (in case of second allo-SCT if relapse occurs 6 months after allo-SCT) in second or subsequent CR;

4. MDS with complex karyotype or -7, transfusion dependent or neutropenic with < 10% blasts or in CR after induction therapy;

5. ALL with t(9;22), t(4;11), and other 11q23 abnormalities, and hypodiploidy; complex abnormalities (≥ 5), excluding hyperdiploidy; high WBC at diagnosis (B-ALL > 30x109/l, T-ALL > 100x109/l) in first CR, or no CR after first induction but in CR after rescue chemotherapy;

6. Relapsed ALL (in case of second allo-SCT if relapse occurs 6 months after allo-SCT) in second or subsequent CR.

Exclusion criteria

1. Relapse of allo-SCT within 6 months after allo-SCT;

2. Relapse acute promyelocyten leukemia;

3. Bilirubin and/or transaminases > 2.5 x normal value;

4. Creatinine clearance < 40 ml/min;

5. Cardiac dysfunction as defined by:

A. Unstable angina;

B. Unstable cardiac arrhythmias.

6. Active, uncontrolled infection;

7. HIV positivity.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2011
Enrollment:	30
Type:	Actual

Ethics review

Not applicable

Application type:	Not applicable

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	NL2356
NTR-old	NTR2463
Other	METC / ABR : 10-257 / NL33076.000.10 ;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A