Sequential FLAMSA chemotherapy and T cell depleted reduced intensity conditioning allogeneic stem cell transplantation (TCD FLAMSA-RIC alloSCT) in elderly acute myeloid leukemia and high risk myelodysplasia patients

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• To assess feasibility and safety of a sequential treatment regime in which standard intensive chemotherapy (fludarabin-amsacrin-cytarabin) is directly followed by standard allogeneic stem cell transplantation (T cell depleted RIC alloSCT with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON39744

Source
ToetsingOnline

Brief title
FLAMSA-RIC alloSCT

Condition

- Leukaemias

Synonym
acute myeloid leukemia (AML), leukemia, myelodysplasia (MDS)

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acute Myeloid Leukemia, Allogeneic stem cell transplantation, FLAMSA-RIC, Myelodysplasia

Outcome measures

Primary outcome

• The number of patients eligible for DLI at 6 months after transplantation

• Incidence of non-hematological grade 3-4 toxicity from the start of

chemotherapy until 9 months after transplantation

• Incidence of serious adverse events from the start of chemotherapy until 9

months after transplantation

• Incidence of severe grade 3 or 4 acute GvHD and incidence of extensive

chronic GvHD in the first 9 months after transplantation

• Non-relapse mortality at 3 and 12 months after transplantation

Secondary outcome

• 1-year progression free survival after transplantation

• 1-year overall survival after transplantation

Study description

Background summary

Elderly patients aged over 60 years with AML or high risk MDS have a poor

prognosis, the only way to achieve long term survival is transplantation with an allogeneic donor after achieving complete remission with intensive chemotherapy. Most patients starting with intensive chemotherapy are not transplanted, due to not achieving a complete remission with intensive chemotherapy, due to declining condition during the multiple courses of intensive chemotherapy with long periods of neutropenia or due to early relapse after chemotherapy. Patients that are in remission after the first induction chemotherapy and stay in remission after the second induction chemotherapy are good candidates for standard reduced intensity conditioning allogeneic stem cell transplantation. Patients that are not in remission after the first induction chemotherapy (50% of patients starting with induction chemotherapy) have a poor prognosis even if they are treated with the intention to reach allogeneic stem cell transplantation. They either stop with the chemotherapy treatments due to declining condition, they relapse before transplantation, or relapse early after transplantation.

In this study we want to explore the feasibility of the sequential use of FLAMSA chemotherapy and our standard T cell depleted reduced intensity conditioning allogeneic stem cell transplantation, followed by our standard donor lymphocyte infusion regimen for high risk disease starting at 3 months after transplantation. This treatment regimen combines a well known effective induction regimen (amsacrine-cytarabine) with a relatively non-toxic allogeneic transplantation conditioning regimen in combination with donor lymphocyte infusion at 3 and 6 months after transplantation.

With this TCD FLAMSA-RIC alloSCT regimen we hope to cure patients that are not in remission after the first induction therapy, a patient group known to have a poor prognosis when treated with further chemotherapy courses followed by allogeneic stem cell transplantation. Patients in remission after induction chemotherapy and in continuous remission after consolidation therapy have a good curative chance with standard RIC alloSCT and will therefore not be included in the study.

Study objective

• To assess feasibility and safety of a sequential treatment regime in which standard intensive chemotherapy (fludarabin-amsacrin-cytarabin) is directly followed by standard allogeneic stem cell transplantation (T cell depleted RIC alloSCT with donor lymphocyte infusion at 3 and 6 months) , in elderly patients with AML or high risk myelodysplastic syndrome (IPSS >=1.5).
• To evaluate the incidence of non-relapse mortality.
• To evaluate progression free survival and overall survival

Study design

Phase 1-2 feasibility study.

Intervention

Patients will receive FLAMSA chemotherapy over the course of 5 days. After a 3 day rest, the conditioning of the allogeneic stem cell transplantation is started. T cell depletion of the patient consists of alemtuzumab in patients transplanted with a related donor and alemtuzumab in combination with rabbit ATG (Thymoglobulin) in unrelated patients. No further immunosuppressive drugs are given after transplantation. All patients are to be treated with donor lymphocyte infusions at 3 and 6 months after transplantation. A total of 15 patients will be included in the study.

Study burden and risks

Elderly patients with AML or high risk MDS have a poor prognosis; the only way to achieve long term survival is transplantation with an allogeneic donor. Most patients starting with intensive chemotherapy are not transplanted, due to not achieving a complete remission with intensive chemotherapy, due to declining condition during the courses of intensive chemotherapy with long periods of neutropenia or due to early relapse after achieving a complete remission. Especially patients that are not in remission after the first induction chemotherapy have a dismal prognosis with current therapies. In a retrospective analysis of 20 patients not in remission after first induction chemotherapy, 16 patients received a second induction chemotherapy; 10 of these patients achieved a CR, 7 patients received a third chemotherapy course for consolidation, and 4 underwent RIC alloSCT. However, there were no long-term survivors in this group of 20 patients.
At the moment our standard therapy for high risk acute myeloid leukemia is induction chemotherapy followed by consolidation chemotherapy in case of the achievement of a complete remission, followed by T cell depleted reduced intensity allogeneic stem cell transplantation and donor lymphocyte infusion at 3 and 6 months after transplantation. Because of the dismal prognosis that patients have when they are not in complete remission after the first induction, even despite further intensive chemotherapy and allogeneic stem cell transplantation, further treatment with standard chemotherapy and transplantation protocols is questionable in these patients.
In this study we explore the feasibility of the sequential use of FLAMSA chemotherapy and T cell depleted reduced intensity conditioning allogeneic stem cell transplantation followed by donor lymphocyte infusion at 3 and 6 months after transplantation in patients that are not in complete remission after the first induction chemotherapy. This treatment regimen combines an effective chemotherapy regimen (amsacrine-cytarabine) with a relatively non-toxic allogeneic transplantation conditioning regimen and a short time between chemotherapy and the time point of DLI administration (3 months). With this TCD FLAMSA-RIC alloSCT regimen we hope to be able to treat and cure more elderly patients with AML and high risk MDS with allogeneic transplantation. The benefit this treatment offers is a chance of curation, the risk is non-relapse

mortality which will be between 10 and 20%.

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 AML or high risk MDS
• Not in remission after first intensive induction chemotherapy
• 60-75 years, inclusive
• HLA-identical sibling or unrelated donor completely matched (10/10 for HLA A, B, C, DR, DQ)
• WHO-performance status 0-2
• Written informed consent

Exclusion criteria

• Previous autologous or allogeneic SCT
• Acute promyelocytic leukemia
• Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix B);
• Severe cardiac dysfunction (NYHA classification 3-4, see appendix C).
• Significant hepatic dysfunction (serum bilirubin or transaminases >= 3 times upper limit of normal);
• Significant renal dysfunction (creatinine clearance < 30 ml/min after rehydration);
• Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.);
• Severe neurological or psychiatric disease;
• Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
• Patient known to be HIV-positive

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-07-2014
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amsidine
Generic name:	amsacrine

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	cytarabine
Generic name:	cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MabCampath
Generic name:	alemtuzumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Thymoglobuline
Generic name:	anti-human thymocyte immunoglobulin (ATG)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-04-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	14-04-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2012-004421-24-NL
CCMO	NL42222.058.13

Study results

Date completed: 08-07-2020

Actual enrolment: 13