Prevention of severe GVHD after allogeneic hematopoietic stem cell transplantation, applied as consolidation immunotherapy in patients with hematological malignancies. A prospective randomized phase III trial.

Published: 27-08-2009
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Objectives: - to increase the proportion of patients with non-severe GVHD within 180 days post-allo-SCT - to reduce the progression rate - to improve the progression free survival- to asses the impact on the quality of life using a time restricted...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON47822

Source
ToetsingOnline

Brief title
HOVON 96 GVHD

Condition

- Haematological disorders NEC

Synonym
Graft versus Host Disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Graft versus Host Disease, Immunosuppresion, Profylaxe

Outcome measures

Primary outcome

Proportion of patients with non-severe GVHD (acute GVHD grade I, grade II

without gut infiltration, or chronic GVHD not requiring systemic treatment)

within D180 after randomization / registration.

Secondary outcome

- time to acute GVHD grade I, II, III, IV

- cumulative incidence of progression

- progression-free survival (defined as time from randomization 1 until

progression or death, whichever occurs first)

- cumulative incidence of non-relapse mortality

- overall survival

- time to chronic GVHD limited and extensive

- adverse events

- Quality of life (of randomized patients) as defined by the EORTC QLQ-C30 and

the FACT-BMT definitions

Study description

Background summary

Allogeneic hematopoietic stem cell transplantation (SCT) has been established as the powerful treatment modality for patients with acute leukemia. Especially, the immunotherapeutic effect, known as the graft versus leukemia effect, significantly reduces the rate of relapse in leukemic patients, receiving their allograft as consolidation therapy in first or subsequent remission. In addition, the graft versus tumor effect can also be observed in patients with malignant lymphoma or multiple myeloma. That immunotherapeutic effect is strongly associated with the occurrence of acute and/or chronic graft versus host disease (GVHD). However, patients with severe acute grade III-IV or chronic extensive GVHD may experience excess mortality and thereby severe GVHD remains the most important complication of allogeneic SCT. Currently, different immunosuppressive regimens are used in order to prevent GVHD. The optimal duration of GVHD prevention is, however, not known and a subject of continuing debate. In the current study 3 regimens will be compared: a prolonged immunosuppressive regimen, a time-restricted regimen and a short-course GVHD prophylaxis consisting of post-transplant cyclophosphamide. The aim of the study is to make optimal use of the immunotherapeutic effect of the allo-SCT by increasing the number of patients with non-severe GVHD, without compromising this by a substantial increase of serious GVHD.

Study objective

Objectives:
- to increase the proportion of patients with non-severe GVHD within 180 days post-allo-SCT
- to reduce the progression rate
- to improve the progression free survival
- to asses the impact on the quality of life
using a time restricted immunosuppressive regimen or a short-course post-transplant GVHD prophylaxis consisting of high-dose cyclophosphamide as compared to a prolonged, standard immunosuppressive regimen

Additional objectives:
- to develop a predictive score, by means of clinical and laboratory parameters (using genomic and proteomic approaches) that allows for accurate identification of patients at high risk of severe GVHD as well as for identification of patients, who will not develop GVHD

Study design

A phase III randomized trial.

Intervention

Prevention of GvHD
3 regimens will be compared: a time-restricted immunosuppressive regimen (Myfortic for 28 days and Cyclosporine A for 84 days), a prolonged regimen (Myfortic for 84 days and Cyclosporine A for 180 days) and a short-course post-transplant GVHD prophylaxis consisting of high-dose cyclophosphamide

Study burden and risks

The extra burden associated with participation is
- once an extra bloodsample (during regular bloodsamping) of 48 ml
- filling out 5 Qol questionnaires.
Since patients are already very thorougly followed after allo SCT, the extra burden associated with particpation in this trial is limited.

On theoretical grounds there could occur more severe GVHD in a time-restricted immunosuppressive regimen. However, from previous experience the chance of this happening is small. This study is deemed justified from the fact that a time-restricted immunosuprresive regimen can accomplish a lower relapse rate. The main risk of arm 3 is increased mucosal toxicity and a prolonged duration of admission. However, if in the setting of arm 1 or 2 the patient will be treated with a myeloablative conditioning regimen, mucosal toxicity will be worse compared to arm 3. World-wide experience with arm 3 has shown no other specific risks. Compared to arm 1 and 2 , the chance to develop severe GvHD or fatal infections might be less.

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

-Age 18-70 inclusive
-AML, MDS, ALL, MM, CML, CLL, NHL, HL, or a myeloproliferative disease (MPD)
-Planned allogeneic stem cell transplantation
-Related or unrelated donor with a 8/8 HLA match (HLA A, B, C, DRB1)
-WHO performance status 0-2
-Written Informed Consent
-Negative pregnancy test (if applicable)
-Patients who are willing and capable to use adequate contraception during Myfortic treatment (all pre-menopausal women)

Exclusion criteria

- Renal dysfunction (serum creatinine > 150 mmol/L or clearance < 50 ml/min)
- Patients with active, uncontrolled infection
- Cord Blood transplantation
- Patients receiving ATG pre-transplantation as part of the conditioning regimen
- Patients with progressive disease in case of MM, CLL, NHL, HL
- Patients with > 5% marrow blasts in case of AML, ALL, CML
- Patients with EMD in case of AML, ALL, CML

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-04-2010
Enrollment:	497
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ciclosporin
Generic name:	Ciclosporin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cyclophosphamide
Generic name:	cyclophosphamide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Myfortic
Generic name:	mycophenolic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	27-08-2009

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-02-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-10-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-11-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-08-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2013
Application type:	Amendment
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Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	06-08-2020
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	EUCTR2008-003540-11-NL
CCMO	NL27061.078.09