Treatment of severe acute GVHD after allogeneic hematopoietic stem cell transplantation with steroids versus MSC and steroids.
A prospective double-blind placebo-controlled randomized phase III trial

Published: 14-06-2013
Last updated: 14-12-2024

To improve the response rate to treatment of severe acute GVHD (grade II-IV with gut involvement) by adding infusion of Mesenchymal Stroma Cells to standard high dose prednisolone.

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

Summary

ID

NL-OMON41587

Source
ToetsingOnline

Brief title
HOVON 112 MSC

Condition

- Other condition
- Haematological disorders NEC

Synonym
Graft versus Host Disease

Health condition

stamceltransplantatie gerelateerde complicatie: Graft versus Host ziekte

Research involving
Human

Sponsors and support

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

Intervention

Keyword: allogeneic stem cell transplanation, GVHD, MSC, steroids

Outcome measures

Primary outcome

Primary

- Proportion of patients in each treatment arm who experience a CR-GVHD or

PR-GVHD at day 57, without treatment failure (initiation of secondary

treatment)

Secondary outcome

Secondary

- Proportion of patients in each treatment arm who experience a CR-GVHD or

PR-GVHD at dindicated timepoints (until 2 years), without treatment failure

(initiation of secondary treatment)

- Time to CR-GVHD or PR-GVHD

- Amount of immune suppression at indicated days

- Adverse events

- The (immunological) phenotype before and after application of MSC/placebo of

responders and non-responders in both groups at different sites (see Appendix E and F)

- The immunological genotype of responders and non-responders as well as donors in both groups (see Appendix E and F)

- Quality of life

- Cost-effectiveness

- Relapse of the underlying disease (e.g. hematological malignancy)

- Progression-free survival

- Incidence and severity of chronic GVHD

- Overall survival

Study description

Background summary

Allogeneic hematopoietic stem cell transplantation (allo-SCT) is an established and powerful treatment modality for patients with multiple hematological malignancies and inborn errors. In particular, the immunotherapeutic effect, known as the graft versus leukemia (GVL) effect, significantly reduces the rate of relapse in leukemia patients, receiving their allograft as consolidation therapy in first or subsequent remission However, GVL is strongly associated with the occurrence of acute and/or chronic graft versus host disease (GVHD)]. GVHD occurs in 35%-50% of the transplanted patients, still substantially limiting the outcome and the more widespread use of allo-SCT .Thus, allo-SCT strategies which separate GVHD from GVL effects and therapies which treat effectively GVHD are urgently needed.
The core of acute GVHD treatment consists of immunosuppression, with 1-2mg/kg/d prednisolone as the standard first line treatment. Several studies demonstrate an overall complete response rate to prednisolone in approximately 40-50% of all patients, with a lower response rate and a higher recurrence in patients with more severe GVHD.[One interesting alternative therapeutic option for patients with severe GVHD comes from recent data of the application of mesenchymal stroma cells (syn., Mesenchymal stem cells) from others] and our center.The so far published data as well as data of our cohort strongly support the notion that MSC need to be studied in larger and more stringent randomized

clinical trials for patients with acute GVHD. They could be more effective when administered early in GVHD treatment thus leading to a better survival. This is the rational for this Phase lll trial comparing steroids and MSC as first line therapy against steroids alone. The study includes selectively patients suffering from gut and/or liver grade II-IV GVHD in first-line, thus patients with an expected survival of less than 25%.

Study objective

To improve the response rate to treatment of severe acute GVHD (grade II-IV with gut involvement) by adding infusion of Mesenchymal Stroma Cells to standard high dose prednisolone.

Study design

Prospective, multicenter, double blind, placebo- controlled, randomized

Intervention

Patients are randomized for treatment with
-high dose prednisolone 2 mg/kg/day i.v. and placebo
-high dose prednisolone 2 mg/kg/day i.v. and MSC at day 1, day 8, and Day 22 i.v.

Cyclosporine A + Mycophenolate prevention regimens will be (re)started or continued according to prevention schedule (Cyclosporine A through levels 0.20-0,35 mmol/l).

Study burden and risks

Burden consists of repetitive infusions of MSC, additional blood draws, bone marrow apirate and biopsy of the organ of GVHD after resolution of GVHD. So far no severe side effects have been reported of MSC. Theoretical risks are support of leukemia-growth, and severe infection. However, considering the life-threatining nature of GVHD and the side-effects of steroids, we expect an overall-benefit in terms of improved survival and less use of steroids.

Contacts

Public
HOVON

HOVON Centraal Bureau, VUMC, De Boelelaan 1117
Amsterdam 1081 HV

NL
Scientific
HOVON

HOVON Centraal Bureau, VUMC, De Boelelaan 1117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Any age;
- Previously treated with allo-SCT/ DLI;
- Acute GVHD grade II iIV nvolving gut and/or liver,
- WHO performance 0-3 ;
- Negative pregnancy test (if applicable);
- Patients must be willing and capable to use adequate contraception during therapy ;
- Written Informed Consent by the patient and/or parent(s) or legal guardian(s);

Exclusion criteria

- Patients with active, uncontrolled infection;
- Rapid progressive hematological malignancy;
- Patients pre-treated with prednisolone > 1 mg/kg for GVHD, for more than 72 hours prior to randomization/application of MSC/placebo;
- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.)

- Any psychological, familial, sociological and/or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- Known uncontrolled toxicity for DMSO;

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-05-2014
Enrollment:	140
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO

Date:	14-06-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	21-11-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-05-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-04-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-05-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 29599
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2011-003237-33-NL
CCMO	NL41506.000.13
OMON	NL-OMON29599