TREATMENT WITH CMV PP65 SPECIFIC T CELLS GENERATED BY USE OF A CMV PP65 PROTEIN-SPANNING PEPTIDE POOL IN PATIENTS WITH CMV REACTIVATION OR CMV DISEASE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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• To assess the feasibility, tolerability and safety of administration of donor or patient derived CMV pp65-specific T cells in patients with CMV reactivation or CMV disease after alloSCT.• To determine the presence of CMV specific T cells at...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON36436

Source
ToetsingOnline

Brief title
CMV pp65 specific T cells

Condition

- Viral infectious disorders

Synonym
CMV reactivation

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: AlloSCT, CMV, T cells

Outcome measures

Primary outcome

- The number of events of acute GvHD, death and all other adverse events.

Secondary outcome

- The number of CMV specific T cells at different time points after infusion of

CMV pp65-specific T cells.

- The number of complete responses or partial responses of CMV reactivation or

CMV disease after infusion of CMV pp65-specific T cells.

Study description

Background summary

In immunocompromised recipients of allogeneic stem cell transplantation (alloSCT), cytomegalovirus (CMV) reactivation can cause serious disease due to absence of adequate CMV-specific T cells. After alloSCT, pre-emptive treatment with antiviral therapy in patients with a positive CMV DNA load is usually performed to prevent CMV disease. However, pharmacological treatment of CMV reactivation is limited by toxicity and not sufficient for long-term anti-viral control. Adoptive transfer of selected CMV-specific T cells is safe and can result in clearance of CMV DNA load. However, the current method is restricted to certain human leukocyte antigen (HLA)-type of the patient/donor (HLA-A02 of HLA-B07), results in selection of CD8+ T cells only and is time consuming. In this study we will use a new method using a pool of overlapping 15-mer peptides for CMV pp65 to generate CMV-specific CD4+ and CD8+ donor T-cells regardless of the HLA-type, which makes it applicable to all patients with a CMV seropositive

donor.

Study objective

• To assess the feasibility, tolerability and safety of administration of donor or patient derived CMV pp65-specific T cells in patients with CMV reactivation or CMV disease after alloSCT.
• To determine the presence of CMV specific T cells at different time points after infusion of CMV pp65-specific T cells.
• To evaluate whether administration of CMV pp65-specific T cells in patients with persistent CMV reactivation or CMV disease after alloSCT leads to complete or partial responses.

Study design

This is an open-label non-randomized phase I/II feasibility study to treat patients with persistent CMV reactivation or CMV disease after alloSCT with administration of CMV pp65-specific T cells generated by use of a CMV pp65 protein-spanning peptide pool.
Patients after alloSCT with a CMV seropositive donor will be monitored weekly for CMV reactivation using PCR for the detection of CMV DNA. In case of CMV reactivation (defined as CMV DNA load >1000 cp/ml) patients will be treated with antiviral therapy according to standard protocols.
For patients with CMV reactivation who fail antiviral therapy (defined as CMV reactivation treatment failure: persistent CMV DNA load of more than 1000 cp/ml or CMV disease after 2 weeks of adequate treatment with antiviral therapy or relapse of CMV DNA load of more than 1000 cp/ml within 4 weeks after adequate treatment with antiviral therapy or contraindication for treatment with antiviral therapy at the discretion of the physician) or develop CMV disease (organ dysfunction (pneumonitis, enteritis, retinitis, encephalitis, hepatitis, and bone marrow suppression) due to CMV infection), CMV pp65-specific CD4+ and CD8+ T cells will be generated from donor PBMC by overnight in vitro stimulation with CMV pp65 peptide pools. CMV-specific CD4+ and CD8+ T cells will be isolated based on their IFNg production and administered to the patient directly after quality control. If alloSCT was performed using CD34 positive cell selection and the CD34 negative subfraction has been cryopreserved at a GMP facility, this fraction can also be used for selection of CMV-specific T cells. Antiviral therapy will be continued after infusion of CMV pp65-specific T cells according to standard antiviral treatment protocols at the discretion of the physician.
In case of ongoing CMV reactivation or CMV disease the infusion of CMV pp65-specific T cells may be repeated 2 times with at least 4 weeks interval.
The patient will be monitored for adverse events and for effect on CMV DNA load. Follow-up of patients will be performed until 6 months after infusion of CMV pp65-specific T cells or until subsequent DLI, whichever comes first.

Intervention

Infusion of CMV pp65-specific T cells

Study burden and risks

Patient will be hospitalized for administration of the T cells.
During or shortly after infusion of CMV pp65-specific T cells patients may experience mild side effects like fever and chills. These symptoms respond well to aminocetophen.
If no side effects occur, patients will go home the same day.
Normally, blood tests will be done once a week. In this study two extra blood tests will be done in the week after administration of CMV pp65-specific T cells. Thereafter, during 8 weeks blood tests will be done once a week and thereafter once a month for 4 more months. Blood tests will be combined with standard blood tests done after allogeneic stem cell transplantation.
A few weeks after infusion of the cells graft versus host disease can develop. The chance of developing this side effect is less than after infusion of non specific cultured donor lymphocytes.

Contacts

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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

* age 0-75 year
* recipient of alloSCT for standard indication according to national- and European Group for blood and Marrow Transplantation-guidelines (see appendix D)
* Possibility to obtain PBMC by leukapheresis from the CMVseropositive donor or availability of peripheral blood stem cell graft (PBSCT) or of a CD34-negative subfraction of a CD34-positively selected PBSCT product of the donor prepared and cryopreserved at a GMP-facility or stem cell center.
* CMV reactivation treatment failure (persistent CMV DNA load of more than 1000 cp/ml or CMV disease after 2 weeks of adequate treatment with antiviral therapy or relapse of CMV DNA load of more than 1000 cp/ml within 4 weeks after adequate treatment with antiviral therapy or contraindication for treatment with antiviral therapy at the discretion of the physician) or CMV disease (organ dysfunction (pneumonitis, enteritis, retinitis, encephalitis, hepatitis, and bone marrow suppression) due to CMV infection).
* Written informed consent by the patient and/or parent(s) or legal guardian(s).

Exclusion criteria

- Life expectation < 3 months.
- End stage irreversible multi-system organ failure.
- Pregnant or lactating women.
- Severe psychological disturbances.
- Patient HIV positive.
- Donor 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:	Recruitment stopped
Start date (anticipated):	17-04-2012
Enrollment:	15
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	26-09-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	01-11-2011
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-024307-27-NL
CCMO	NL35080.000.11

Study results

Date completed:	01-01-2016
Actual enrolment:	16