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CytoMegaloVirus~IMmunoProphylactic Adoptive Cellular Therapy study

Submission date
20/02/2008

Recruitment status
No longer recruiting

Registration date
04/03/2008

Overall study status
Completed

Last Edited
10/05/2019

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Following the transplant, a patients immune system will not work properly for several months. During this time they may develop serious infections that are usually easily controlled by people with healthy immune systems. The most common of these infections following transplant is cytomegalovirus or CMV. CMV infection can lead to pneumonia and even death in some patients. Antiviral drugs are the current standard of care for the treatment of CMV infection, but these drugs do not always work and even when they do the infection can recur when they are stopped. A new treatment strategy has been developed that relies on boosting a patients immunity to the CMV rather than using antiviral drugs. This is achieved by using blood cells from the transplant donor and processing them in the laboratory in order to enrich the immune cells that react against the CMV virus. There are now different ways to select cells specific for CMV but the relative advantages of each are unknown.

Who can participate?
Patients aged 18 or over receiving allogeneic haematopoietic stem cell transplants, where donor and recipient are both CMV seropositive.

What does the study involve?
Participants will be randomly allocated to either the treatment or the control group. For the participants in the treatment group, their donor will be asked to donate further cells 2 weeks after the transplant. In the laboratory immune cells from the donor will be selected which will provide an immune response against CMV. These immune cells will be given to the patient 27 days following the transplant. As part of this study an extra 50 ml of blood (the equivalent to three tablespoons) will be collected on the day of the planned infusion, then every week for 4 weeks, then monthly until 7 months after the transplant. Participants in the control group will receive the standard best available antiviral drug therapy, and an extra 50 ml of blood will be collected (the equivalent to three tablespoons) on day 27 following transplantation, then every week for 4 weeks, then monthly until 7 months after the transplant.

What are the possible benefits and risks of participating?
It is hoped that the cell treatment will help fight CMV infection. It has been already shown that these cells are capable of expanding to control CMV infection in patients who were treated after

the infection. It is hoped that the transfusion of the donor cells will restore a patients immunity to the CMV virus and prevent or treat infection. The transfusion of the donor cells may cause fever and chills that can occur with any blood or platelet transfusion. Any transfusion carries a risk of transmitting infection. This risk has been minimised since the donor will be screened for infections and by checking that the cells given are free from bacteria. The transfusion could cause Graft Versus Host Disease, in which the donor immune cells react against your own body organs and tissue. There are both acute and chronic forms of this complication. GVHD may never appear, may be mild and transient, or may lead to severe complications. GVHD can cause skin rash, diarrhoea, or inflammation and injury to the liver (hepatitis). Every effort has been made to reduce the risk of this potential complication. Firstly, the selection process in the laboratory positively selects immune cells which are responsible for immunity against CMV and does not select for cells which are responsible for GVHD. Secondly, the number of selected cells you receive is relatively small, and this will reduce the likelihood of GVHD. The transfusion may not prevent recurring CMV infections. If this occurs, you will receive our standard best available antiviral drug therapy for the treatment of CMV infection.

Where is the study run from?
UCL Cancer Institute (UK)

When is the study starting and how long is it expected to run for?
The study ran from April 2008 to August 2014

Who is funding the study?
Wellcome Trust Technology Translation Award (UK)

Who is the main contact?
Dr Karl Peggs

Contact information

Type(s)
Scientific

Contact name
Dr Karl Peggs

Contact details
UCL Cancer Institute
Paul O'Gorman Building
University College London
72 Huntley Street
London
United Kingdom
WC1E 6BT

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01077908

Protocol serial number
CM-2008-01

Study information

Scientific Title
A phase III randomised study to investigate the use of adoptive cellular therapy (ACT) in combination with conventional antiviral drug therapy for the treatment of cytomegalovirus reactivation episodes in patients following allogeneic haematopoietic stem cell transplant

Acronym
CMV~IMPACT

Study objectives
Hypothesis:
Evaluation of the potential clinical benefit of prophylactic cytomegalovirus (CMV)-specific adoptive cellular therapy (ACT) following T cell depleted allogeneic haematopoietic stem cell transplant (HSCT) for reducing recurrent CMV reactivation.

Study aim:
The study will investigate whether ACT will reduce the number of patients experiencing a recurrent episode of CMV reactivation after primary reactivation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Royal Free Hospital's Ethics Committee, 20/02/2008

Primary study design
Interventional

Study design
Open-label randomised multicentre study comparing immunoprophylaxis with adoptive cellular therapy (ACT)

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cytomegalovirus (CMV) infection in patients receiving allogeneic haematopoietic stem cell transplants (allo-HSCT)

Interventions
The study is divided into three arms. All patients receive current best available antiviral drug therapy when a positive CMV viraemia test is observed. Two arms of the study will additionally receive prophylactic adoptive cellular therapy (ACT). The study is divided as follows:
1. 42 patients receiving standard best available antiviral drug therapy
2. 35 patients receiving ACT prepared using gamma catch selection in combination with standard best available antiviral drug therapy

3. 35 patients receiving ACT prepared using multimer selection in combination with standard best available antiviral drug therapy

Treatment is a single dose ACT infusion at day 27 post-allo-HSCT, follow up is for six months post ACT infusion.

Intervention Type
Other

Phase
Phase III

Primary outcome(s)
Number of patients experiencing a recurrent episode of CMV reactivation after primary reactivation, measured for six months post-ACT infusion.

Key secondary outcome(s)
1. Incidence and severity of GVHD, measured at baseline, on a weekly basis for 100 days post infusion and then on a monthly basis up to six months post infusion
2. Duration of antiviral drug therapy (total days) and of viraemia (total days), measured at baseline, on a weekly basis for 100 days post infusion and then on a monthly basis up to six months post infusion
3. Incidence of CMV disease, measured at baseline, on a weekly basis for 100 days post infusion and then on a monthly basis up to six months post infusion
4. Laboratory evidence of reconstitution and persistence of CMV-specific immunity, measured at baseline, on a weekly basis for 100 days post infusion and then on a monthly basis up to six months post infusion

Completion date
01/08/2014

Eligibility

Key inclusion criteria
1. Sibling T cell depleted allogeneic HSCT recipients where donor and recipient are both CMV seropositive
2. Aged 18 years or over

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
75

Key exclusion criteria
1. Pregnant or lactating women
2. Co-existing medical problems that would place the patient at significant risk of death due to graft-versus-host disease (GVHD) or its sequelae
3. Human immunodeficiency virus (HIV) infection

To be assessed prior to CMV-specific T cell infusion (confirmed prior to product release):
4. Active acute GVHD greater than grade I
5. Concurrent use of systemic corticosteroids
6. Organ dysfunction as measured by:
6.1. Creatinine greater than 200 uM/l
6.2. Bilirubin greater than 50 uM/l
6.3. Alanine aminotransferase (ALT) greater than three times normal

Date of first enrolment
11/04/2008

Date of final enrolment
01/08/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
UCL Cancer Institute
London
United Kingdom
WC1E 6BT

Sponsor information

Organisation
Cell Medica Ltd (UK)

ROR

https://ror.org/027q99w81

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust Technology Translation Award (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	results abstract	06/12/2014	10/05/2019	No	No