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Randomised adoptive transfer of cytomegalovirus-specific cytotoxic T lymphocytes (CMV CTLs) after stem cell transplant

Submission date 11/07/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 19/08/2008	**Overall study status** Completed	
Last Edited 13/03/2019	**Condition category** Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01220895

Secondary identifying numbers

RG_07-186

Study information

Scientific Title
A prospective randomised, phase II study to investigate the efficacy and safety of pre-emptive cytomegalovirus (CMV) adoptive cellular therapy in patients receiving allogeneic haematopoietic stem cell transplant from an unrelated donor

Acronym
CMV-ASPECT (Alternate donor Study of Pre-Emptive Cellular Therapy)

Study objectives
Cytomegalovirus (CMV) infection remains a significant cause of morbidity and mortality following allogeneic stem cell transplant (SCT). We hypothesise that prophylactic adoptive transfer of human leukocyte antigen (HLA)-multimer selected cytomegalovirus-specific cytotoxic T lymphocytes (CMV-CTLs) after SCT will reduce CMV-related morbidity and mortality through lower frequencies of CMV reactivation during the first year following SCT.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands Research Ethics Committee, 21/04/2008, ref: 08/H1208/17

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request patient information material

Health condition(s) or problem(s) studied
Cytomegalovirus (CMV) infection after haemopoietic stem cell transplant

Interventions
Current interventions as of 22/02/2011:
This trial aims to recruit 36 patients with unrelated donors. Patients will be randomised into one

of two arms: pre-emptive infusion with CMV-specific T cells selected by the streptamer selection technique plus standard CMV antiviral therapy versus standard CMV antiviral therapy alone. Patients randomised to receive therapy will be given a single infusion upon CMV reactivation in conjunction with standard best available antiviral drug therapy following SCT.

Previous interventions:
This trial aims to recruit 18 patients with sibling donors and 21 patients with unrelated donors on each treatment arm (78 patients estimated in total). Patients will be randomised into one of two arms - standard practice (control) versus prophylactic infusion of CMV CTLs. Patients randomised to receive therapy will be given a single infusion on day 21 (+/-3 days if infusion falls on a weekend or bank holiday) following SCT. This will consist of up to 10^6/kg donor CMV-specific CD8+ T cells. Patients randomised to the control group will not receive an infusion of CMV-CTL.

Intervention Type
Biological/Vaccine

Phase
Phase II

Primary outcome measure
The frequency of CMV reactivation measured by quantitative polymerase chain reaction (PCR) during the first year following transplantation

Secondary outcome measures
1. CMV-specific immune reconstitution by detection of circulating T-cell responses to CMV in the first year following transplant
2. Clinical outcomes (total duration of follow-up: 12 months):
2.1. Time to CMV reactivation
2.2. Use of antiviral therapy
2.3. Incidence of secondary CMV reactivation and CMV disease
2.4. Incidence of acute and chronic graft-versus-host-disease (GvHD)

Overall study start date
01/10/2010

Completion date
01/06/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 22/02/2011:
1. Age 16 years or older
2. CMV-seropositive allogeneic T cell depleted (alemtuzumab-containing conditioning regimen) HSCT recipient with CMV-seropositive unrelated donor
3. Patient informed consent
4. Prepared to undergo additional study procedures as per study schedule
5. Patient has undergone counselling about risk
6. Donor engraftment (neutrophils > 0.5x10^9/l) (to be assessed prior to CMV-specific T-cell infusion)

7. Single positive CMV PCR result (and to be assessed prior to CMV-specific T-cell infusion)
8. The donor will be selected from the Anthony Nolan Trust registry or other donor registries that have approved the protocol and consent procedure.
9. Donor must have met requirements of EU Tissue and Cells Directive (2004/23/EC) as amended and the UK statutory instruments pursuant therein.
10. Healthy, CMV-seropositive donor - having passed medical for stem cell donation
11. Subject and donor must have negative serology for HIV, hepatitis B and C, syphilis
12. HLA type A*0101, A*0201, A*2402, B*0702, B*0801, B*3501
13. Donor informed consent for stem cell mobilisation leucapheresis and storage

Previous inclusion criteria:
1. Both males and females, aged 16 years or over
2. Patients considered fit for allogeneic peripheral blood stem cell transplant
3. Sibling or matched unrelated allogeneic peripheral blood stem cell transplant (PBSCT) using alemtuzemab
4. CMV-seropositive patient and donor
5. Patients and donor sharing at least one of the following HLA alleles:- HLA-A*0101, HLA*0201, HLA-A*1101, HLA-A*2402, HLA-B*0702, HLA-B*0801, HLA-B*3502
6. Patient willing and able to give consent and comply with trial protocol

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
36

Key exclusion criteria
Current exclusion criteria as of 22/02/2011:
1. Pregnant or lactating women
2. Co-existing medical problems that would place the patient at significant risk of death due to GVHD or its sequelae
3. HIV infection
4. Active acute GVHD > Grade I (to be assessed prior to CMV-specific T-cell infusion)
5. Concurrent use of systemic corticosteroids (to be assessed prior to CMV-specific T-cell infusion)
6. Organ dysfunction (to be assessed prior to CMV-specific T-cell infusion) as measured by:
6.1. Creatinine > 200 uM/l
6.2. Bilirubin > 50 uM/l
6.3. Alanine transferase > 3x upper limit of normal
7. Donor pregnant or lactating
8. Donor platelets < 50x10^9/l

Previous exclusion criteria:
1. Donors whose stem cells have already been collected and cryopreserved prior to transplant
2. Patients whose donor stem cell harvests are <4.0 x 10^6 CD34 cells/kg will not proceed with

the study
3. Bone marrow transplants

Date of first enrolment
01/10/2010

Date of final enrolment
01/06/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cell Medica Ltd
London
United Kingdom
W1T 6ES

Sponsor information

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Sponsor type
Industry

Website
http://www.cellmedica.co.uk

ROR
https://ror.org/027q99w81

Funder(s)

Funder type
Charity

Funder Name
Leukaemia Research Fund (UK) - new grant award (ref: 05071)

Funder Name
Cell Medica Ltd

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration