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Adenovirus Specific Paediatric Immune Reconstitution

Submission date
09/03/2012

Recruitment status
No longer recruiting

Registration date
12/04/2012

Overall study status
Completed

Last Edited
21/06/2019

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
Adenovirus (ADV) infections account for 10% of acute respiratory infections in children but are unlikely to cause serious complications in healthy patients. Following bone marrow transplant, ADV infection occurs in about 30% of paediatric patients and may be responsible for as many as 10% of post-transplant paediatric deaths. Antiviral drugs have some success, but no drug available is indicated for this patient group; current treatment options do not restore immune function. Additionally, currently available antiviral drugs have side effects that may increase the levels of morbidity (illness) in these patients. This study will look at the safety of adenovirus-specific T-cells (ADV-specific immune cells) given to high-risk paediatric patients after bone marrow transplant to treat reactivation of adenovirus.

Who can participate?
Patients considered at highest risk of infection: paediatric patients (aged 16 or younger) with unrelated donors, mismatched family donors or haploidentical (half-matched) donors.

What does the study involve?
Following transplant, patients are routinely monitored for ADV viraemia (presence of ADV virus) and following two consecutive positive results, the selected cell dose will be infused. If a patient is still exhibiting uncontrolled ADV viraemia four weeks following the cell infusion, they will be infused with a higher cell dose. Throughout the study the patients will be asked to give blood samples to assess their immune function and will be closely monitored for side effects through routine medical assessments. Evidence of the treatment's effectiveness, demonstrated by clearance of ADV virus, will also be recorded.

What are the possible benefits and risks of participating?
The benefits are, if the treatment works, the ADV infection will be better controlled and immunity will be restored, preventing further infection. The main concern for participating is an increase in the incidence of graft-versus-host-disease, in which the white blood cells of the transplanted bone marrow react against the patient's own body organs and tissues. There are both acute and chronic forms of this complication and it may cause skin rash, diarrhoea and liver inflammation. Because of the methods used, it is unlikely that this increase will be seen; the process will specifically increase the numbers of adenovirus-specific cells only and the number of

white blood cells given to the patient is very small, which reduces the risks overall. Additional risks associated with infusion are fever, allergic reactions, infection, inflammation and inefficacy.

Where is the study run from?
The study runs over three hospitals in the UK – Great Ormond Street Hospital, London; Royal Victoria Infirmary, Newcastle and Royal Children's Hospital, Manchester.

When is the study starting and how long is it expected to run for?
From December 2012 to July 2016.

Who is funding the study?
Cell Medica Ltd and the Technology Strategy Board (UK).

Who is the main contact?
Dr Shreenal Patel
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Contact information

Type(s)
Scientific

Contact name
Dr Waseem Qasim

Contact details
Institute of Child Health
Great Ormond Street Hospital
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United Kingdom
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Additional identifiers

Clinical Trials Information System (CTIS)
2011-001788-36

ClinicalTrials.gov (NCT)
NCT01822093

Protocol serial number
2011-001788-36

Study information

Scientific Title
A phase I/II study to investigate the safety of adenovirus-specific T-cells given to high-risk paediatric patients post allogeneic haematopoietic stem cell transplant (HSCT) to prevent or treat reactivation of adenovirus

Acronym
ASPIRE

Study objectives
Human Adenovirus-specific T-cells can persist and augment impaired adenovirus immune response post allogeneic haematopoietic stem cell transplant, and reduce the requirement for antiviral therapy without toxicity or increasing the occurrence of Graft Versus Host Disease.

On 28/04/2015 the following changes were made to the trial record:
1. The overall trial start date was changed from 01/07/2012 to 01/12/2012.
2. The overall trial end date was changed from 31/12/2014 to 01/07/2016.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Initial EC approval (NRES Committee London – Riverside) dated 23/08/2012
2. Substantial Amendment 001 approved on 04/10/2012
3. Substantial Amendment 002 approved on 21/06/2013
4. Substantial Amendment 003 approved on 14/04/2014
5. Substantial Amendment 004 approved on 18/09/2014

Study design
Phase I/IIa open-label safety study, assessing the effects of administering adenovirus-specific T-cells (Cytovir ADV) to paediatric patients post haematopoietic stem cell transplant

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Allogeneic hematopoietic stem cell transplantation (HSCT) patients considered at high risk of developing adenovirus (ADV) infection

Interventions
Current interventions as of 28/04/2015:
Adenovirus-specific T-cells (Cytovir-ADV)

A single dose 1x10e4 CD3+ T cells/kg patient weight of Cytovir ADV is prescribed to patients on exhibiting two consecutive PCR positive Adenovirus viraemia results > 1000 copies/ml. Patients are followed up by continued monitoring of Adenovirus viraemia results. If patients exhibit uncontrolled ADV viraemia at ≥ 4 weeks following the first cell dose, they will be prescribed a second cell dose of 1x10e5 CD3+ T cell/kg. Patients will be monitored for 6 months following infusion of Cytovir ADV.

This is a feasibility/pilot study and has no control group

Previous interventions:
Adenovirus-specific T-cells (Cytovir-ADV)

A single dose 5x10e4 CD3+ T cells/kg patient weight of Cytovir ADV is prescribed to patients on exhibiting two consecutive PCR positive Adenovirus viraemia results > 1000 copies/ml. Patients are followed up by continued monitoring of Adenovirus viraemia results. If patients exhibit uncontrolled ADV viraemia at ≥ 4 weeks following the first cell dose, they will be prescribed a second cell dose of 10e5 CD3+ T cell/kg. Patients will be monitored for 6 months following infusion of Cytovir ADV.

This is a feasibility/pilot study and has no control group

Intervention Type
Other

Primary outcome(s)
Current primary outcome measures as of 28/04/2015:
1. Number of subjects with new onset GvHD; Time Frame: 180 days
2. Number of subjects developing NCI Grade 3-4 adverse events; Time Frame: 180 days

Previous primary outcome measures:
1. Toxicity
2. Incidence and severity of GVHD
3. Cytopenias
4. Grade 3-4 adverse events.

Key secondary outcome(s))
1. Number of reported serious adverse events (SAEs) (Suspected, Unexpected Serious Adverse Reactions [SUSARs] and Suspected, Expected Serious Adverse Reactions [SESARs])
2. Number of detectable HAdV-specific T-cells in vivo at each time point
3. Requirement for second infusion of ADV specific T cells
4. Number of treatment days with antiviral drugs.
5. Number of treatment days with other anti-infective drugs
6. Number of in-hospital days during study period

Completion date
31/07/2016

Eligibility

Key inclusion criteria
Patients:
1. Age 16 years or younger
2. Scheduled to undergo an allogeneic HSCT with an unrelated donor, mismatched unrelated donor, mismatched family donor or haplo identical donor
3. The subject (or legally acceptable representative) must give informed consent (and assent for subjects ≥ 12 years). All subjects will have a parent or guardian provide informed consent and the subject will provide witnessed verbal assent
4. Negative serology for HIV 1 + 2, HepB, HepC, Syphilis, hCG.

Donors (for manufacturing only):
1. Meets requirements of Directive 2004/23/EC as amended and the UK statutory instruments pursuant therein
2. Negative serology for HIV 1 + 2, HepB, HepC, Syphilis, hCG
3. Passed medical assessment for stem cell donation
4. HdADV seropositive
5. Signed informed consent
6. Age 16 years or older

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Upper age limit
16 years

Sex
All

Total final enrolment
8

Key exclusion criteria
Patients
1. Pregnant or lactating females
2. Co-existing medical problems that would place the patient at significant risk of death due to GVHD or its sequelae
3. Human Immunodeficiency Virus (HIV) infection

Donors
1. Pregnant or lactating females
2. (assessed prior to apheresis) Platelets < 50x109/L

Date of first enrolment
01/12/2012

Date of final enrolment
30/06/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Child Health
London
United Kingdom
WC1N 1EH

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Royal Manchester Children's Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
Cell Medica Ltd (UK)

ROR
https://ror.org/027q99w81

Funder(s)

Funder type
Industry

Funder Name
Cell Medica Ltd (UK)

Funder Name
Technology Strategy Board (UK)

Alternative Name(s)
TSB

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2018	16/04/2019	Yes	No
Basic results			21/06/2019	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes