

Human herpes virus (HHV) specific immune effector (IE) cell therapy for HHV-related diseases

Submission date
05/02/2009

Recruitment status
No longer recruiting

☐ Prospectively registered

☐ Protocol

Registration date
27/02/2009

Overall study status
Completed

☐ Statistical analysis plan

☐ Results

Last Edited
01/09/2020

Condition category
Infections and Infestations

☐ Individual participant data

☐ Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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201100

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title

Human herpes virus (HHV) specific immune effector (IE) cells for prevention and treatment of HHV-related diseases

Study objectives

Human herpes viruses, including Epstein-Barr virus (EBV), cytomegalovirus (CMV) and HHV type 6 (HHV6) are common pathogens in humans. In healthy individuals, HHV infection is often self-resolved. However, in immune compromised individuals such as transplant patients, or young and elderly individuals, HHV-related diseases can be lethal. The development of an effective immune response is the best solution to treating HHV diseases. We hypothesise that HHV-specific immune effector cells can be used to prevent or cure HHV infections including EBV-associated lymphomas. Such immune effector cells can come from the recipients own blood, or their allogeneic transplant donors' blood. HHV-specific immune effector (IE) cells will be generated in culture and infused into patients. The safety of this approach, and virus titre and HHV-associated diseases will be closely monitored. The study will determine if HHV-specific IE cells can be used to prevent HHV infections and treat HHV-related diseases.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Institutional Review Board of Shanghai Dao-Pei Hospital, Institute of Hematology, Fu Dan University gave approval on the 10/05/07 (ref: SHDP-2007-0510)

Study design

Phase I/II trial, non-blind, single-site, single-group (compared with historical database) study

Primary study design

Interventional

Secondary study design

Non randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Prevention

Participant information sheet

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

Health condition(s) or problem(s) studied

Human herpes virus (HHV) infections

Interventions

The trial enrolls paediatric and adult patients with potential of developing HHV-related diseases to receive immune cell infusions. The pre-emptive/preventive arm of treatment is a Phase I/II trial, non-blind, single-site, single-group (compared with historical database) study, and the subjects will be followed up for one year after treatment. Each subject will receive four infusions of HHV-specific immune effector cells after haematopoietic stem cell transplantation, with seven follow-ups: one week after the last infusion, one month thereafter for three months, and every three months thereafter until the end of the trial.

The previous sponsor for this trial (up to 02/07/2013) was:

Vectorite Biomedica Inc.

WR-09, 17th Fl

3 Yuan Qu Street

Taipei

001

Taiwan

Intervention Type

Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

EBV-specific immune effector cells

Primary outcome measure

1. Patients' immediate clinical response after IE cell infusion, i.e. body temperature and symptoms related to GvHD
2. Virus titre or DNA copy in blood or tissue biopsy
3. HHV-associated diseases such as EBV-associated post-transplant lymphoproliferative disorder (PTLD)

Outcomes are measured at 24 hours, day 2, day 3, day 4, day 5, day 6, day 7, week 2, week 4, month 2, month 3, month 6 and year 1.

Secondary outcome measures

1. Production: IE cell preparation success rate - the minimal IE cell number can be generated per subject
2. Efficacy:
 - 2.1. Tracking HHV titre or copy number
 - 2.2. HHV IE cell function analysis in vitro and its correlation with in vivo effect
 - 2.3. Effect on PTLD - for subjects with EBV-PTLD
 - 2.4. Effect on mononucleosis - body temperature and HHV titre will be monitored
 - 2.5. Survival rate and the time required to recover completely from HHV diseases
3. Prevention: determine the time and frequency of HHV disease incidence in subjects after the first IE cell infusion, in comparison to historically-documented uninfused subjects
4. Safety:
 - 4.1. Adverse effect documentation
 - 4.2. National Cancer Institute Common Toxicity Criteria (NCI-CTC) grade 3 or above response
 - 4.3. Changes in biochemical parameters
 - 4.4. Complete blood count (CBC)

- 4.5. SGPT (aspartate aminotransferase [AST]), SGOT (alanine aminotransferase [ALT]), total bilirubin, gamma-glutamyl transferase (g-GT)
- 4.6. Creatinine, blood urea nitrogen (BUN), uric acid
- 4.7. Physical response
- 4.8. Life sign changes
- 4.9. Blood pressure
- 4.10. Pulse
- 4.11. Temperature

Outcomes are measured at 24 hours, day 2, day 3, day 4, day 5, day 6, day 7, week 2, week 4, month 2, month 3, month 6 and year 1.

Overall study start date

25/06/2007

Completion date

25/06/2015

Eligibility

Key inclusion criteria

1. The participants should meet at least one of the following conditions:
 - 1.1. Bone marrow transplant (BMT) or solid organ transplant (SOT) patient:
 - 1.1.1. High-risk subject of lymphoproliferative disease: e.g. donor is HHV sero-positive (human herpes virus viral capsid antigen immunoglobulin G positive [HHV VCA IgG+]) and recipient is HHV sero-negative (HHV VCA IgG-) at time of transplantation
 - 1.1.2. The subject has history of human herpes virus-associated lymphoproliferative disorder (HHV-LPD) or HHV-related malignancy
 - 1.1.3. The subject develops HHV diseases and not considered suitable for conventional treatment
 - 1.1.4. The subject shows human herpes virus deoxyribonucleic acid (HHV DNA) greater than or equal to 1000 genome copies/ μ g in the peripheral blood (with or without LPD) in two consecutive samplings (24 hours apart)
 - 1.1.5. HHV reactivation
 - 1.2. HHV-infected subjects:
 - 1.2.1. Subject develops HHV LPD and not suitable for conventional treatment
 - 1.2.2. The subject shows HHV DNA greater than or equal to 1000 genome copies/ μ g in the peripheral blood (with or without LPD) in two consecutive samplings (24 hours apart)
 - 1.2.3. HHV reactivation
2. Aged less than or equal to 65 years, either sex
3. Subject blood:
 - 3.1. White blood cell count (WBC) greater than or equal to 3500/ μ l
 - 3.2. Blood lymphocytes greater than or equal to 750/ μ l
4. Liver and kidney function:
 - 4.1. Creatinine less than or equal to 1.25 time of upper limit
 - 4.2. Bilirubin less than or equal to 1.5 time of upper limit
 - 4.3. Serum glutamic oxaloacetic transaminase (SGOT) less than or equal to 3 time of upper limit
 - 4.4. Serum glutamic pyruvic transaminase (SGPT) less than or equal to 3 time of upper limit
5. Donor condition:
 - 5.1. No chemo- or radiation-therapy within 4 weeks of blood collection; no steroid use within 1 week of blood collection
 - 5.2. WBC greater than or equal to 3500/ μ l

5.3. Lymphocytes greater than or equal to 750/ μ l

6. Signed informed consent

Participant type(s)

Patient

Age group

Other

Sex

Both

Target number of participants

300

Key exclusion criteria

1. Donor or recipient shows hepatitis C virus (HCV), human immunodeficiency virus (HIV) or tuberculosis (TB) positive
2. Recipient develops grade IV graft-versus-host disease (GvHD)
3. Recipient is albumin-intolerant
4. Recipient life expectancy less than 8 weeks
5. Recipient received alternative cell therapy within 30 days
6. Recipient is pregnant

Date of first enrolment

25/06/2007

Date of final enrolment

25/06/2015

Locations

Countries of recruitment

China

Study participating centre

Shanghai Dap-Pei Hospital

Shanghai

China

201100

Sponsor information

Organisation

America Yuva Biomed Inc. (China)

Sponsor details

B105
Zhongguancun Biomedical Garden
Kaituo rd.no.5
Haidian District
Beijing
China
100085

Sponsor type

Industry

Website

<http://www.usayuva.com>

Funder(s)**Funder type**

Industry

Funder Name

Current sources of funding as of 02/07/13:

Funder Name

America Yuva Biomed Inc. (China)

Funder Name

Previous sources of funding:

Funder Name

Vectorite Biomedica Inc. (Taiwan)

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