ISRCTN44627941 https://doi.org/10.1186/ISRCTN44627941

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

Submission date	Recruitment status	[_] Prospectively registered
05/02/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/02/2009	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
01/09/2020	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Daopei Lu

Contact details
Shanghai Dap-Pei Hospital
Minhang County
Shanghai
China
201100

Additional identifiers

Protocol serial number
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

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Human herpes virus (HHV) infections

Interventions
The trial enrols 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(s)
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.

Key secondary outcome(s))
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 respose
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.

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/μg 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/μg 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/μl
3.2. Blood lymphocytes greater than or equal to 750/μl
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/μl
5.3. Lymphocytes greater than or equal to 750/μl
6. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Other

Sex
All

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)

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration