

Pre-emptive treatment of epstein-barr virus (EBV)-associated lymphoproliferative disorder (LPD) and post-transplantational lymphoproliferative disorder (PTLD) with EBV-specific immune effector cell (EBV-IE)

Submission date 05/03/2009	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 13/03/2009	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 13/03/2009	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Li-Min Huang

Contact details
College of Medicine and College of Public Health
Division of Infectious Diseases
Department of Paediatrics
National Taiwan University Hospital
7 Chung-Shan South Road
Taipei
Taiwan
100

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title

Epstein-barr virus (EBV)-specific immune effector cell (EBV-IE) for pre-emptive/preventive and therapeutic treatment of EBV-related diseases such as lymphoproliferative disorder (LPD) and post-transplantation lymphoproliferative disorder (PTLD)

Study objectives

Epstein-barr virus (EBV) is a common human pathogen. In healthy individuals, EBV infection is often self-resolved. However, in immune compromised individuals such as transplant patients, or young and elderly individuals, EBV-related diseases can be lethal. The development of an effective immune response is the best solution to treating EBV diseases. We hypothesise that EBV-specific immune effector cells can be used to prevent or cure EBV-associated disorders including lymphomas. Such immune effector cells can come from the patient's own blood, or human leukocyte antigen (HLA)-matched donors' blood. EBV-specific immune effector (IE) cells will be generated in ex-vivo culture and infused into patients. The safety of this approach, and virus titre and EBV-associated diseases will be closely monitored. The study will determine if EBV-specific IE cells can be used to prevent EBV infections and treat EBV-related diseases.

Ethics approval required

Old ethics approval format

Ethics approval(s)

The 144th meeting of Research Ethics Committee of the National Taiwan University Hospital approved on the 14th November 2008 (ref: 200809044D); approved duration: 05/12/2008 - 04/12/2009

Study design

Interventional phase I/II single-arm single-centre trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

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

EBV-related diseases

Interventions

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 EBV-specific immune effector cells, 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 data collected in this trial will be compared with historical data.

Intervention Type

Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

EBV-specific immune effector cells

Primary outcome measure

Patients' immediate clinical response after IE cell infusion, e.g., body temperature and symptoms related to GvHD. In addition, virus titre or DNA copy in blood or tissue biopsy will be monitored.

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

To evaluate the rate of successful EBV-IE generation and ability of EBV-IE for anti-EBV efficacy and EBV reactivation prophylaxis:

1. Production: IE cell preparation success rate - the minimal IE cell number can be generated per subject
2. Efficacy:
 - 2.1. Tracking EBV titre or copy number
 - 2.2. EBV 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 EBV titer will be monitored
 - 2.5. Survival rate and the time required to recover completely from EBV-related diseases (LPD, PTLD)
3. Prevention: determine the time and frequency of EBV-related 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:
 - 4.3.1. Complete blood count (CBC)
 - 4.3.2. SGPT (aspartate aminotransferase [AST]), SGOT (alanine aminotransferase [ALT]), total bilirubin, gamma glutamyl transferase (g-GT)
 - 4.3.3. Creatinine, blood urea nitrogen (BUN), uric acid
 - 4.4. Physical response

4.5. Life sign changes:

4.5.1. Blood pressure

4.5.2. Pulse

4.5.3. 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

01/05/2009

Completion date

01/05/2011

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 developing LPD: donor is EBV sero-positive (EBV-VCA IgG+) while subject is EBV sero-negative (EBV-VCA IgG-)
 - 1.1.2. The subject has history of EBV-LPD or EBV-related malignancy
 - 1.1.3. The subject with EBV-LPD and is not adaptable for conventional treatment
 - 1.1.4. The subject shows EBV 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. The subject with the symptoms of EBV reactivation (fever, diarrhoea or lymphadenopathy) and confirmed by biopsy examination, regardless of the EBV level
 - 1.2. EBV-infected subjects without BMT/SOT:
 - 1.2.1. Subject develops EBV-LPD and not suitable for conventional treatment
 - 1.2.2. The subject shows EBV 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. The subject with the symptoms of EBV reactivation (fever, diarrhoea or lymphadenopathy) and confirmed by biopsy examination, regardless of the EBV level
2. Aged less than or equal to 65 years old
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 times of upper limit
 - 4.2. Bilirubin less than or equal to 1.5 times of upper limit
 - 4.3. Serum glutamic oxaloacetic transaminase (SGOT) less than or equal to 3 times of upper limit
 - 4.4. Serum glutamic pyruvic transaminase (SGPT) less than or equal to 3 times of upper limit
5. Donor condition:
 - 5.1. No chemo- or radiotherapy 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

Adult

Sex

Both

Target number of participants

12

Key exclusion criteria

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

Date of first enrolment

01/05/2009

Date of final enrolment

01/05/2011

Locations**Countries of recruitment**

China

Taiwan

Study participating centre

College of Medicine and College of Public Health

Taipei

Taiwan

100

Sponsor information**Organisation**

Vectorite Biomedica Inc. (Taiwan)

Sponsor details

c/o Mr Mike Chen

WR-09, 17th Fl.

3 Yuan Qu Street
Taipei
Taiwan
001

Sponsor type
Industry

Website
<http://www.vectorite.com>

ROR
<https://ror.org/00mjfwd15>

Funder(s)

Funder type
Industry

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