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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	Recruitment status	[X] Prospectively registered
05/03/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/03/2009	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
13/03/2009	Infections and Infestations	[_] Record updated in last year

Plain English Summary
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

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 hypothesis
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

Condition
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

Overall study end date
01/05/2011

Eligibility

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

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
12

Participant 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

Recruitment start date
01/05/2009

Recruitment end date
01/05/2011

Locations

Countries of recruitment
China

Taiwan

Study participating centre
College of Medicine and College of Public Health
Taipei
Taiwan
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Sponsor information

Organisation
Vectorite Biomedica Inc. (Taiwan)

Sponsor details
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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