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# Study to evaluate the use of allogeneic mesenchymal stromal cells for the treatment of skin disease in children with recessive dystrophic epidermolysis bullosa

**Submission date**
11/06/2012

**Recruitment status**
No longer recruiting

**Registration date**
08/08/2012

**Overall study status**
Completed

**Last Edited**
01/03/2019

**Condition category**
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims:
Recessive Dystrophic Epidermolysis Bullosa (RDEB) is a severe inherited skin disease caused by lack of collagen VII - the protein that 'sticks' the top and bottom layer of the skin together. It is a severe condition leading to skin fragility, blisters and wounds which are slow to heal or leave non-healing open wounds. There is desperate need to develop new treatments for RDEB and attempts are being made to develop studies using different types of treatment. The aim of this study is to find out if using a particular type of cell is safe to use and can improve the skin disease in this genetic disease.

Who can participate?
Children with a diagnosis of RDEB, aged 1 to 17

What does the study involve?
The study consists of a total of 7 visits. The first visit consists of a screening consultation with a study doctor where the study is thoroughly explained and questions answered. If the parent and child decide to participate, an informed consent form is signed. Six further visits are scheduled after this, during which different procedures are carried out: cell infusions, blood tests and skin biopsies. Also, various assessments of the wounds, pain and quality of life are done using different scoring systems.

What are the possible benefits and risks of participating?
If the treatment works, the skin disease may become milder with fewer blisters and wounds that hopefully heal faster. However, it is not known how long the effects will last. The child is followed up for 6 months and information is collected about the skin disease during the routine clinical appointments for up to 1 year. If the cell treatment proves safe and study participants benefit from it, there is the possibility to administer further cell treatments. It is also hoped that the information gathered will contribute to future studies for therapies of individuals with RDEB. Mesenchymal Stem Cells (MSCs) have been used for other medical conditions with no

severe side effects recorded and recent studies using MSCs for children with RDEB in other countries have reported no serious adverse reactions. Although not expected, the infusion of any blood product carries a small risk of complications such as allergic reaction, infection or other unpredicted reactions that could potentially require medical care and hospitalisation. Blood taking and skin biopsies could result in pain, bruising and/or infection at the injection site. Infection can be treated with a short course of oral antibiotics.

Where is the study run from?
Great Ormond Street Hospital for Children (UK)

When is the study starting and how long is it expected to last for?
June 2013 to December 2014

Who is funding the study?
Dystrophic Epidermolysis Bullosa Research Association (DebRA) (UK)

Who is the main contact?
Prof. John McGrath
john.mcgrath@kcl.ac.uk

# Contact information

### Type(s)
Scientific

### Contact name
Prof John Alexander McGrath

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# Additional identifiers

### Clinical Trials Information System (CTIS)
2012-001394-87

### Protocol serial number
19312-1

# Study information

## Scientific Title
A prospective phase I/II study to evaluate the use of allogeneic mesenchymal stromal cells for the treatment of skin disease in children with recessive dystrophic epidermolysis bullosa

## Acronym
EBSTEM

## Study objectives
Mesenchymal stromal cells (also known as mesenchymal stem cells, MSC) have been identified as bone marrow derived multipotent stem cells of non-haematopoetic lineage that are present in tiny quantities in the circulation (1 in 104 nucleated cells). MSCs can be isolated from bone marrow but also from subcutaneous fat, umbilical cord blood, placenta and definitive teeth. MSCs have been shown to differentiate into a number of different cell types of stromal lineage including osteoblasts, adipocytes and chondrocytes. There is an intense amount of research interest in the clinical application of MSCs in the treatment of degenerative or inflammatory diseases. Mesenchymal stem cells (MSC) have been shown to home to wounded tissue and mediate wound healing. It is, therefore, anticipated that bone marrow derived tissue cultured MSCs, if injected systemically, will lead to increased amounts of type VII collagen production as well as the production of a variety of growth factors and cytokines both to stimulate wound healing as well as inducing type VII collagen synthesis in the patient's own keratinocytes and fibroblasts. Recent studies in animal models and humans have demonstrated that MSCs have the potential to improve skin function. This project aims to translate those initial findings into a clinical trial of MSCs given intravenously into children with RDEB. The goal is to see whether this is safe, feasible and of potential value to those living with this condition.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
NRES Committee London-Bloomsbury, 23/11/2012, ref: 12/LO/1258

## Study design
Phase I/II non-randomised open-label single-centre proof of concept

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Recessive dystrophic epidermolysis bullosa

## Interventions
Children with RDEB from Great Ormond Street NHS Trust will be invited to take part in the study. Each subject will undergo an initial screening including physical examination, vital signs and disease severity assessment. This will also include a skin biopsy and blood test investigations. All study participants will receive three intravenous MSC infusions at baseline Day 0, Day 7 and Day 28. The patients will then be additionally reviewed at Day 60, Day 100 and Day 180 after the first infusion (total 7 visits, including screening visit). During the study visits, the participant will be reviewed by a doctor who will assess the disease severity, blister counts,

pain and quality of life issues. Blood tests will be performed on six occasions. A skin biopsy will be repeated at screening and Day 60. At Day 0 and Day 100 the time taken to form a small suction blister will be assessed. The parents of each child will be invited to have their skin fragility tested as well, by measuring the time to forming a suction blister and this will be correlated with their child's time. Suction blisters times provide a functional measurement of skin integrity and resistance to blistering. Photographs of body areas will be taken by the participants' parents/guardians at different timepoints during dressing changes. Investigators will also take clinical photographs during the study visits to assess the appearance of affected body areas. After the first 6 months the children will be followed up clinically every 3 to 6 months by the GOSH clinical team and no scheduled interventions are planned unless they are clinically indicated

### Intervention Type
Biological/Vaccine

### Phase
Phase I/II

### Primary outcome(s)
Current primary outcome measures as of 15/01/2015:
The safety of allogeneic intravenously administered MSCs in children with RDEB over a 12-month period

Previous primary outcome measures:
The safety of allogeneic intravenously administered MSCs in children with RDEB over a 24-month period

### Key secondary outcome(s))
1. Increase in collagen VII deposition at the DEJ post treatment
2. Quantitative analysis of the donor cells dermal chimerism
3. Improvement of haematological and serological markers of generalised inflammation
4. General clinical appearance of the skin based on medical photographs, generalised severity score and BEBSS score
5. Improved quality of life
6. Pain scoring
7. Reduction in blister numbers
8. Increase in skin strength measured by increased time to blister formation after skin suction at screening and D120

### Completion date
11/12/2014

## Eligibility

### Key inclusion criteria
1. Subjects who have a diagnosis of recessive dystrophic epidermolysis bullosa (RDEB) characterised by partial or complete collagen VII deficiency
2. Subjects who are ≥ 12 months and ≤ 17 years of age at the time of enrolment
3. Subjects whose responsible relative/guardian has voluntary signed and dated an Informed

Consent Form (ICF) prior to the first study intervention. Whenever the minor child is able to give consent, the minor's assent will be obtained in addition to the signed consent of the minor's legal guardian

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Child

## Lower age limit
12 months

## Upper age limit
17 years

## Sex
All

## Key exclusion criteria
Current exclusion criteria as of 10/09/2013:
1. Subjects who have had other investigational medicinal products within 90 days prior to screening or during the treatment phase
2. Subjects who have received immunotherapy including oral corticosteroids for more than 1 week (intranasal and topical preparations are permitted) or chemotherapy within 60 days of enrolment into this study
3. Subjects with a known allergy to any of the constituents of the investigational product
4. Subjects with signs of active infection
5. Subjects with a medical history or evidence of malignancy, including cutaneous squamous cell carcinoma
6. Subjects with both positive C7 ELISA and a positive indirect immunofluorescence (IIF) with binding to the base of salt split skin
7. Subjects who are pregnant or of child-bearing potential who are not abstinent or practicing an acceptable means of contraception, as determined by the Investigator, for the duration of the treatment phase

Previous exclusion criteria:
1. Subjects who have had other investigational medicinal products within 90 days prior to screening or during the treatment phase
2. Subjects who have received immunotherapy including oral corticosteroids for more than 1 week (intranasal and topical preparations are permitted) or chemotherapy within 60 days of enrolment into this study
3. Subjects with a known allergy to any of the constituents of the investigational product
4. Subjects with signs of active infection
5. Subjects with a medical history or evidence of malignancy, including cutaneous squamous cell carcinoma
6. Subjects with positive serum antibodies to C7 confirmed by ELISA
7. Subjects who are pregnant or of child-bearing potential who are not abstinent or practicing an

acceptable means of contraception, as determined by the Investigator, for the duration of the treatment phase

**Date of first enrolment**
14/06/2013

**Date of final enrolment**
03/10/2013

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**Great Ormond Street Hospital for Children NHS Foundation Trust**
Great Ormond Street
London
United Kingdom
WC1N 3JH

# Sponsor information

**Organisation**
King's College London (UK)

**ROR**
https://ror.org/0220mzb33

# Funder(s)

**Funder type**
Charity

**Funder Name**
Dystrophic Epidermolysis Bullosa Research Association

**Alternative Name(s)**
Dystrophic Epidermolysis Bullosa Research Association UK, Dystrophic Epidermolysis Bullosa Research Association, DEBRA

### Funding Body Type
Government organisation

### Funding Body Subtype
Associations and societies (private and public)

### Location
United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. John McGrath (john.mcgrath@kcl.ac.uk).

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/09/2015 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |