

# Mesenchymal stromal cell therapy for children with recessive dystrophic epidermolysis bullosa

<b>Submission date</b> 18/03/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 25/03/2021	<b>Overall study status</b> Ongoing	<input checked="" type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 22/05/2025	<b>Condition category</b> Skin and Connective Tissue Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Recessive Dystrophic Epidermolysis Bullosa (RDEB) is an inherited skin blistering disease. RDEB is a severe form of epidermolysis bullosa (EB) caused by loss-of-function mutations in type VII collagen gene (COL7A1) leading to skin blistering following a minor injury to the skin. There is no effective treatment for RDEB and management is mainly supportive. The use of mesenchymal stromal cells (MSCs) in children with RDEB has been studied before and was found to improve wound quality and reduce skin itching and pain without significant side effects.

The aim of this study is to assess the safety of treatment with MSCs in children with RDEB. The study will also assess the efficacy of MSCs in improving the disease severity, quality of life, and symptoms (e.g. pain and itch) including the cost-effectiveness compared to the usual care over the 15-month period in children with severe RDEB.

### Who can participate?

Children aged between 6 months and 16 years with a diagnosis of RDEB

### What does the study involve?

Participants will be allocated to one of two groups, with an equal chance of being in either group (like tossing a coin) for the first half of the study. In the second half of the study, participants will receive the treatment that they did not receive in the first half of the study. The treatments are either mesenchymal stromal cells (MSCs) or placebo (an inactive treatment with a similar appearance) which will both be given as a liquid into a vein. Participants will not know the order in which they receive the different treatments. The study will last 15 months with the option for participants to continue for a further 12 months with the MSC treatment after the trial. Participants will be assessed for the severity of disease, quality of life, and symptoms (e.g. pain and itch), and will undergo routine safety blood tests throughout the trial.

### What are the possible benefits and risks of participating?

If the treatment works, the participant's skin may become less painful, wounds less red, and may heal faster. Participants may have a better quality of life due to reduced pain, reduced itch, and improved sleeping. However, it is not known exactly how long the effects will last. Based on a previous trial, it is expected that the effects will last between 3 and 6 months after the last dose. It is also hoped that this study will show that UC-MSCs are safe and helpful for children with

RDEB and will provide evidence to the NHS EB service funders to continue funding the treatment.

Although very unlikely, the infusion of UC-MSCs carries a small risk of complications such as allergic reaction, itching, tummy ache, headaches, mild fever, nausea, transient heart rate changes, transient garlic smell, or infection. These complications could potentially require medical care and hospitalisation. However, the cells have been given before in other medical conditions with no severe side effects recorded, and in a recent study with RDEB patients, no severe adverse events were reported. Participants are encouraged to talk to their clinical team if they have any concerns.

The MSCs will be administered in a designated area for clinical trials at Great Ormond Street Hospital and Birmingham Children's Hospital where all the required equipment and trained staff will be available should an unexpected reaction takes place. To reduce the risk of an allergic reaction, premedication with chlorphenamine (antihistamine) will be given. The aforementioned side effects have been encountered after some MSC infusions in the previous trials, but in all cases the children have recovered fully.

Where is the study run from?

Great Ormond Street Hospital (UK)

When is the study starting and how long is it expected to run for?

From August 2020 to October 2025

Who is funding the study?

National Research Collaboration Programme (NIHR127963), an NHS England and National Institute for Health Research partnership. Additional funds were provided by Cure EB, an EB medical research charity incorporated organization. Please see <http://www.cure-eb.org/> or email [research@cure-eb.org](mailto:research@cure-eb.org) for more information.

Who is the main contact?

Kate Hutchence, [k.j.hutchence@sheffield.ac.uk](mailto:k.j.hutchence@sheffield.ac.uk)

### **Study website**

<https://www.sheffield.ac.uk/scharr/research/centres/ctr/missionebeb>

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

Dr Anna Martinez

### **ORCID ID**

<https://orcid.org/0000-0003-1738-8008>

### **Contact details**

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Great Ormond Street  
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United Kingdom  
WC1N 3JH  
+44 (0)207 8297808  
anna.martinez@gosh.nhs.uk

**Type(s)**  
Scientific

**Contact name**  
Dr Gabriela Petrof

**Contact details**  
Great Ormond Street Hospital for Children NHS Foundation Trust  
Great Ormond Street  
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United Kingdom  
WC1N 3JH  
+44 (0)207 8297808  
gabriela.petrof@gosh.nhs.uk

## **Additional identifiers**

**EudraCT/CTIS number**  
2020-005049-18

**IRAS number**  
281748

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
CPMS 48230, IRAS 281748

## **Study information**

**Scientific Title**  
Double-blinded placebo-controlled crossover study of Mesenchymal Intravenous Stromal cell Infusions in children with recessive dystrophic Epidermolysis Bullosa

**Acronym**  
MissionEB

**Study objectives**  
Repeated intravenous infusions of allogeneic (unrelated) UC-MSCs are safe and can benefit children with recessive dystrophic epidermolysis bullosa (RDEB).

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

Approved 17/03/2021, North East – York (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN; +44 (0)207 104 8079; york.rec@hra.nhs.uk), ref: 21/NE/0016

**Study design**

Prospective double-blind randomized placebo-controlled cross-over trial incorporating a phase 1 de-escalation study and a possible continued treatment follow-on open-label study

**Primary study design**

Interventional

**Secondary study design**

Randomised cross over trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

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

**Health condition(s) or problem(s) studied**

Congenital disorders of the skin, recessive dystrophic epidermolysis bullosa

**Interventions**

Current intervention as of 22/04/2022:

This is a prospective, randomised, placebo-controlled, double-blinded cross-over trial incorporating a phase 1 de-escalation study in the first 3 months and a 12 month continued treatment follow-on open-label study following review of the data by NIHR. The trial will be conducted at 2 sites that both specialise in paediatric dermatology: Great Ormond Street Hospital and Birmingham Children's Hospital.

**Screening visit (Visit 1):**

Each child will undergo an initial screening consisting of confirmation of consent from parent /guardian, physical examination, assessment of vital signs, disease severity assessment, concomitant medication review, routine safety bloods. Blood will be taken for DNA analysis and a skin biopsy performed for immunofluorescence testing if this information is not already available. Menstruating and sexually active participants will be asked to take a pregnancy test. Patients will be also asked if they would like to consent to the storage of blood samples for future research.

**Randomisation:**

All study participants will be randomised to receive two consecutive intravenous MSCs or placebo infusions at 0 and 14 days. After the outcome assessment at 9 months, all children will be crossed over and receive either MSCs or placebo at 9 months and 14 days later. The placebo effect is expected to tail off by 3 months.

Follow up visits (Randomised crossover study, including phase I):

All children will be followed up every 3 months for the first year following the first infusion.

Outcome measures will be taken at 3, 6, 12, and 15 months. Infusion visits will be at day 0 and 14 days, 9 months and 2 weeks later.

1. On day 0 (Visit 2), participants will receive the first infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessment, pain and itch assessment, quality of life questionnaire, pain and itch medication review, concomitant medication review, research blood tests, photography of wounds, and adverse event assessment.
2. On day 14 (Visit 3), participants will receive the second infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, concomitant medication review, research blood tests, photography of wounds, and adverse event assessment.
3. At 3 months (Visit 4), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, changes to analgesia/itch meds review, pain and itch medication review, concomitant medication review, photography of wounds, adverse event assessment, pregnancy test (menstruating and sexually active participants only), physical examination.
4. At 6 months (Visit 5), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, concomitant medication review, photography of wounds, adverse event assessment, pregnancy test (menstruating and sexually active participants only), physical examination.
5. At 9 months (Visit 6), participants will receive the third infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, quality of life questionnaire, pain and itch assessment, concomitant medication review, pain and itch medication review, safety bloods and research blood tests, photography of wounds, and adverse event assessment.
6. At 9 months + 2 weeks (Visit 7), participants will receive the fourth infusion and be assessed for pregnancy test (menstruating and sexually active participants only,) physical examination, vital signs, pain and itch assessment, concomitant medication review, research blood tests, photography of wounds, and adverse event assessment
7. At 12 months (Visit 8), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, changes to analgesia review, pain and itch medication review, concomitant medication review, photography of wounds, adverse event assessment, pregnancy test (menstruating and sexually active participants only), physical examination.
8. At 15 months (Visit 9), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, concomitant medication review, photography of wounds, adverse event assessment, pregnancy test (menstruating and sexually active participants only), physical examination.

Phase I study:

Participants will partake in the phase I trial. The first cohort of 4 patients will receive IMP or placebo in a 3:1 ratio. If there are no safety concerns the second cohort of 5 patients will receive IMP or placebo (3:2). Participants involved in the phase I trial will undergo the assessments as outlined above for their infusion visits. If there are no safety concerns they will continue through the crossover trial with the assessments as outlined above.

If there 2 or more toxicities the phase I trial will be halted and re-started using half the dose of IMP, with a new cohort of 4 + 5 patients. Those patients that took part in the original phase I trial will be followed up for 3 months. Safety data will be collected (AEs and SAEs). Due to the small population of patients with this disease, these participants will be reentered into the crossover trial to receive half the dose of IMP, after a washout period of 9 months.

#### Open-label study:

The open-label study will go ahead if the treatment is found to be effective without safety concerns. Participants of the cross-over trial will be invited to consent to the open-label study and be given two infusions at 4 monthly intervals (at day 0, month 4, and month 8) and followed up at month 12. We will explore the acceptability of the treatment by conducting interviews with children and parents in both arms following the crossover period.

1. At 0 months (Visit 10), participants will receive the fifth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, pain and itch medication review, quality of life questionnaire, safety and research blood tests, adverse event assessment, and concomitant medication assessment.
2. At 0 months + 2 weeks (Visit 11), participants will receive the sixth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, research blood tests, adverse event assessment, and concomitant medication assessment.
3. At 4 months (Visit 12), participants will receive the seventh infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, changes to analgesia/itch meds review, pain and itch medication review, quality of life questionnaire, research and safety blood tests, adverse event assessment, concomitant medication assessment.
4. At 4 months + 2 weeks (Visit 13), participants will receive the eighth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, research blood tests, adverse event assessment, and concomitant medication assessment.
5. At 8 months (Visit 14), participants will receive the ninth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, changes to analgesia/itch meds review, pain and itch medication review, quality of life questionnaire, safety and research blood tests, adverse event assessment, and concomitant medication assessment.
6. At 8 months + 2 weeks (Visit 15), participants will receive the tenth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, research blood tests, adverse event assessment, and concomitant medication assessment.
7. At 12 month (Visit 16), participants will undergo disease severity assessments, pain and itch assessment, photography of wounds, changes to analgesia/itch meds review, pain and itch medication review, quality of life questionnaire, safety blood tests, adverse event assessment, concomitant medication assessment, pregnancy test (menstruating and sexually active participants only), physical examination.

The maximum duration of treatment of a subject will 24 months. An evaluation of costs associated with treatment will also be undertaken.

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#### Previous intervention:

This is a prospective, randomised, placebo-controlled, double-blinded cross-over trial incorporating a phase 1 de-escalation study in the first 3 months and a 12 month continued

treatment follow-on open-label study following review of the data by NIHR. The trial will be conducted at 2 sites that both specialise in paediatric dermatology: Great Ormond Street Hospital and Birmingham Children's Hospital.

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Each child will undergo an initial screening consisting of confirmation of consent from parent /guardian, physical examination, assessment of vital signs, disease severity assessment, concomitant medication review, routine safety bloods. Blood will be taken for DNA analysis and a skin biopsy performed for immunofluorescence testing if this information is not already available. Menstruating and sexually active participants will be asked to take a pregnancy test. Patients will be also asked if they would like to consent to the storage of blood samples for future research.

#### Randomisation:

All study participants will be randomised to receive two consecutive intravenous MSCs or placebo infusions at 0 and 14 days. After the outcome assessment at 9 months, all children will be crossed over and receive either MSCs or placebo at 9 months and 14 days later. The placebo effect is expected to tail off by 3 months.

#### Follow up visits (Randomised crossover study, including phase I):

All children will be followed up every 3 months for the first year following the first infusion. Outcome measures will be taken at 3, 6, 12, and 15 months. Infusion visits will be at day 0 and 14 days, 9 months and 2 weeks later.

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3. At 3 months (Visit 4), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, analgesia review, concomitant medication review, photography of wounds, adverse event assessment, and pregnancy test (menstruating and sexually active participants only)
4. At 6 months (Visit 5), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, analgesia review, concomitant medication review, photography of wounds, adverse event assessment, and pregnancy test (menstruating and sexually active participants only)
5. At 9 months (Visit 6), participants will receive the third infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, concomitant medication review, analgesia review, safety bloods and research blood tests, photography of wounds, and adverse event assessment
6. At 9 months + 2 weeks (Visit 7), participants will receive the fourth infusion and be assessed for pregnancy test (menstruating and sexually active participants only,) physical examination, vital signs, pain and itch assessment, quality of life questionnaire, analgesia review, concomitant medication review, research blood tests, photography of wounds, and adverse event assessment
7. At 12 months (Visit 8), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, analgesia review, concomitant medication review, photography of wounds, adverse event assessment, and pregnancy test (menstruating and sexually active participants only)

8. At 15 months (Visit 9), participants will undergo disease severity assessment, pain and itch assessment, quality of life questionnaire, analgesia review, concomitant medication review, photography of wounds, adverse event assessment, and pregnancy test (menstruating and sexually active participants only)

#### Phase I study:

Participants will partake in the phase I trial. The first cohort of 4 patients will receive IMP or placebo in a 3:1 ratio. If there are no safety concerns the second cohort of 5 patients will receive IMP or placebo (3:2). Participants involved in the phase I trial will undergo the assessments as outlined above for their infusion visits. If there are no safety concerns they will continue through the crossover trial with the assessments as outlined above.

If there 2 or more toxicities the phase I trial will be halted and re-started using half the dose of IMP, with a new cohort of 4 + 5 patients. Those patients that took part in the original phase I trial will be followed up for 3 months. Safety data will be collected (AEs and SAEs). Due to the small population of patients with this disease, these participants will be reentered into the crossover trial to receive half the dose of IMP, after a washout period of 9 months.

#### Open-label study:

The open-label study will go ahead if the treatment is found to be effective without safety concerns. Participants of the cross-over trial will be invited to consent to the open-label study and be given two infusions at 4 monthly intervals (at day 0, month 4, and month 8) and followed up at month 12. We will explore the acceptability of the treatment by conducting interviews with children and parents in both arms following the crossover period.

1. At 0 months (Visit 10), participants will receive the fifth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, analgesia review, quality of life questionnaire, safety and research blood tests, adverse event assessment, and concomitant medication assessment

2. At 0 months + 2 weeks (Visit 11), participants will receive the sixth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, research blood tests, adverse event assessment, and concomitant medication assessment

3. At 4 months (Visit 12), participants will receive the seventh infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, analgesia review, quality of life questionnaire, research and safety blood tests, adverse event assessment, concomitant medication assessment

4. At 4 months + 2 weeks (Visit 13), participants will receive the eighth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, photography of wounds, research blood tests, adverse event assessment, and concomitant medication assessment

5. At 8 months (Visit 14), participants will receive the ninth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, disease severity assessments, pain and itch assessment, photography of wounds, analgesia review, quality of life questionnaire, safety and research blood tests, adverse event assessment, and concomitant medication assessment

6. At 8 months + 2 weeks (Visit 15), participants will receive the tenth infusion and be assessed for pregnancy test (menstruating and sexually active participants only), physical examination, vital signs, pain and itch assessment, photography of wounds, research blood tests, adverse event assessment, and concomitant medication assessment



7. At 12 month (Visit 16), participants will undergo disease severity assessments, pain and itch assessment, photography of wounds, analgesia review, quality of life questionnaire, safety blood tests, adverse event assessment, concomitant medication assessment, and pregnancy test (menstruating and sexually active participants only)

The maximum duration of treatment of a subject will 24 months. An evaluation of costs associated with treatment will also be undertaken.

### **Intervention Type**

Biological/Vaccine

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

CORDStrom

### **Primary outcome measure**

Current primary outcome measure as of 22/04/2022:

Internal phase I dose de-escalation trial:

Toxicity measured using the incidence of a Suspected Unexpected Serious Adverse Reaction (SUSAR) within 48 h of a patient receiving an infusion

Main cross-over trial:

Disease severity measured using the total score across all 5 domains of the Epidermolysis Bullosa Disease Activity and Scarring Index (EBDASI) at day 0 and 3 months post-infusion of UC-MSCs

Open-label non-randomised study:

Disease severity measured using the total score across all 5 domains of the Epidermolysis Bullosa Disease Activity and Scarring Index (EBDASI) at 4, 8, and 12 months of the open-label study

NB: MissionEB is not an adequately powered study for feasibility reasons and as such, the judgement on efficacy of UC-MSCs will be based on totality of evidence from all clinical (primary and secondary) outcomes.

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Previous primary outcome measure:

Internal phase I dose de-escalation trial:

Toxicity measured using the incidence of a Suspected Unexpected Serious Adverse Reaction (SUSAR) within 48 h of a patient receiving an infusion

Main cross-over trial:

Disease severity measured using the total score across all 5 domains of the Epidermolysis Bullosa Disease Activity and Scarring Index (EBDASI) at day 0 and 3 months post-infusion of UC-MSCs

Open-label non-randomised study:

Disease severity measured using the total score across all 5 domains of the Epidermolysis

Bullosa Disease Activity and Scarring Index (EBDASI) at 4, 8, and 12 months of the open-label study

## Secondary outcome measures

Current secondary outcome measures as of 22/04/2022:

1. Change in disease severity as measured by EBDASI at 6 months post infusion (from day 0, period baseline) for the cross-over study, and at 0, 4, 6, and 12 months for the open-label study.
2. Change in disease severity measured using instrument for scoring clinical outcomes of research for epidermolysis bullosa (iscorEB) at 3- and 6-months post infusion (from day 0, period baseline) for the cross-over study and at 0, 4, 6, and 12 months for the open-label study.
3. Change in general clinical appearance of skin disease measured using clinical photography at 3- and 6-months post infusion (from day 0, period baseline) for the cross-over study, and at 0 months, 0 months + 2 weeks, 4 months, 4 months + 2 weeks, 8 months, and 8 months + 2 weeks infusion visits and 12-month follow-up for the open-label study
4. Change to pain and itch as assessed by the Wong-Baker FACES Pain scale for children over 6 years old and Leuven itch scale scores at 3- and 6-months post infusion (from day 0, period baseline) for the cross-over study and 0 months, 0 months + 2 weeks, 4 months, 4 months + 2 weeks, 8 months, and 8 months + 2 weeks infusion visits and 12 month follow up for the open-label study.
5. Change to pain and itch as assessed by the amount of analgesia and itch medications required. Participants or their guardians will be asked to detail what pain and itch medication the participant has taken in the last 48 hours, including dose and frequency. At 3 months post infusion, clinicians blinded to treatment allocation will compare whether this is unchanged, increased or decreased since baseline (day 0, period baseline) for the cross-over study and at 0, 4, 8, and 12 months for the open-label study.
6. Change in quality of life according to validated Child Health Utility 9D (CHUD-9D) scoring system in children aged  $\geq 7$  years (an age appropriate by proxy version will be used for children aged 3 – 6) at 3- and 6-months post infusion (from day 0, period baseline) for the cross-over study at 0, 4, 8, and 12 months for the open-label study.
7. Health economic analysis to assess the costs and consequences of treatment with UC-MSCs versus usual care.
8. Safety measured using monitoring of AEs and SAEs throughout the trial.

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Previous secondary outcome measures:

1. Disease severity measured using instrument for scoring clinical outcomes of research for epidermolysis bullosa (iscorEB) at day 0 (day of infusion), 3, and 6 months post-infusion for the cross-over study and at 0, 4, 6, and 12 months for the open-label study
2. General clinical appearance of skin disease measured using clinical photography at 0 day and 9 months infusions visits and 3, 6, 12, and 15 month follow-up for the cross-over study and at 0 months, 0 months + 2 weeks, 4 months, 4 months + 2 weeks, 8 months, and 8 months + 2 weeks infusion visits and 12 month follow-up for the open-label study
3. Improved pain and itch measured using the Wong-Baker FACES Pain scale for children over 6 years old and the Leuven itch scale scores, measured at 0 days, 14 days, 9 months, and 9 months + 2 weeks infusion visits and 3, 6, 9, 12, and 15 months follow-up for the cross-over study and 0 months, 0 months + 2 weeks, 4 months, 4 months + 2 weeks, 8 months, and 8 months + 2 weeks infusion visits and 12 month follow up for the open-label study
4. Improved pain measured using the amount of analgesia required, the type of analgesia required, including dose and frequency, and whether this use is unchanged, increased, or decreased in the last 48 h reported using a question to participants or their guardian at 0 day and 9 month infusion visits and 3, 6 12 and 15 months follow-up for the cross-over study and at

0, 4, 8, and 12 months for the open-label study

5. Improved quality of life measured using the validated Child Health Utility 9D (CHUD-9D) scoring system in children aged  $\geq 7$  years (A by proxy version will be used for children aged 3 to 6 years) at 0 day and 9 month infusion visits and 3, 6, 12, and 15 months follow up for the cross-over study at 0, 4, 8, and 12 months for the open-label study

6. Health economic analysis to assess the costs and consequences of treatment with UC-MSCs versus usual care

7. Safety measured using monitoring of AEs and SAEs throughout the trial

**Overall study start date**

01/08/2020

**Completion date**

31/10/2025

## **Eligibility**

**Key inclusion criteria**

1. Diagnosis of RDEB characterised by partial or complete C7 deficiency including generalised severe and generalised intermediate subtypes

2. Aged  $>6$  months and  $<16$  years at time of enrolment

3. Responsible parent/guardian has voluntarily 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

**Age group**

Child

**Lower age limit**

6 Months

**Upper age limit**

16 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 36; UK Sample Size: 36

**Total final enrolment**

37

**Key exclusion criteria**

Current participant exclusion criteria as of 07/03/2023:

1. Other subtypes of EB such as EB simplex, EB junctional, dominant dystrophic EB, and Kindler EB

2. Received oral or topical corticosteroids for >7 consecutive days within 30 days or enrolment into this study, except for treatment with oral budesonide
3. Known allergy to any of the constituents of the investigational product
4. Signs of active infection that require treatment with oral or intravenous antibiotics within 7 days of screening
5. History or evidence of active malignancy, including cutaneous squamous cell carcinoma
6. Positive C7 ELISA and positive indirect immunofluorescence (IIF) with binding to the base of salt split skin at screening
7. 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
8. Received MSC infusions in the last 9 months
9. Simultaneous or previous participation in any interventional trial within 3 months before entering this trial. Participation in simultaneous registry and diagnostic trials during the trial is allowed.

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Previous participant exclusion criteria as of 22/04/2022 to 07/03/2023:

1. Other subtypes of EB such as EB simplex, EB junctional, dominant dystrophic EB, and Kindler EB
2. Received oral or topical corticosteroids for >7 consecutive days within 30 days or enrolment into this study, except for treatment with oral budesonide
3. Known allergy to any of the constituents of the investigational product
4. Signs of active infection that require treatment with oral or intravenous antibiotics within 7 days of screening
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6. Positive C7 ELISA and positive indirect immunofluorescence (IIF) with binding to the base of salt split skin
7. 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
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Previous participant exclusion criteria:

1. Other subtypes of EB such as EB simplex, EB junctional, dominant dystrophic EB, and Kindler EB
2. Received oral or topical corticosteroids for >1 week within 30 days of enrolment into this study
3. Known allergy to any of the constituents of the investigational product
4. Signs of active infection that require treatment with oral or intravenous antibiotics within 7 days of screening
5. History or evidence of active malignancy, including cutaneous squamous cell carcinoma
6. Positive C7 ELISA and positive indirect immunofluorescence (IIF) with binding to the base of salt split skin
7. 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

8. Received MSC infusions in the last 9 months

9. Simultaneous or previous participation in any interventional trial within 3 months before entering this trial. Participation in simultaneous registry and diagnostic trials during the trial is allowed.

**Date of first enrolment**

13/09/2021

**Date of final enrolment**

05/01/2023

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Great Ormond Street Hospital**

Great Ormond Street Hospital for Children NHS Foundation Trust

Great Ormond Street

London

United Kingdom

WC1N 3JH

**Study participating centre**

**Birmingham Children's Hospital**

Birmingham Women's And Children's NHS Foundation Trust

Steelhouse Lane

Birmingham

United Kingdom

B4 6NH

## **Sponsor information**

**Organisation**

Great Ormond Street Hospital for Children NHS Foundation Trust

**Sponsor details**

R&D office

Great Ormond Street Hospital

Great Ormond Street

London  
England  
United Kingdom  
WC1N 3JH  
+44 (0)2074059200  
research.governance@gosh.nhs.uk

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.gosh.nhs.uk/>

**ROR**

<https://ror.org/03zydm450>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

**Funder Name**

Cure EB

## **Results and Publications**

Publication and dissemination plan

Planned publication of results in a high-impact peer-reviewed journal. Planned publication of study protocol which will be available at <https://www.sheffield.ac.uk/scharr/research/centres/ctru/missioneib>.

**Intention to publish date**

31/07/2025

**Individual participant data (IPD) sharing plan**

All data generated or analysed during this study will be included in the subsequent results publication

**IPD sharing plan summary**

Published as a supplement to the results publication, Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol file</a>	version 8.1	17/12/2024	21/03/2025	No	No
<a href="#">Statistical Analysis Plan</a>	version 2.0	30/04/2024	17/04/2025	No	No
<a href="#">Protocol article</a>		21/05/2025	22/05/2025	Yes	No