

**Clinical trial results:**

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

Summary

EudraCT number	2012-001394-87
Trial protocol	GB
Global end of trial date	11 December 2014

Results information

Result version number	v1 (current)
This version publication date	28 October 2018
First version publication date	28 October 2018
Summary attachment (see zip file)	EBSTEM Final Clinical Study Report (EBSTEM Clinical Study Report_ 28 Sep 2015.pdf)

Trial information**Trial identification**

Sponsor protocol code	EBSTEM001
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Additional study identifiers

ISRCTN number	ISRCTN46615946
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Dept of Genetics and Molecular Med., Prof. John A. McGrath, 0044 0207188 6409, john.mcgrath@kcl.ac.uk
Scientific contact	Dept of Genetics and Molecular Med., Prof. John A. McGrath, 0044 0207188 6409, john.mcgrath@kcl.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2014
Global end of trial reached?	Yes
Global end of trial date	11 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of allogeneic intravenously administered MSCs in children with RDEB over a 24-month period.

Protection of trial subjects:

The study subjects can continue to receive their regular medication(s). All IMP administration is completed in a specialist hospital environment.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	04 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	4
Children (2-11 years)	6
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Ten children were enrolled at Great Ormond Street Hospital (London, UK).

Pre-assignment

Screening details:

Eleven children with RDEB were screened for inclusion into the trial. One child was excluded because of both positive ELISA for C7 antibodies and positive indirect immunofluorescence microscopy (IIF) with binding of the antibodies to the dermal-epidermal junction (DEJ) within the base of salt-split skin.

Period 1

Period 1 title	Whole Group (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

n/a

Arms

Arm title	Full study
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Arm description:

Single Arm Study. All study participants will receive three intravenous MSC infusions at baseline Day 0, D7 and D28 and will be followed up for a 24-month period following the last infusion

Arm type	Experimental
Investigational medicinal product name	Mesenchymal stromal cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Third-party bone marrow-derived mesenchymal stromal cells administered by intravenous infusion on 3 occasions.

Number of subjects in period 1	Full study
Started	10
Completed	10

Baseline characteristics

Reporting groups

Reporting group title	Whole Group
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Reporting group description: -

Reporting group values	Whole Group	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
12months to 3 years	3	3	
4 to 6 years	3	3	
7 to 10years	2	2	
11 to 14 years	2	2	
Gender categorical Units: Subjects			
Female	5	5	
Male	5	5	

End points

End points reporting groups

Reporting group title	Full study
Reporting group description: Single Arm Study. All study participants will receive three intravenous MSC infusions at baseline Day 0, D7 and D28 and will be followed up for a 24-month period following the last infusion	

Primary: Primary safety endpoint

End point title	Primary safety endpoint ^[1]
End point description: To evaluate the safety of allogeneic intravenously administered MSCs in children with RDEB over a 24-month period	
End point type	Primary
End point timeframe: 0 to 24 months	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Please see attached documents for results	

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: whole	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Efficacy Parameters

End point title	Secondary Efficacy Parameters
End point description: Incidence of infusional toxicity. Increase in C7 deposition at the DEJ post treatment at D0 and D60. Quantitative analysis of the donor cells chimerism at D60. Improvement of haematological and serological markers of generalised inflammation at D0, D7, D28, D60 and D180 compared to baseline. Improvement in the clinical appearances of the skin. Improved quality of life according to validated paediatric QoL scoring systems at screening, D60, D100 and D180. Pain scoring at screening, D0, D7, D28, D60, D100 and D180. Reduction in blister occurrence over entire body surface at D0, D7, D28, D60, D100 and D180 as compared to baseline. Increase in skin strength measured by time to blister formation after skin suction at screening and D100.	
End point type	Secondary
End point timeframe: 0 to day 180	

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: whole	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to day 180

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Whole Trial
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Reporting group description: -

Serious adverse events	Whole Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Injury, poisoning and procedural complications			
Accidental injuries			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	18		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Oesophageal dilatation			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		
Routine surgical procedure related to complications of EB			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Dental procedure subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Ear and labyrinth disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Sore Throat subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Corneal abrasion subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 20		
Sore eyes subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Reflux subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Constipation subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Diarrhea			

subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 9		
Increased appetite subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Nausea subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 3		
Vomiting subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 6		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 4		
Respiratory tract infection subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 10		
Skin infections subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 7		
Skin and subcutaneous tissue disorders			
Skin/mucosal blisters/wounds subjects affected / exposed occurrences (all)	9 / 10 (90.00%) 16		
Dry skin subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Fine hair growth subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Milia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Pruritus			

<p>subjects affected / exposed occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed occurrences (all)</p>	<p>4 / 10 (40.00%) 4</p> <p>2 / 10 (20.00%) 4</p>		
<p>Renal and urinary disorders</p> <p>Oliguria</p> <p>subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Joint pain</p> <p>subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p>		
<p>Infections and infestations</p> <p>Fever</p> <p>subjects affected / exposed occurrences (all)</p> <p>Urinary tract infections</p> <p>subjects affected / exposed occurrences (all)</p>	<p>2 / 10 (20.00%) 2</p> <p>1 / 10 (10.00%) 1</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2014	Reduction of Data Monitoring Committee meetings detailed in the protocol
25 September 2014	To change primary end point and reduce follow up period from 24 months to 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25905587>