



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 |
|-----------------------|-----------|

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 |
|-----------|------------|

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 |
|-----------------------|-------------|

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Whole Trial |
|-----------------------|-------------|

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 | | | |

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

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