



## Clinical trial results:

**A phase I safety and tolerability study of infusing the autologous progeny of an adult CD34+ subset into patients with type I diabetes mellitus and a successful renal transplant.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2006-002328-40 |
| Trial protocol           | GB             |
| Global end of trial date | 31 May 2013    |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 13 November 2019 |
| First version publication date | 13 November 2019 |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | HHSC/005 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00788827 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Imperial College London  |
| Sponsor organisation address | South Kensington Campus, London, United Kingdom, SW7 2AZ                         |
| Public contact               | Charles Pusey, Imperial College London, +44 20 8383 2308, c.pusey@imperial.ac.uk |
| Scientific contact           | Charles Pusey, Imperial College London, +44 20 8383 2308, c.pusey@imperial.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:

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**Results analysis stage**

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|  |             |
|--|-------------|
| Analysis stage                                       | Final       |
| Date of interim/final analysis                       | 30 May 2014 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 31 May 2013 |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 31 May 2013 |
| Was the trial ended prematurely?                     | No          |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety and tolerance of a high dose of autologous expanded progeny of adult CD34+ stem cell subset (InsulinCytes) when introduced into either the body or tail of the pancreas.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 03 November 2008 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Worldwide total number of subjects   | 7                 |
| EEA total number of subjects         | 7                 |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |
| Adults (18-64 years)                      | 7 |
| From 65 to 84 years                       | 0 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited at Imperial College NHS Healthcare Trust, Hammersmith Hospital between November 2008 and May 2013

### Pre-assignment

Screening details:

A total of seven participants were eligible for the study

### Period 1

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

### Arms

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Autologous CD34+ Stem Cells |
|------------------|-----------------------------|

Arm description:

Patients received Autologous CD34+ Stem Cells

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | CD34+ Stem Cells                |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Other use                       |

Dosage and administration details:

The expanded autologous CD34+ cells were infused into the right hepatic artery of the patients in the imaging department.

| Number of subjects in period 1 | Autologous CD34+ Stem Cells |
|--------------------------------|-----------------------------|
| Started                        | 7                           |
| Completed                      | 5                           |
| Not completed                  | 2                           |
| Lack of efficacy               | 2                           |

## Baseline characteristics

### Reporting groups

|                                |         |
|--------------------------------|---------|
| Reporting group title          | Overall |
| Reporting group description: - |         |

| Reporting group values | Overall | Total |  |
|------------------------|---------|-------|--|
| Number of subjects     | 7       | 7     |  |
| Age categorical        |         |       |  |
| Units: Subjects        |         |       |  |
| Adults (18-64 years)   | 7       | 7     |  |
| Age continuous         |         |       |  |
| Units: years           |         |       |  |
| geometric mean         | 54.6    |       |  |
| standard deviation     | ± 4.2   | -     |  |
| Gender categorical     |         |       |  |
| Units: Subjects        |         |       |  |
| Female                 | 2       | 2     |  |
| Male                   | 5       | 5     |  |

### Subject analysis sets

|  |                             |
|--|-----------------------------|
| Subject analysis set title                                 | Pre Infusion of Stem Cells  |
| Subject analysis set type                                  | Sub-group analysis          |
| Subject analysis set description:                          |                             |
| Mean HbA1c laboratory measurements pre stem cell infusion  |                             |
| Subject analysis set title                                 | Post Infusion of Stem Cells |
| Subject analysis set type                                  | Sub-group analysis          |
| Subject analysis set description:                          |                             |
| Mean HbA1c laboratory measurements post stem cell infusion |                             |

| Reporting group values | Pre Infusion of Stem Cells | Post Infusion of Stem Cells |  |
|------------------------|----------------------------|-----------------------------|--|
| Number of subjects     | 5                          | 5                           |  |
| Age categorical        |                            |                             |  |
| Units: Subjects        |                            |                             |  |
| Adults (18-64 years)   | 5                          | 5                           |  |
| Age continuous         |                            |                             |  |
| Units: years           |                            |                             |  |
| geometric mean         |                            |                             |  |
| standard deviation     | ±                          | ±                           |  |
| Gender categorical     |                            |                             |  |
| Units: Subjects        |                            |                             |  |
| Female                 |                            |                             |  |
| Male                   |                            |                             |  |

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Autologous CD34+ Stem Cells |
| Reporting group description:<br>Patients received Autologous CD34+ Stem Cells                   |                             |
| Subject analysis set title  | Pre Infusion of Stem Cells  |
| Subject analysis set type   | Sub-group analysis          |
| Subject analysis set description:<br>Mean HbA1c laboratory measurements pre stem cell infusion  |                             |
| Subject analysis set title  | Post Infusion of Stem Cells |
| Subject analysis set type   | Sub-group analysis          |
| Subject analysis set description:<br>Mean HbA1c laboratory measurements post stem cell infusion |                             |

### Primary: Number of Participants Who Experienced Adverse Events\_Haematoma at femoral catheter insertion

|                                 |  |
|---------------------------------|--|
| End point title                 | Number of Participants Who Experienced Adverse Events_Haematoma at femoral catheter insertion <sup>[1]</sup> |
| End point description:          |  |
| End point type                  | Primary  |
| End point timeframe:<br>14 days |  |

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: No statistical analyses due to low number of participants.

| End point values            | Autologous CD34+ Stem Cells |  |  |  |
|-----------------------------|-----------------------------|--|--|--|
| Subject group type          | Reporting group             |  |  |  |
| Number of subjects analysed | 7                           |  |  |  |
| Units: Participants         | 1                           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants Who Experienced Adverse Events\_Fatigue

|                                 |  |
|---------------------------------|--|
| End point title                 | Number of Participants Who Experienced Adverse Events_Fatigue <sup>[2]</sup> |
| End point description:          |  |
| End point type                  | Primary  |
| End point timeframe:<br>14 days |  |

Notes:

[2] - 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: No statistical analyses due to low number of participants.

|                             |                             |  |  |  |
|-----------------------------|-----------------------------|--|--|--|
| <b>End point values</b>     | Autologous CD34+ Stem Cells |  |  |  |
| Subject group type          | Reporting group             |  |  |  |
| Number of subjects analysed | 7                           |  |  |  |
| Units: Participants         | 7                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Hba1C Data of Pre and Post Stem Cell Infusion

|                        |   |
|------------------------|---|
| End point title        | Hba1C Data of Pre and Post Stem Cell Infusion |
| End point description: |   |
| End point type         | Secondary                                     |
| End point timeframe:   |   |
| 12 weeks               |   |

|                                     |                            |                             |  |  |
|-------------------------------------|----------------------------|-----------------------------|--|--|
| <b>End point values</b>             | Pre Infusion of Stem Cells | Post Infusion of Stem Cells |  |  |
| Subject group type                  | Subject analysis set       | Subject analysis set        |  |  |
| Number of subjects analysed         | 5                          | 5                           |  |  |
| Units: percentage                   |                            |                             |  |  |
| geometric mean (standard deviation) | 7.2 (± 1.3)                | 7.24 (± 1.2)                |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Hba1C Data of Pre and Post Stem Cell Infusion            |
| Comparison groups                       | Pre Infusion of Stem Cells v Post Infusion of Stem Cells |
| Number of subjects included in analysis | 10   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | < 0.05   |
| Method                                  | Mixed models analysis                                    |

## Secondary: Insulin level

|                 |               |
|-----------------|---------------|
| End point title | Insulin level |
|-----------------|---------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

12 weeks

| End point values                    | Pre Infusion of Stem Cells | Post Infusion of Stem Cells |  |  |
|-------------------------------------|----------------------------|-----------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set        |  |  |
| Number of subjects analysed         | 5                          | 5                           |  |  |
| Units: iu/day                       |                            |                             |  |  |
| geometric mean (standard deviation) | 59.4 (± 25.7)              | 54.06 (± 18.2)              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Amylase Level

|                 |               |
|-----------------|---------------|
| End point title | Amylase Level |
|-----------------|---------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

12 weeks

| End point values                    | Pre Infusion of Stem Cells | Post Infusion of Stem Cells |  |  |
|-------------------------------------|----------------------------|-----------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set        |  |  |
| Number of subjects analysed         | 5                          | 5                           |  |  |
| Units: units/L                      |                            |                             |  |  |
| geometric mean (standard deviation) | 48.49 (± 25.2)             | 75.52 (± 34.2)              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Serum Creatinine

|                 |                  |
|-----------------|------------------|
| End point title | Serum Creatinine |
|-----------------|------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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End point timeframe:

12 weeks

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| <b>End point values</b>             | Pre Infusion of Stem Cells | Post Infusion of Stem Cells |  |  |
|-------------------------------------|----------------------------|-----------------------------|--|--|
| Subject group type                  | Subject analysis set       | Subject analysis set        |  |  |
| Number of subjects analysed         | 5                          | 5                           |  |  |
| Units: umol/L                       |                            |                             |  |  |
| geometric mean (standard deviation) | 128.22 (± 11.9)            | 118.64 (± 15.5)             |  |  |

### **Statistical analyses**

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 weeks

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 10 |
|--------------------|----|

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Autologous CD34+ Stem Cells |
|-----------------------|-----------------------------|

Reporting group description:

Patients received Autologous CD34+ Stem Cells

| Serious adverse events                            | Autologous CD34+ Stem Cells |  |  |
|---|-----------------------------|--|--|
| Total subjects affected by serious adverse events |                             |  |  |
| subjects affected / exposed                       | 0 / 7 (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                            | Autologous CD34+ Stem Cells |  |  |
|---|-----------------------------|--|--|
| Total subjects affected by non-serious adverse events |                             |  |  |
| subjects affected / exposed                           | 7 / 7 (100.00%)             |  |  |
| Nervous system disorders                              |                             |  |  |
| Fatigue   |                             |  |  |
| subjects affected / exposed                           | 7 / 7 (100.00%)             |  |  |
| occurrences (all)                                     | 7                           |  |  |
| Blood and lymphatic system disorders                  |                             |  |  |
| Haematoma   |                             |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%)              |  |  |
| occurrences (all)                                     | 1                           |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported