



## Clinical trial results:

### The pharmacological effects of granulocyte-colony stimulating factor (GCSF) on frataxin expression in patients with Friedreich Ataxia

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-003084-34 |
| Trial protocol           | GB             |
| Global end of trial date | 12 April 2019  |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 26 January 2020   |
| First version publication date    | 26 January 2020   |
| Summary attachment (see zip file) | FA GCSF result synopsis (Clinical_Study_Synopsis_GCSF FA.pdf) |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | GCSF_FRDA_v1 |
|-----------------------|--------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | University of Bristol  |
| Sponsor organisation address | Research and Enterprise Development One Cathedral Square, Bristol, United Kingdom, BS1 5DD |
| Public contact               | Alastair Wilkins, University of Bristol, research-governance@bristol.ac.uk                 |
| Scientific contact           | Alastair Wilkins, University of Bristol, 44 1174147802, alastair.wilkins@bristol.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                       | 19 December 2019 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 12 April 2019    |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Does administration of GCSF lead to improvements in blood markers of Friedreich Ataxia?

We will study a small number of patients with the condition and will administer GCSF (at identical doses to those given to 'healthy' people prior to bone marrow donation) for a short period of time. We will define whether administration of the drug leads to changes in blood markers which would indicate a positive response to the drug. The study will also allow us to decide what blood markers we can monitor in the subsequent trial. This has not been studied before and is a vital step in the development of a stem cell research trial. Once information has been obtained from this study, a larger trial of GCSF in FRDA can be developed.

Protection of trial subjects:

The trial was carried out using the principles of Good Clinical Practice and was approved by UK Medicines and Healthcare products Regulatory Agency (MHRA), Health Research Authority (HRA) and Research Ethics Committee (REC).

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 01 October 2017 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### 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:

### 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)  | 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:

7 participants:

Inclusion criteria:

Genetic diagnosis of Friedreich's Ataxia (FA)

Inclusion criteria: Genetic diagnosis of FA; Age of over 18

### Pre-assignment

Screening details:

Patients attending local/ regional or national atxia clinic were screened

Genetic diagnosis of Friedreich's Ataxia (FA)

Inclusion criteria: Genetic diagnosis of FA; Age of over 18

### Period 1

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

Blinding implementation details:

N/A

### Arms

|           |               |
|-----------|---------------|
| Arm title | Overall trial |
|-----------|---------------|

Arm description:

Single arm; all participants received the same intervention

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Granulocyte-colony stimulating factor |
| Investigational medicinal product code |                                       |
| Other name                             | Lenograstim, Granocyte                |
| Pharmaceutical forms                   | Powder for suspension for injection   |
| Routes of administration               | Subcutaneous use                      |

Dosage and administration details:

1.28 million units/kg daily for 5 days

| Number of subjects in period 1 | Overall trial |
|--------------------------------|---------------|
| Started                        | 7             |
| Completed                      | 7             |

## Baseline characteristics

### Reporting groups

|   |               |
|---|---------------|
| Reporting group title                                       | Overall trial |
| Reporting group description:                                |               |
| Single arm; all participants received the same intervention |               |

| Reporting group values                             | Overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 7             | 7     |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 7             | 7     |  |
| From 65-84 years                                   | 0             | 0     |  |
| 85 years and over                                  | 0             | 0     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 4             | 4     |  |
| Male   | 3             | 3     |  |

## End points

### End points reporting groups

|   |               |
|---|---------------|
| Reporting group title                                       | Overall trial |
| Reporting group description:                                |               |
| Single arm; all participants received the same intervention |               |

### Primary: Change in frataxin expression in peripheral blood cells after granulocyte-colony stimulating factor (G-CSF) administration to patients with Friedreich's Ataxia

|                 |  |
|-----------------|--|
| End point title | Change in frataxin expression in peripheral blood cells after granulocyte-colony stimulating factor (G-CSF) administration to patients with Friedreich's Ataxia <sup>[1]</sup> |
|-----------------|--|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 5-19 after commencement of administration of IMP

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: All participants received the IMP. No control comparator

| End point values            | Overall trial    |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 6 <sup>[2]</sup> |  |  |  |
| Units: pg/μg of protein     |                  |  |  |  |
| number (not applicable)     | 6                |  |  |  |

Notes:

[2] - 1 participant did not complete trial

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Between commencement of administration of IMP and day 19 of the study in each participant

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Single arm |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events                            | Single arm    |  |  |
|---|---------------|--|--|
| 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: 5 %

| Non-serious adverse events                            | Single arm     |  |  |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 3 / 7 (42.86%) |  |  |
| Nervous system disorders                              |                |  |  |
| headache  |                |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%) |  |  |
| occurrences (all)                                     | 1              |  |  |
| Musculoskeletal and connective tissue disorders       |                |  |  |
| bone pain   |                |  |  |
| subjects affected / exposed                           | 2 / 7 (28.57%) |  |  |
| occurrences (all)                                     | 2              |  |  |

## 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