



Clinical trial results:

'Stem cell Trial of recovery EnhanceMent after Stroke 3' (STEMS 3)- a pilot randomised controlled trial of G-CSF and therapy in chronic stroke Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-001684-50 |
| Trial protocol | GB |
| Global end of trial date | 30 October 2013 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 24 February 2019 |
| First version publication date | 24 February 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 11015 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|----------------|
| ISRCTN number | ISRCTN16714730 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | University of Nottingham |
| Sponsor organisation address | Jubilee Campus, Triumph Road, Nottingham, United Kingdom, NG8 1DH |
| Public contact | Nikola Sprigg, University of Nottingham, +44 115 8231765, nikola.sprigg@nottingham.ac.uk |
| Scientific contact | Angela Shone, University of Nottingham, +44 115 8467906, angela.shone@nottingham.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 | 04 February 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 October 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 October 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the safety, feasibility, and tolerability of delivering the drug G-CSF and or rehabilitation therapy in chronic stroke patients.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 17 November 2011 |
| 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: 60 |
| Worldwide total number of subjects | 60 |
| EEA total number of subjects | 60 |

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) | 26 |
| From 65 to 84 years | 32 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Recruitment commenced on 17th November 2011 and was completed on 1st July 2013

Pre-assignment

Screening details:

Participants had to demonstrate disability, mRs greater than 1 and no longer be receiving ongoing rehabilitation therapy.

3 months - 2 years post stroke

Period 1

| | |
|------------------------------|---|
| Period 1 title | Baseline |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|------|
| Are arms mutually exclusive? | No |
| Arm title | GCSF |

Arm description: -

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Filgastrim |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

1 x 10E6 iu/kg injection once per day for 5 days

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Normal Saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.9% solution once per day for 5 days

| | |
|------------------|---------|
| Arm title | Therapy |
|------------------|---------|

Arm description: -

| | |
|---|------------------------|
| Arm type | Received physiotherapy |
| No investigational medicinal product assigned in this arm | |

| | |
|------------------|------------|
| Arm title | No therapy |
|------------------|------------|

Arm description: -

| | |
|---|---------------|
| Arm type | Standard care |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | GCSF | Placebo | Therapy |
|--------------------------------|------|---------|---------|
| Started | 30 | 30 | 30 |
| Completed | 30 | 30 | 30 |

| Number of subjects in period 1 | No therapy |
|--------------------------------|------------|
| Started | 30 |
| Completed | 30 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Day 90 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|------|
| Are arms mutually exclusive? | Yes |
| Arm title | GCSF |

Arm description: -

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Filgastrim |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

1 x 10E6 iu/kg injection once per day for 5 days

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Normal Saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.9% solution once per day for 5 days

| | |
|------------------|---------|
| Arm title | Therapy |
|------------------|---------|

Arm description: -

| | |
|----------|------------------------|
| Arm type | Received physiotherapy |
|----------|------------------------|

| | |
|---|---------------|
| No investigational medicinal product assigned in this arm | |
| Arm title | No therapy |
| Arm description: - | |
| Arm type | Standard care |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | GCSF | Placebo | Therapy |
|---------------------------------------|------|---------|---------|
| Started | 30 | 30 | 30 |
| Completed | 30 | 27 | 28 |
| Not completed | 0 | 3 | 2 |
| Lost to follow-up | - | 3 | 2 |

| Number of subjects in period 2 | No therapy |
|---------------------------------------|------------|
| Started | 30 |
| Completed | 29 |
| Not completed | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|------------|
| Reporting group title | GCSF |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Therapy |
| Reporting group description: - | |
| Reporting group title | No therapy |
| Reporting group description: - | |

| Reporting group values | GCSF | Placebo | Therapy |
|------------------------|--------|---------|---------|
| Number of subjects | 30 | 30 | 30 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 12 | 14 | 14 |
| From 65-84 years | 18 | 14 | 16 |
| 85 years and over | 0 | 2 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 66.8 | 65.6 | 65.6 |
| standard deviation | ± 8.33 | ± 12.8 | ± 9.46 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 11 | 11 |
| Male | 17 | 19 | 19 |

| Reporting group values | No therapy | Total | |
|------------------------|------------|-------|--|
| Number of subjects | 30 | 60 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 12 | 26 | |
| From 65-84 years | 16 | 32 | |
| 85 years and over | 2 | 2 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 66.9 | - | |
| standard deviation | ± 11.97 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 24 | |
| Male | 17 | 36 | |

End points

End points reporting groups

| | |
|--------------------------------|------------|
| Reporting group title | GCSF |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Therapy |
| Reporting group description: - | |
| Reporting group title | No therapy |
| Reporting group description: - | |
| Reporting group title | GCSF |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Therapy |
| Reporting group description: - | |
| Reporting group title | No therapy |
| Reporting group description: - | |

Primary: Day 90 mRs

| | |
|------------------------|------------|
| End point title | Day 90 mRs |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| Day 90 | |

| End point values | GCSF | Placebo | Therapy | No therapy |
|--------------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 27 | 28 | 29 |
| Units: Mean mRs | | | | |
| arithmetic mean (standard deviation) | 2.8 (\pm 1.03) | 2.9 (\pm 0.91) | 2.9 (\pm 1.04) | 2.8 (\pm 0.90) |

Statistical analyses

| | |
|----------------------------|-----------------|
| Statistical analysis title | GCSF comparison |
| Comparison groups | GCSF v Placebo |

| | |
|---|-----------------|
| Number of subjects included in analysis | 57 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.46 |
| Method | t-test, 2-sided |

| | |
|---|----------------------|
| Statistical analysis title | Therapy comparison |
| Comparison groups | No therapy v Therapy |
| Number of subjects included in analysis | 57 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9 |
| Method | t-test, 2-sided |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Day 90

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Non-serious adverse events not recorded

| Serious adverse events | All patients | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 60 (20.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| General disorders and administration site conditions | | | |
| SAE | | | |
| subjects affected / exposed | 12 / 60 (20.00%) | | |
| occurrences causally related to treatment / all | 0 / 44 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | All patients | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|-----|
| N/A |
|-----|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27610616>