



## Clinical trial results:

### A Calcium channel or Angiotensin converting enzyme inhibitor/Angiotensin receptor blocker Regimen to reduce Blood pressure variability in acute ischaemic Stroke (CAARBS): A Feasibility Trial

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-002560-41 |
| Trial protocol           | GB             |
| Global end of trial date | 31 March 2019  |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 03 December 2019 |
| First version publication date | 03 December 2019 |

#### Trial information

##### Trial identification

|                       |      |
|-----------------------|------|
| Sponsor protocol code | 0611 |
|-----------------------|------|

##### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN10853487 |
| ClinicalTrials.gov id (NCT number) | -              |
| WHO universal trial number (UTN)   | -              |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University of Leicester   |
| Sponsor organisation address | Leicester General Hospital, Gwendolen Road, Leicester, United Kingdom, LE5 4PW              |
| Public contact               | Professor Thompson Robinson, University of Leicester, +44 01162523182, tgr2@leicester.ac.uk |
| Scientific contact           | Professor Thompson Robinson, University of Leicester, +44 01162523182, tgr2@leicester.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                       | 20 April 2019   |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 22 January 2019 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 31 March 2019   |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

In this feasibility study, patient recruitment and reasons for non-eligibility will be recorded. Accordingly, a screening log of all patients referred to the stroke services will be collected, and the reasons for non-inclusion in the study recorded.

Protection of trial subjects:

Subjects randomised to receive an angiotensin converting enzyme inhibitor or angiotensin receptor blocker had a blood test to monitor their renal function at the first follow-up visit, in line with standard clinical practise.

Background therapy:

Participants in both arms of the trial received standard stroke secondary prevention treatment in addition to the investigational treatment.

Evidence for comparator:

Work exploring the effects of commonly used antihypertensive medications in patients with hypertension has indicated that different classes of antihypertensive medication have different effects on the variability of blood pressure despite having similar impacts on average blood pressure levels. Specifically, blood pressure variability is reduced by calcium channel blockers, but increased by angiotensin converting enzyme inhibitors and angiotensin receptor blockers. Furthermore, these differential effects on blood pressure variability correlate with the risk of stroke seen in patients taking these medications.

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 01 September 2017 |
| 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: 14 |
| Worldwide total number of subjects   | 14                 |
| EEA total number of subjects         | 14                 |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 3  |
| From 65 to 84 years       | 11 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment for the trial commenced on 3rd January 2018 and was undertaken at three sites within the UK. The trial closed to recruitment on 31st December 2018.

### Pre-assignment

Screening details:

All patients presenting to stroke services at the involved trial sites (both in-patient and out-patient services at two of the sites and only out-patients at one site) were screened for potential inclusion in the trial.

### Period 1

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

Blinding implementation details:

The trial was open-label.

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | CCB arm |

Arm description:

Patients randomised to this arm were allocated to treatment with a medication from the class dihydropyridine calcium channel blockers, with the specific choice of medication from within that class being at the discretion of the treating physician.

|  |   |
|--|---|
| Arm type                               | Experimental                            |
| Investigational medicinal product name | Dihydropyridine calcium channel blocker |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Tablet                                  |
| Routes of administration               | Oral use                                |

Dosage and administration details:

Administer orally once daily for the duration of the trial. To be started at the introductory dose and titrated up at the first follow-up visit if blood pressure remained above the pre-specified target value.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | ACEI/ARB arm |
|------------------|--------------|

Arm description:

Patients randomised to this arm were allocated to treatment with a medication from the class angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, with the specific choice of medication from within the allocated class being at the discretion of the treating physician.

|  |   |
|--|---|
| Arm type                               | Active comparator                       |
| Investigational medicinal product name | Angiotensin-converting enzyme inhibitor |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Tablet                                  |
| Routes of administration               | Oral use                                |

Dosage and administration details:

Administered orally once daily for the duration of the trial. To be commenced at the introductory dose and titrated up at the first follow-up visit if blood pressure was above the pre-specified target value.

|  |                              |
|--|------------------------------|
| Investigational medicinal product name | Angiotensin receptor blocker |
| Investigational medicinal product code |                              |
| Other name                             |                              |

|                          |          |
|--------------------------|----------|
| Pharmaceutical forms     | Tablet   |
| Routes of administration | Oral use |

Dosage and administration details:

Administered orally once daily for the duration of the trial. To be commenced at the introductory dose and titrated up at the first follow-up visit if blood pressure was above the pre-specified target value.

| <b>Number of subjects in period 1</b> | CCB arm | ACEI/ARB arm |
|---------------------------------------|---------|--------------|
| Started                               | 6       | 8            |
| Completed                             | 4       | 5            |
| Not completed                         | 2       | 3            |
| Consent withdrawn by subject          | 1       | 1            |
| Screening failure                     | 1       | 1            |
| Protocol deviation                    | -       | 1            |

## Baseline characteristics

### Reporting groups

|   |              |
|---|--------------|
| Reporting group title   | CCB arm      |
| Reporting group description:  |              |
| Patients randomised to this arm were allocated to treatment with a medication from the class dihydropyridine calcium channel blockers, with the specific choice of medication from within that class being at the discretion of the treating physician.   |              |
| Reporting group title   | ACEI/ARB arm |
| Reporting group description:  |              |
| Patients randomised to this arm were allocated to treatment with a medication from the class angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, with the specific choice of medication from within the allocated class being at the discretion of the treating physician. |              |

| Reporting group values                             | CCB arm | ACEI/ARB arm | Total |
|--|---------|--------------|-------|
| Number of subjects                                 | 6       | 8            | 14    |
| Age categorical<br>Units: Subjects                 |         |              |       |
| In utero   |         |              | 0     |
| Preterm newborn infants (gestational age < 37 wks) |         |              | 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)                               |         |              | 0     |
| From 65-84 years                                   |         |              | 0     |
| 85 years and over                                  |         |              | 0     |
| Age continuous<br>Units: years                     |         |              |       |
| arithmetic mean                                    | 74.8    | 64.9         |       |
| standard deviation                                 | ± 4.2   | ± 9.1        | -     |
| Gender categorical<br>Units: Subjects              |         |              |       |
| Female   | 1       | 3            | 4     |
| Male   | 4       | 4            | 8     |
| Not recorded                                       | 1       | 1            | 2     |
| Ethnicity categorical<br>Units: Subjects           |         |              |       |
| White - British                                    | 4       | 6            | 10    |
| White - other                                      | 1       | 1            | 2     |
| Not recorded                                       | 1       | 1            | 2     |
| Diagnosis categorical<br>Units: Subjects           |         |              |       |
| Stroke   | 2       | 4            | 6     |
| TIA  | 3       | 3            | 6     |
| Not recorded                                       | 1       | 1            | 2     |
| Smoking status categorical<br>Units: Subjects      |         |              |       |

|  |         |          |    |
|--|---------|----------|----|
| Never smoked   | 2       | 2        | 4  |
| Ex-smoker  | 3       | 2        | 5  |
| Current smoker   | 0       | 3        | 3  |
| Not recorded   | 1       | 1        | 2  |
| Past medical history of hypertension categorical<br>Units: Subjects          |         |          |    |
| Yes  | 3       | 1        | 4  |
| No   | 2       | 6        | 8  |
| Not recorded   | 1       | 1        | 2  |
| Past medical history of diabetes categorical<br>Units: Subjects              |         |          |    |
| Yes  | 1       | 0        | 1  |
| No   | 4       | 7        | 11 |
| Not recorded   | 1       | 1        | 2  |
| Body mass index continuous<br>Units: Kg/m2                                   |         |          |    |
| arithmetic mean  | 28.2    | 27.1     |    |
| standard deviation   | ± 4.6   | ± 5.8    | -  |
| Alcohol consumption continuous<br>Units: units/week                          |         |          |    |
| median   | 5       | 14       |    |
| inter-quartile range (Q1-Q3)   | 0 to 17 | 12 to 38 | -  |
| Mean enhanced clinic SBP continuous<br>Units: mmHg                           |         |          |    |
| arithmetic mean  | 163.6   | 152.7    |    |
| standard deviation   | ± 17.3  | ± 14.5   | -  |
| Mean enhanced clinic DBP continuous<br>Units: mmHg                           |         |          |    |
| arithmetic mean  | 81.8    | 83.1     |    |
| standard deviation   | ± 5.9   | ± 6.5    | -  |
| Standard deviation of enhanced clinic SBP continuous<br>Units: mmHg          |         |          |    |
| arithmetic mean  | 8.4     | 6.8      |    |
| standard deviation   | ± 5.2   | ± 5.3    | -  |
| Standard deviation of enhanced clinic DBP continuous<br>Units: mmHg          |         |          |    |
| arithmetic mean  | 5.6     | 6.0      |    |
| standard deviation   | ± 3.0   | ± 3.4    | -  |
| Coefficient of variation of enhanced clinic SBP continuous<br>Units: percent |         |          |    |
| arithmetic mean  | 4.9     | 4.5      |    |
| standard deviation   | ± 2.6   | ± 3.4    | -  |
| Coefficient of variation of enhanced clinic DBP continuous<br>Units: percent |         |          |    |
| arithmetic mean  | 7.0     | 7.2      |    |
| standard deviation   | ± 3.9   | ± 4.0    | -  |
| Mean beat-to-beat SBP continuous   |         |          |    |

|  |                |                 |   |
|--|----------------|-----------------|---|
| Units: mmHg<br>arithmetic mean<br>standard deviation   | 156.6<br>± 5.7 | 151.0<br>± 11.9 | - |
| Mean beat-to-beat DBP continuous<br>Units: mmHg<br>arithmetic mean<br>standard deviation                           | 79.8<br>± 7.1  | 82.6<br>± 6.1   | - |
| Standard deviation of beat-to-beat SBP continuous<br>Units: mmHg<br>arithmetic mean<br>standard deviation          | 9.9<br>± 3.9   | 9.2<br>± 5.5    | - |
| Standard deviation of beat-to-beat DBP continuous<br>Units: mmHg<br>arithmetic mean<br>standard deviation          | 5.2<br>± 2.2   | 5.1<br>± 2.4    | - |
| Coefficient of variation of beat-to-beat SBP continuous<br>Units: percent<br>arithmetic mean<br>standard deviation | 6.3<br>± 2.5   | 6.0<br>± 2.6    | - |
| Coefficient of variation of beat-to-beat DBP continuous<br>Units: percent<br>arithmetic mean<br>standard deviation | 6.6<br>± 2.6   | 6.3<br>± 3.0    | - |



## End points

### End points reporting groups

|   |              |
|---|--------------|
| Reporting group title   | CCB arm      |
| Reporting group description:<br>Patients randomised to this arm were allocated to treatment with a medication from the class dihydropyridine calcium channel blockers, with the specific choice of medication from within that class being at the discretion of the treating physician.   |              |
| Reporting group title   | ACEI/ARB arm |
| Reporting group description:<br>Patients randomised to this arm were allocated to treatment with a medication from the class angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, with the specific choice of medication from within the allocated class being at the discretion of the treating physician. |              |

### Primary: Feasibility of recruitment and retention

|  |   |
|--|---|
| End point title  | Feasibility of recruitment and retention <sup>[1]</sup> |
| End point description:<br>Firstly, the proportion of patients screened who were eligible for, and agreed to participate in the trial was recorded from the screening logs and is presented in the CONSORT flow diagram. Reasons for ineligibility were also assessed and quantified, and are presented in the accompanying table. Secondly, the rate of retention in the trial was assessed by recording the number of recruited participants who did and did not complete the trial follow-up period. |   |
| End point type   | Primary   |
| End point timeframe:<br>The number of patients screened who were recruited to the trial and the number of recruited participants who completed the trial was assessed over the whole trial period (15 months).   |   |
| Notes:<br>[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.<br>Justification: As this was a feasibility trial only descriptive analyses were carried out, with no formal statistical testing of any of the primary or secondary end-points.  |   |

| End point values              | CCB arm         | ACEI/ARB arm    |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 6               | 8               |  |  |
| Units: Number of participants |                 |                 |  |  |
| Completed the trial           | 4               | 5               |  |  |
| Did not complete the trial    | 2               | 3               |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | CONSORT flow diagram/Figure 1 CAARBS CONSORT Flow Table of reasons for exclusion.docx |
|-----------------------------------|---|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance with trial treatment

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Compliance with trial treatment |
|-----------------|---------------------------------|

End point description:

Compliance was assessed using a self-report questionnaire. If participants were taking the trial medication >80% of the time then they were considered to be compliant.

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

End point timeframe:

Compliance with trial treatment was assessed in each participant who completed the three month follow-up period.

| End point values              | CCB arm         | ACEI/ARB arm    |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 6               | 8               |  |  |
| Units: Number of participants |                 |                 |  |  |
| >80% compliant                | 4               | 4               |  |  |
| <80% compliant                | 0               | 1               |  |  |
| Not recorded                  | 2               | 3               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Completion rate of enhanced clinic blood pressure measurements

|                 |  |
|-----------------|--|
| End point title | Completion rate of enhanced clinic blood pressure measurements |
|-----------------|--|

End point description:

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

End point timeframe:

Compliance with trial measurement methods was assessed by recording completion rates of each blood pressure measurement over the three month follow-up period.

| End point values              | CCB arm         | ACEI/ARB arm    |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 6               | 8               |  |  |
| Units: Number of participants |                 |                 |  |  |
| Complete                      | 4               | 5               |  |  |
| Incomplete                    | 0               | 0               |  |  |
| Not recorded                  | 2               | 3               |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Completion rate of beat-to-beat blood pressure measurements**

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|                 |   |
|-----------------|---|
| End point title | Completion rate of beat-to-beat blood pressure measurements |
|-----------------|---|

End point description:

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

End point timeframe:

Compliance with trial measurement methods was assessed by recording completion rates of each blood pressure measurement over the three month follow-up period.

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| End point values              | CCB arm         | ACEI/ARB arm    |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 6               | 8               |  |  |
| Units: Number of participants |                 |                 |  |  |
| Complete                      | 4               | 3               |  |  |
| Incomplete                    | 0               | 2               |  |  |
| Not recorded                  | 2               | 3               |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Standard deviation of enhanced clinic systolic blood pressure variability after three months**

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|                 |  |
|-----------------|--|
| End point title | Standard deviation of enhanced clinic systolic blood pressure variability after three months |
|-----------------|--|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

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| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: mmHg                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 5.1 (± 2.1)     | 3.9 (± 1.7)     |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Standard deviation of enhanced clinic diastolic blood pressure variability after three months**

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|                 |   |
|-----------------|---|
| End point title | Standard deviation of enhanced clinic diastolic blood pressure variability after three months |
|-----------------|---|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

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| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: mmHg                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 4.3 (± 2.2)     | 3.1 (± 1.7)     |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Coefficient of variation of enhanced clinic systolic blood pressure variability after three months**

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|                 |  |
|-----------------|--|
| End point title | Coefficient of variation of enhanced clinic systolic blood pressure variability after three months |
|-----------------|--|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

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| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: percent                       |                 |                 |  |  |
| arithmetic mean (standard deviation) | 4.0 (± 1.7)     | 3.1 (± 1.5)     |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Coefficient of variation of enhanced clinic diastolic blood pressure**

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**variability after three months**

|                 |   |
|-----------------|---|
| End point title | Coefficient of variation of enhanced clinic diastolic blood pressure variability after three months |
|-----------------|---|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: percent                       |                 |                 |  |  |
| arithmetic mean (standard deviation) | 5.8 (± 2.7)     | 4.3 (± 1.6)     |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Standard deviation of beat-to-beat systolic blood pressure variability after three months**

|                 |   |
|-----------------|---|
| End point title | Standard deviation of beat-to-beat systolic blood pressure variability after three months |
|-----------------|---|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: mmHg                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 6.2 (± 3.0)     | 8.7 (± 5.9)     |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Standard deviation of beat-to-beat diastolic blood pressure variability after three months**

|   |  |
|---|--|
| End point title   | Standard deviation of beat-to-beat diastolic blood pressure variability after three months |
| End point description:  |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Blood pressure variability was assessed at three month follow-up. |  |

| End point values                     | CCB arm          | ACEI/ARB arm     |  |  |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed          | 4                | 5                |  |  |
| Units: mmHg                          |                  |                  |  |  |
| arithmetic mean (standard deviation) | 2.8 ( $\pm$ 1.4) | 3.9 ( $\pm$ 2.7) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Coefficient of variation of beat-to-beat systolic blood pressure variability after three months

|   |   |
|---|---|
| End point title   | Coefficient of variation of beat-to-beat systolic blood pressure variability after three months |
| End point description:  |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Blood pressure variability was assessed at three month follow-up. |   |

| End point values                     | CCB arm          | ACEI/ARB arm     |  |  |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed          | 4                | 5                |  |  |
| Units: percent                       |                  |                  |  |  |
| arithmetic mean (standard deviation) | 4.5 ( $\pm$ 2.1) | 6.0 ( $\pm$ 2.9) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Coefficient of variation of beat-to-beat diastolic blood pressure variability after three months

|                 |  |
|-----------------|--|
| End point title | Coefficient of variation of beat-to-beat diastolic blood pressure variability after three months |
|-----------------|--|

End point description:

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

End point timeframe:

Blood pressure variability was assessed at three month follow-up.

| End point values                     | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: percent                       |                 |                 |  |  |
| arithmetic mean (standard deviation) | 3.8 (± 1.8)     | 4.9 (± 2.9)     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Modified Rankin score at three months

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Modified Rankin score at three months |
|-----------------|---------------------------------------|

End point description:

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Functional outcome was assessed using the modified Rankin score at three month follow-up.

| End point values                      | CCB arm         | ACEI/ARB arm    |  |  |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type                    | Reporting group | Reporting group |  |  |
| Number of subjects analysed           | 4               | 5               |  |  |
| Units: mRS points                     |                 |                 |  |  |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 1)      | 0 (0 to 1)      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Montreal Cognitive Assessment score at three months

|                 |   |
|-----------------|---|
| End point title | Montreal Cognitive Assessment score at three months |
|-----------------|---|

End point description:

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

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End point timeframe:

Cognition was assessed using the Montreal Cognitive Assessment at the three month follow-up visit.

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| <b>End point values</b>              | CCB arm         | ACEI/ARB arm    |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 5               |  |  |
| Units: MoCA points                   |                 |                 |  |  |
| arithmetic mean (standard deviation) | 23.5 (± 2.7)    | 23.6 (± 3.7)    |  |  |

### **Statistical analyses**

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No statistical analyses for this end point



## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Data on adverse events was collected over the whole three month follow-up period for each participant. Only serious adverse events were reported in this feasibility trial.

Adverse event reporting additional description:

Data regarding adverse events were collected by research staff initiated questionnaire at each trial follow-up visit. There were no serious adverse events recorded during the trial.

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

### Dictionary used

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

|                    |        |
|--------------------|--------|
| Dictionary version | 10.0.0 |
|--------------------|--------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | CCB arm |
|-----------------------|---------|

Reporting group description:

Patients randomised to this arm were allocated to treatment with a medication from the class dihydropyridine calcium channel blockers, with the specific choice of medication from within that class being at the discretion of the treating physician.

|                       |              |
|-----------------------|--------------|
| Reporting group title | ACEI/ARB arm |
|-----------------------|--------------|

Reporting group description:

Patients randomised to this arm were allocated to treatment with a medication from the class angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, with the specific choice of medication from within the allocated class being at the discretion of the treating physician.

| Serious adverse events                            | CCB arm       | ACEI/ARB arm  |  |
|---|---------------|---------------|--|
| Total subjects affected by serious adverse events |               |               |  |
| subjects affected / exposed                       | 0 / 5 (0.00%) | 0 / 7 (0.00%) |  |
| number of deaths (all causes)                     | 0             | 0             |  |
| number of deaths resulting from adverse events    |               |               |  |

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

| Non-serious adverse events                            | CCB arm       | ACEI/ARB arm  |  |
|---|---------------|---------------|--|
| Total subjects affected by non-serious adverse events |               |               |  |
| subjects affected / exposed                           | 0 / 5 (0.00%) | 0 / 7 (0.00%) |  |

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: Only data on serious adverse events was collected in this feasibility trial.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment  |
|----------------|--|
| 09 August 2018 | A substantial amendment was made to the trial eligibility criteria in order to try and improve recruitment figures. This was done following discussion with the Trial Management Group and Trial Steering Committee based on analysis of screening log data. Specifically, the inclusion criteria which stipulated that patients should be recruited within 72 hours of the qualifying clinical event (i.e. ischaemic stroke or transient ischaemic attack) was altered to allow inclusion of patients up to 7 days following the qualifying clinical event. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30782930>