



## Clinical trial results: Anglo-Scandinavian Cardiac Outcomes Trial; Post Trial Follow-Up Study Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-023875-24 |
| Trial protocol           | GB             |
| Global end of trial date | 30 May 2015    |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 08 November 2019 |
| First version publication date | 08 November 2019 |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | CRO1777 |
|-----------------------|---------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01499511 |
| 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               | Judith A Mackay, Imperial College London, +44 2075941395, judith.mackay@imperial.nhs.uk |
| Scientific contact           | Judith A Mackay, Imperial College London, +44 2075941395, judith.mackay@imperial.nhs.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                       | 31 January 2017 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 30 May 2015     |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 30 May 2015     |
| 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:

The principal research objective is to see whether there are long-term differences between the study treatments used in the original ASCOT study (atenolol-based vs perindopril-based treatment on blood pressure lowering, and atorvastatin versus placebo treatment on cholesterol lowering) in terms of cardiovascular disease (heart attacks, strokes and death from cardiovascular disease). Followup study without treatment

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

|                                                           |                     |
|-----------------------------------------------------------|---------------------|
| Actual start date of recruitment                          | 09 January 2012     |
| Long term follow-up planned                               | Yes                 |
| Long term follow-up rationale                             | Scientific research |
| Long term follow-up duration                              | 16 Years            |
| 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: 1718 |
| Worldwide total number of subjects   | 1718                 |
| EEA total number of subjects         | 1718                 |

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)                      | 173  |
| From 65 to 84 years                       | 1417 |

|                   |     |
|-------------------|-----|
| 85 years and over | 128 |
|-------------------|-----|

## Subject disposition

### Recruitment

Recruitment details:

ASCOT-10 is a follow-up study of surviving participants in the United Kingdom (UK) arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) which was conducted between 2000 and 2005.

### Pre-assignment

Screening details:

It is follow up group from the ASCOT study, after 5.5 years treatment.

### Period 1

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

### Arms

|                              |                               |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes                           |
| <b>Arm title</b>             | ASCOT participants amlodipine |

Arm description:

It is follow up group from the ASCOT study, after treatment with amlodipine for 5.5 years. No treatment only follow up.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | no intervention |
| Investigational medicinal product name | No product      |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Capsule         |
| Routes of administration               | Other use       |

Dosage and administration details:

no intervention

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | ASCOT Participants Atenolol |
|------------------|-----------------------------|

Arm description:

It is follow up group from the ASCOT study, after treatment with atenolol for 5.5 years. No treatment only follow up.

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

| Number of subjects in period 1 | ASCOT participants amlodipine | ASCOT Participants Atenolol |
|--------------------------------|-------------------------------|-----------------------------|
| Started                        | 885                           | 833                         |
| Completed                      | 884                           | 833                         |
| Not completed                  | 1                             | 0                           |
| death                          | 1                             | -                           |

## Baseline characteristics

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### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | ASCOT participants amlodipine |
|-----------------------|-------------------------------|

Reporting group description:

It is follow up group from the ASCOT study, after treatment with amlodipine for 5.5 years. No treatment only follow up.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | ASCOT Participants Atenolol |
|-----------------------|-----------------------------|

Reporting group description:

It is follow up group from the ASCOT study, after treatment with atenolol for 5.5 years. No treatment only follow up.

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| Reporting group values                | ASCOT participants amlodipine | ASCOT Participants Atenolol | Total |
|---------------------------------------|-------------------------------|-----------------------------|-------|
| Number of subjects                    | 885                           | 833                         | 1718  |
| Age categorical<br>Units: Subjects    |                               |                             |       |
| Adults (18-64 years)                  | 85                            | 88                          | 173   |
| From 65-84 years                      | 731                           | 686                         | 1417  |
| more than 85 years                    | 69                            | 59                          | 128   |
| Age continuous<br>Units: years        |                               |                             |       |
| median                                | 75                            | 74.51                       |       |
| full range (min-max)                  | 53.97 to 92.54                | 52.36 to 91.03              | -     |
| Gender categorical<br>Units: Subjects |                               |                             |       |
| Female                                | 739                           | 720                         | 1459  |
| Male                                  | 146                           | 113                         | 259   |

## End points

### End points reporting groups

|                                                                                                                                                         |                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| Reporting group title                                                                                                                                   | ASCOT participants amlodipine |
| Reporting group description:<br>It is follow up group from the ASCOT study, after treatment with amlodipine for 5.5 years. No treatment only follow up. |                               |
| Reporting group title                                                                                                                                   | ASCOT Participants Atenolol   |
| Reporting group description:<br>It is follow up group from the ASCOT study, after treatment with atenolol for 5.5 years. No treatment only follow up.   |                               |

### Primary: Morbidity after 16 years in patients recruited into the Anglo-Scandinavian Outcomes trial\_non fatal myocardial infarction

|                                  |                                                                                                                           |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title                  | Morbidity after 16 years in patients recruited into the Anglo-Scandinavian Outcomes trial_non fatal myocardial infarction |
| End point description:           |                                                                                                                           |
| End point type                   | Primary                                                                                                                   |
| End point timeframe:<br>16 years |                                                                                                                           |

| End point values            | ASCOT participants amlodipine | ASCOT Participants Atenolol |  |  |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group               | Reporting group             |  |  |
| Number of subjects analysed | 877                           | 828                         |  |  |
| Units: Participants         | 35                            | 37                          |  |  |

### Statistical analyses

|                                         |                                                             |
|-----------------------------------------|-------------------------------------------------------------|
| Statistical analysis title              | non fatal myocardial infarction                             |
| Comparison groups                       | ASCOT participants amlodipine v ASCOT Participants Atenolol |
| Number of subjects included in analysis | 1705                                                        |
| Analysis specification                  | Pre-specified                                               |
| Analysis type                           | superiority                                                 |
| P-value                                 | = 0.624                                                     |
| Method                                  | ANOVA                                                       |
| Parameter estimate                      | Cox proportional hazard                                     |

### Primary: Morbidity After 16 Years in Patients Recruited Into the Anglo-Scandinavian Outcomes trial\_non Fatal Stroke/TIA (Transient Ischaemic Attack)

|                        |                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Morbidity After 16 Years in Patients Recruited Into the Anglo-Scandinavian Outcomes trial_non Fatal Stroke/TIA (Transient Ischaemic Attack) |
| End point description: |                                                                                                                                             |
| End point type         | Primary                                                                                                                                     |
| End point timeframe:   |                                                                                                                                             |
| 16 years               |                                                                                                                                             |

| End point values            | ASCOT participants amlodipine | ASCOT Participants Atenolol |  |  |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group               | Reporting group             |  |  |
| Number of subjects analysed | 877                           | 823                         |  |  |
| Units: Participants         | 29                            | 52                          |  |  |

### Statistical analyses

|                                         |                                                             |
|-----------------------------------------|-------------------------------------------------------------|
| <b>Statistical analysis title</b>       | non Fatal Stroke/TIA (Transient Ischaemic Attack)           |
| Comparison groups                       | ASCOT participants amlodipine v ASCOT Participants Atenolol |
| Number of subjects included in analysis | 1700                                                        |
| Analysis specification                  | Pre-specified                                               |
| Analysis type                           | superiority                                                 |
| P-value                                 | = 0.004                                                     |
| Method                                  | ANOVA                                                       |

### Secondary: Number of participants who have developed diabetes since the end of the ASCOT trial

|                        |                                                                                     |
|------------------------|-------------------------------------------------------------------------------------|
| End point title        | Number of participants who have developed diabetes since the end of the ASCOT trial |
| End point description: |                                                                                     |
| End point type         | Secondary                                                                           |
| End point timeframe:   |                                                                                     |
| 16 years               |                                                                                     |

| End point values            | ASCOT participants amlodipine | ASCOT Participants Atenolol |  |  |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group               | Reporting group             |  |  |
| Number of subjects analysed | 871                           | 825                         |  |  |
| Units: Participants         | 322                           | 325                         |  |  |

### Statistical analyses

|                                         |                                                             |
|-----------------------------------------|-------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Diabetes                                                    |
| Comparison groups                       | ASCOT participants amlodipine v ASCOT Participants Atenolol |
| Number of subjects included in analysis | 1696                                                        |
| Analysis specification                  | Pre-specified                                               |
| Analysis type                           | superiority                                                 |
| P-value                                 | = 0.304                                                     |
| Method                                  | ANOVA                                                       |

### Secondary: Number of Participants Who Have Undergone Coronary/Peripheral Re-vascularisation Procedures Since the End of the ASCOT Trial

|                        |                                                                                                                              |
|------------------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Number of Participants Who Have Undergone Coronary/Peripheral Re-vascularisation Procedures Since the End of the ASCOT Trial |
| End point description: |                                                                                                                              |
| End point type         | Secondary                                                                                                                    |
| End point timeframe:   |                                                                                                                              |
| 16 years               |                                                                                                                              |

| End point values            | ASCOT participants amlodipine | ASCOT Participants Atenolol |  |  |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group               | Reporting group             |  |  |
| Number of subjects analysed | 872                           | 822                         |  |  |
| Units: Participants         | 39                            | 33                          |  |  |

### Statistical analyses

|                                         |                                                             |
|-----------------------------------------|-------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Coronary/Peripheral Re-vascularisation Procedures           |
| Comparison groups                       | ASCOT participants amlodipine v ASCOT Participants Atenolol |
| Number of subjects included in analysis | 1694                                                        |
| Analysis specification                  | Pre-specified                                               |
| Analysis type                           | superiority                                                 |
| P-value                                 | = 0.641                                                     |
| Method                                  | ANOVA                                                       |

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**Secondary: Number of Participants Who Have Required Renal Replacement Therapy (Dialysis or Kidney Transplant) Since the End of the ASCOT Trial**

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|                 |                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants Who Have Required Renal Replacement Therapy (Dialysis or Kidney Transplant) Since the End of the ASCOT Trial |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

16 years

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| End point values            | ASCOT participants amlodipine | ASCOT Participants Atenolol |  |  |
|-----------------------------|-------------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group               | Reporting group             |  |  |
| Number of subjects analysed | 874                           | 826                         |  |  |
| Units: Participants         | 10                            | 9                           |  |  |

**Statistical analyses**

|                                         |                                                             |
|-----------------------------------------|-------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Required Renal Replacement Therapy                          |
| Comparison groups                       | ASCOT participants amlodipine v ASCOT Participants Atenolol |
| Number of subjects included in analysis | 1700                                                        |
| Analysis specification                  | Pre-specified                                               |
| Analysis type                           | superiority                                                 |
| P-value                                 | = 0.915                                                     |
| Method                                  | ANOVA                                                       |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

16 years follow up

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

### Dictionary used

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

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

### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | ASCOT participants amlodipine |
|-----------------------|-------------------------------|

Reporting group description:

It is follow up group from the ASCOT study, after treatment with amlodipine for 5.5 years. No treatment only follow up.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | ASCOT Participants Atenolol |
|-----------------------|-----------------------------|

Reporting group description:

It is follow up group from the ASCOT study, after treatment with atenolol for 5.5 years. No treatment only follow up.

| Serious adverse events                            | ASCOT participants amlodipine            | ASCOT Participants Atenolol |  |
|---------------------------------------------------|------------------------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events |                                          |                             |  |
| subjects affected / exposed                       | 2 / 885 (0.23%)                          | 0 / 833 (0.00%)             |  |
| number of deaths (all causes)                     | 1                                        | 0                           |  |
| number of deaths resulting from adverse events    | 0                                        | 0                           |  |
| Cardiac disorders                                 |                                          |                             |  |
| Stroke                                            | Additional description: Ischaemic stroke |                             |  |
| subjects affected / exposed                       | 1 / 885 (0.11%)                          | 0 / 833 (0.00%)             |  |
| occurrences causally related to treatment / all   | 0 / 1                                    | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0                                    | 0 / 0                       |  |
| Musculoskeletal and connective tissue disorders   |                                          |                             |  |
| Injuries                                          | Additional description: Cycling accident |                             |  |
| subjects affected / exposed                       | 1 / 885 (0.11%)                          | 0 / 833 (0.00%)             |  |
| occurrences causally related to treatment / all   | 0 / 1                                    | 0 / 0                       |  |
| deaths causally related to treatment / all        | 0 / 0                                    | 0 / 0                       |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                                                                                                                                 | ASCOT participants<br>amlodipine                 | ASCOT Participants<br>Atenolol                   |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|--------------------------------------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                                                                              | 4 / 885 (0.45%)                                  | 1 / 833 (0.12%)                                  |  |
| Cardiac disorders<br>High blood pressure<br>subjects affected / exposed<br>occurrences (all)                                                                                      | 1 / 885 (0.11%)<br>1                             | 0 / 833 (0.00%)<br>0                             |  |
| Nervous system disorders<br>Collapse<br>subjects affected / exposed<br>occurrences (all)<br><br>Alcohol dependence withdrawal<br>subjects affected / exposed<br>occurrences (all) | 0 / 885 (0.00%)<br>0<br><br>1 / 885 (0.11%)<br>1 | 1 / 833 (0.12%)<br>0<br><br>0 / 833 (0.00%)<br>0 |  |
| Gastrointestinal disorders<br>Stomach cramp<br>subjects affected / exposed<br>occurrences (all)                                                                                   | 1 / 885 (0.11%)<br>1                             | 0 / 833 (0.00%)<br>0                             |  |
| Respiratory, thoracic and mediastinal disorders<br>Bronchiectasis<br>subjects affected / exposed<br>occurrences (all)                                                             | 1 / 885 (0.11%)<br>1                             | 0 / 833 (0.00%)<br>0                             |  |

## **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