



## Clinical trial results:

### A Phase 2, Double-blind, Active-controlled, Dose-titrating Efficacy and Safety Study of Firibastat (QGC001) Compared to Ramipril Administered Orally, Twice Daily, Over 12 Weeks to Prevent Left Ventricular Dysfunction after Acute Myocardial Infarction

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-003146-17 |
| Trial protocol           | DE SK HU ES GB |
| Global end of trial date | 08 July 2021   |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 18 December 2022                                     |
| First version publication date    | 18 December 2022                                     |
| Summary attachment (see zip file) | CSR Synopsis (CSR_QUORUM_VF_3Fev2022 - Synopsis.pdf) |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | QGC001-2QG4 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03715998 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Quantum Genomics   |
| Sponsor organisation address | 33 rue Marbeuf, Paris, France,   |
| Public contact               | Clinical Project Manager, Quantum Genomics,<br>mariette.codou@quantum-genomics.com |
| Scientific contact           | Clinical Project Manager, Quantum Genomics,<br>mariette.codou@quantum-genomics.com |

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                       | 27 July 2021 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 08 July 2021 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 08 July 2021 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

Comparison of the effects of twice daily (bis in die [BID]) oral administration of 2 doses of firibastat to those of BID oral administration of ramipril on the change from Baseline in left ventricular ejection fraction (LVEF) assessed by cardiac magnetic resonance imaging (CMRI) on Day 84

Protection of trial subjects:

If symptomatic hypotension, symptomatic orthostatic hypotension, or cardiogenic shock occur, the treatment will be discontinued for the remainder of the study, and the event will be recorded as an AE leading to discontinuation.

In case a skin reaction is concomitant to fever, blisters on the skin, and/or the mucous membranes of the mouth, nose, eyes and genitals, peeling and shedding skin, which may suggest erythema multiforme or Stevens-Johnson syndrome, the treatment must be immediately discontinued.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 15 February 2019 |
| 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 | Poland: 74        |
| Country: Number of subjects enrolled | Slovakia: 70      |
| Country: Number of subjects enrolled | Spain: 28         |
| Country: Number of subjects enrolled | United Kingdom: 5 |
| Country: Number of subjects enrolled | France: 40        |
| Country: Number of subjects enrolled | Germany: 11       |
| Country: Number of subjects enrolled | Hungary: 67       |
| Worldwide total number of subjects   | 295               |
| EEA total number of subjects         | 290               |

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)                     | 206 |
| From 65 to 84 years                      | 84  |
| 85 years and over                        | 5   |

## Subject disposition

### Recruitment

Recruitment details:

A total of 295 male and female patients with a diagnosis of first acute anterior MI were randomized. The patients had a primary percutaneous coronary intervention (PCI) of the index-MI-related artery within 24 hours after MI. Patients were randomly assigned to 1 of the 3 treatment groups in a 1:1:1 ratio.

### Pre-assignment

Screening details:

The population for this study corresponds to adults patients with a first acute anterior MI treated with primary PCI and signed an ICF.

### Period 1

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

Blinding implementation details:

Patients were randomly assigned to 1 of the following 3 treatment groups in a 1:1:1 ratio:

- Group 1: Patients received 50 mg firibastat BID for 2 weeks and then 100 mg BID for 10 weeks.
- Group 2: Patients received 250 mg firibastat BID for 2 weeks and then 500 mg BID for 10 weeks.
- Group 3: Patients received 2.5 mg ramipril BID for 2 weeks and then 5 mg BID for 10 weeks.

IP was produced in order to maintain the blind (similar bottles with similar caps). IP allocation via IRT.

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Firibastat 100 mg BID |

Arm description:

50 mg firibastat BID for 2 weeks and then 100 mg BID for 10 weeks

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Firibastat   |
| Investigational medicinal product code | QGC001       |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Firibastat 100 mg BID (2 caps of 50mg twice a day)

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | Firibastat 500mg BID |
|------------------|----------------------|

Arm description:

250 mg firibastat BID for 2 weeks and then 500 mg BID for 10 weeks

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Firibastat   |
| Investigational medicinal product code | QGC001       |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Firibastat 500 mg BID (2 caps of 250mg twice a day)

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Ramipril 5 mg BID |
|------------------|-------------------|

Arm description:

2.5 mg ramipril BID for 2 weeks and then 5 mg BID for 10 weeks.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Ramipril          |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

Ramipril 2.5mg 2 caps twice a day

| <b>Number of subjects in period 1</b> | <b>Firibastat 100 mg<br/>BID</b> | <b>Firibastat 500mg<br/>BID</b> | <b>Ramipril 5 mg BID</b> |
|---------------------------------------|----------------------------------|---------------------------------|--------------------------|
| Started                               | 98                               | 99                              | 98                       |
| Completed                             | 81                               | 80                              | 88                       |
| Not completed                         | 17                               | 19                              | 10                       |
| Adverse event, serious fatal          | 2                                | 1                               | 1                        |
| Adverse event, non-fatal              | 5                                | 10                              | 5                        |
| Subject decision                      | 9                                | 6                               | 2                        |
| Pregnancy                             | 1                                | -                               | -                        |
| Lost to follow-up                     | -                                | 1                               | 1                        |
| Protocol deviation                    | -                                | 1                               | 1                        |

## Baseline characteristics

### Reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Firibastat 100 mg BID |
| Reporting group description:<br>50 mg firibastat BID for 2 weeks and then 100 mg BID for 10 weeks  |                       |
| Reporting group title  | Firibastat 500mg BID  |
| Reporting group description:<br>250 mg firibastat BID for 2 weeks and then 500 mg BID for 10 weeks |                       |
| Reporting group title  | Ramipril 5 mg BID     |
| Reporting group description:<br>2.5 mg ramipril BID for 2 weeks and then 5 mg BID for 10 weeks.    |                       |

| Reporting group values                             | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID |
|--|-----------------------|----------------------|-------------------|
| Number of subjects                                 | 98                    | 99                   | 98                |
| Age categorical<br>Units: Subjects                 |                       |                      |                   |
| In utero   | 0                     | 0                    | 0                 |
| Preterm newborn infants (gestational age < 37 wks) | 0                     | 0                    | 0                 |
| Newborns (0-27 days)                               | 0                     | 0                    | 0                 |
| Infants and toddlers (28 days-23 months)           | 0                     | 0                    | 0                 |
| Children (2-11 years)                              | 0                     | 0                    | 0                 |
| Adolescents (12-17 years)                          | 0                     | 0                    | 0                 |
| Adults (18-64 years)                               | 74                    | 64                   | 68                |
| From 65-84 years                                   | 22                    | 33                   | 29                |
| 85 years and over                                  | 2                     | 2                    | 1                 |
| Gender categorical<br>Units: Subjects              |                       |                      |                   |
| Female   | 30                    | 23                   | 25                |
| Male   | 68                    | 76                   | 73                |

| Reporting group values                             | Total |  |  |
|--|-------|--|--|
| Number of subjects                                 | 295   |  |  |
| 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)                               | 206   |  |  |
| From 65-84 years                                   | 84    |  |  |
| 85 years and over                                  | 5     |  |  |

|                    |     |  |  |
|--------------------|-----|--|--|
| Gender categorical |     |  |  |
| Units: Subjects    |     |  |  |
| Female             | 78  |  |  |
| Male               | 217 |  |  |

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Firibastat 100 mg BID       |
| Reporting group description:<br>50 mg firibastat BID for 2 weeks and then 100 mg BID for 10 weeks   |                             |
| Reporting group title   | Firibastat 500mg BID        |
| Reporting group description:<br>250 mg firibastat BID for 2 weeks and then 500 mg BID for 10 weeks  |                             |
| Reporting group title   | Ramipril 5 mg BID           |
| Reporting group description:<br>2.5 mg ramipril BID for 2 weeks and then 5 mg BID for 10 weeks.   |                             |
| Subject analysis set title  | mITT                        |
| Subject analysis set type   | Modified intention-to-treat |
| Subject analysis set description:<br>The mITT population included 229 patients (77.6% of the randomized population) who received at least 1 dose of the IP and who had at least 1 baseline (before or within 8 hours of taking the first IP) and 1 post-baseline efficacy assessment (LVEF), with 72 (73.5%) patients in the firibastat 100 mg BID group, 77 (77.8%) patients in the firibastat 500 mg BID group and 80 (81.6%) patients in the ramipril group. |                             |
| Subject analysis set title  | ITT                         |
| Subject analysis set type   | Intention-to-treat          |
| Subject analysis set description:<br>The ITT population included all randomized population (N=295) for each treatment groups, with 98 patients in the firibastat 100 mg BID group, 99 patients in the firibastat 500 mg BID group and 98 patients in the ramipril group   |                             |
| Subject analysis set title  | Safety                      |
| Subject analysis set type   | Safety analysis             |
| Subject analysis set description:<br>The safety population included 294 patients (99.7% of the randomized population) who received at least one dose of the IP, with 98 (100%) patients in the firibastat 100 mg BID group, 98 (99.0%) patients in the firibastat 500 mg BID group and 98 (100%) patients in the ramipril group   |                             |
| Subject analysis set title  | PP                          |
| Subject analysis set type   | Per protocol                |
| Subject analysis set description:<br>The PP population included 170 patients (57.6% of the randomized population) without major protocol deviations, with 56 (57.1%) patients in the firibastat 100 mg BID group, 48 (48.5%) patients in the firibastat 500 mg BID group and 66 (67.3%) patients in the ramipril group  |                             |

### Primary: Change from Baseline to Day 84 in LVEF

|   |  |
|---|--|
| End point title   | Change from Baseline to Day 84 in LVEF |
| End point description:<br>Change from Baseline to Day 84 in LVEF assessed by CMRI (central reading) |  |
| End point type  | Primary                                |
| End point timeframe:<br>84 days   |  |



| End point values                               | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID | mITT                 |
|--|-----------------------|----------------------|-------------------|----------------------|
| Subject group type                             | Reporting group       | Reporting group      | Reporting group   | Subject analysis set |
| Number of subjects analysed                    | 72                    | 77                   | 80                | 229                  |
| Units: % of Left Ventricular Ejection Fraction |                       |                      |                   |                      |
| arithmetic mean (standard deviation)           | 5.6 (± 1.2)           | 5.3 (± 1.1)          | 5.7 (± 1.1)       | -0.36 (± 1.32)       |

## Statistical analyses

| Statistical analysis title              | Primary analysis of the primary efficacy endpoint                |
|---|--|
| Comparison groups                       | Firibastat 100 mg BID v Firibastat 500mg BID v Ramipril 5 mg BID |
| Number of subjects included in analysis | 229  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.789  |
| Method                                  | ANCOVA   |

## Secondary: Left-ventricle End-Diastolic Volume

|                        |   |
|------------------------|---|
| End point title        | Left-ventricle End-Diastolic Volume   |
| End point description: | Change from Baseline to Day 84 in left-ventricular end-diastolic and end-systolic volumes assessed by CMRI (centralized reading). |
| End point type         | Secondary   |
| End point timeframe:   | Day 84  |

| End point values                     | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID | mITT                 |
|--------------------------------------|-----------------------|----------------------|-------------------|----------------------|
| Subject group type                   | Reporting group       | Reporting group      | Reporting group   | Subject analysis set |
| Number of subjects analysed          | 72                    | 77                   | 80                | 229                  |
| Units: mL                            |                       |                      |                   |                      |
| arithmetic mean (standard deviation) | 14.2 (± 4.5)          | 12.7 (± 4.3)         | 9.4 (± 4.4)       | 3.29 (± 5.13)        |

## Statistical analyses

| Statistical analysis title        | Analysis of the Secondary Efficacy endpoint                                      |
|-----------------------------------|--|
| Statistical analysis description: | 9.2.2.1 Change in left-ventricular end-diastolic and end-systolic volumes at EOT |
| Comparison groups                 | Firibastat 100 mg BID v Firibastat 500mg BID v Ramipril 5 mg BID                 |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 229           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.521       |
| Method                                  | ANCOVA        |

### Secondary: Left-ventricle End-systolic Volume

|   |                                    |
|---|------------------------------------|
| End point title   | Left-ventricle End-systolic Volume |
| End point description:<br>Change from Baseline to Day 84 in left-ventricular end-systolic volumes assessed by CMRI (centralized reading). |                                    |
| End point type  | Secondary                          |
| End point timeframe:<br>Day 84  |                                    |

| End point values                     | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID | mITT                 |
|--------------------------------------|-----------------------|----------------------|-------------------|----------------------|
| Subject group type                   | Reporting group       | Reporting group      | Reporting group   | Subject analysis set |
| Number of subjects analysed          | 72                    | 77                   | 80                | 229                  |
| Units: mL                            |                       |                      |                   |                      |
| arithmetic mean (standard deviation) | -0.5 (± 3.3)          | -0.4 (± 3.2)         | -3.1 (± 3.2)      | 2.75 (± 3.82)        |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Analysis of the Secondary Efficacy endpoint                      |
| Comparison groups                       | Firibastat 100 mg BID v Firibastat 500mg BID v Ramipril 5 mg BID |
| Number of subjects included in analysis | 229  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.473  |
| Method                                  | ANCOVA   |

### Secondary: MACE (i.e., cardiovascular deaths, new MIs, and cardiac hospitalizations)

|  |   |
|--|---|
| End point title  | MACE (i.e., cardiovascular deaths, new MIs, and cardiac hospitalizations) |
| End point description:<br>Major cardiac events as adjudicated by an independent committee by treatment group |   |
| End point type   | Secondary   |
| End point timeframe:<br>Day 84   |   |

| End point values            | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID | Safety               |
|-----------------------------|-----------------------|----------------------|-------------------|----------------------|
| Subject group type          | Reporting group       | Reporting group      | Reporting group   | Subject analysis set |
| Number of subjects analysed | 98                    | 98                   | 98                | 294                  |
| Units: Event                | 10                    | 8                    | 6                 | 24                   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in NT-proBNP,

|                        |                                    |
|------------------------|------------------------------------|
| End point title        | Change from Baseline in NT-proBNP, |
| End point description: |                                    |
| End point type         | Secondary                          |
| End point timeframe:   |                                    |
| Day 84                 |                                    |

| End point values                     | Firibastat 100 mg BID | Firibastat 500mg BID | Ramipril 5 mg BID  | mITT                 |
|--------------------------------------|-----------------------|----------------------|--------------------|----------------------|
| Subject group type                   | Reporting group       | Reporting group      | Reporting group    | Subject analysis set |
| Number of subjects analysed          | 62                    | 71                   | 70                 | 229                  |
| Units: pg/ml                         |                       |                      |                    |                      |
| arithmetic mean (standard deviation) | -1360.0 (± 1381.7)    | -1596.4 (± 2279.6)   | -1735.6 (± 2326.5) | 246.8 (± 127)        |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Analysis of the Secondary Efficacy endpoint                      |
| Comparison groups                       | Firibastat 100 mg BID v Firibastat 500mg BID v Ramipril 5 mg BID |
| Number of subjects included in analysis | 203  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.053  |
| Method                                  | ANCOVA   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From ICF signature to end of treatment

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 24 |
|--------------------|----|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Firibastat 100mg |
|-----------------------|------------------|

Reporting group description: -

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Firibastat 500mg |
|-----------------------|------------------|

Reporting group description: -

|                       |               |
|-----------------------|---------------|
| Reporting group title | Ramipril 5 mg |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                               | Firibastat 100mg | Firibastat 500mg | Ramipril 5 mg    |
|--|------------------|------------------|------------------|
| Total subjects affected by serious adverse events    |                  |                  |                  |
| subjects affected / exposed                          | 11 / 98 (11.22%) | 18 / 98 (18.37%) | 10 / 98 (10.20%) |
| number of deaths (all causes)                        | 2                | 1                | 1                |
| number of deaths resulting from adverse events       | 2                | 1                | 1                |
| Vascular disorders                                   |                  |                  |                  |
| Aortic aneurysm                                      |                  |                  |                  |
| subjects affected / exposed                          | 0 / 98 (0.00%)   | 1 / 98 (1.02%)   | 0 / 98 (0.00%)   |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypertensive crisis                                  |                  |                  |                  |
| subjects affected / exposed                          | 0 / 98 (0.00%)   | 1 / 98 (1.02%)   | 0 / 98 (0.00%)   |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| General disorders and administration site conditions |                  |                  |                  |
| Chest pain or chest discomfort                       |                  |                  |                  |
| subjects affected / exposed                          | 1 / 98 (1.02%)   | 1 / 98 (1.02%)   | 3 / 98 (3.06%)   |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Death  |                  |                  |                  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 98 (1.02%) | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Vascular stent thrombosis                       |                |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Dry throat                                      |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary oedema                                |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Electrocardiogram QT prolonged                  |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Limb injury                                     |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Periprocedural myocardial infarction            |                |                |                |

|   |                            |                |                |
|---|----------------------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 98 (1.02%)             | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1                      | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                            |                |                |
| Angina pectoris                                 |                            |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%)             | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0                      | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 0          | 0 / 0          |
| Aortic valve incompetence                       |                            |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%)             | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1                      | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 0          | 0 / 0          |
| Cardiac arrest                                  |                            |                |                |
| alternative assessment type: Systematic         |                            |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%)             | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0                      | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 0          | 0 / 1          |
| Cardiac failure                                 |                            |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%)             | 2 / 98 (2.04%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1                      | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 1          | 0 / 0          |
| Cardiac tamponade                               |                            |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%)             | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1                      | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1                      | 0 / 0          | 0 / 0          |
| Coronary artery syndrome                        | Additional description: ae |                |                |
| subjects affected / exposed                     | 2 / 98 (2.04%)             | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2                      | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0                      | 0 / 0          | 0 / 0          |
| Myocardial infarction                           |                            |                |                |
| alternative assessment type: Systematic         |                            |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 98 (1.02%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pericardial Effusion                            |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pericarditis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ventricle rupture                               |                |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%) | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ischaemic stroke                                |                |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anemia  |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 2 / 98 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Retinal detachment                              |                |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%) | 0 / 98 (0.00%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Skin and subcutaneous tissue disorders          |                |                |                |
| Drug eruption                                   |                |                |                |
| alternative assessment type: Systematic         |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rash maculo-papular                             |                |                |                |
| alternative assessment type: Systematic         |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Acute kidney injury                             |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 2 / 98 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hyperplasia Adrenal                             |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Spinal pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 1 / 98 (1.02%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| COVID-19  |                |                |                |
| subjects affected / exposed                     | 1 / 98 (1.02%) | 3 / 98 (3.06%) | 0 / 98 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Staphylococcal bacteraemia                      |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 98 (0.00%) | 0 / 98 (0.00%) | 1 / 98 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | Firibastat 100mg | Firibastat 500mg | Ramipril 5 mg    |
|---|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                  |
| subjects affected / exposed                           | 4 / 98 (4.08%)   | 13 / 98 (13.27%) | 19 / 98 (19.39%) |
| Cardiac disorders                                     |                  |                  |                  |
| Chest discomfort                                      |                  |                  |                  |
| subjects affected / exposed                           | 0 / 98 (0.00%)   | 0 / 98 (0.00%)   | 5 / 98 (5.10%)   |
| occurrences (all)                                     | 0                | 0                | 5                |
| Gastrointestinal disorders                            |                  |                  |                  |
| Diarrhoea   |                  |                  |                  |
| subjects affected / exposed                           | 1 / 98 (1.02%)   | 1 / 98 (1.02%)   | 5 / 98 (5.10%)   |
| occurrences (all)                                     | 1                | 1                | 6                |
| Skin and subcutaneous tissue disorders                |                  |                  |                  |
| Rash  |                  |                  |                  |
| subjects affected / exposed                           | 0 / 98 (0.00%)   | 8 / 98 (8.16%)   | 3 / 98 (3.06%)   |
| occurrences (all)                                     | 0                | 9                | 3                |
| Infections and infestations                           |                  |                  |                  |
| COVID-19  |                  |                  |                  |
| subjects affected / exposed                           | 3 / 98 (3.06%)   | 4 / 98 (4.08%)   | 6 / 98 (6.12%)   |
| occurrences (all)                                     | 3                | 4                | 6                |

## 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