# Clinical trial results:
# A 12-week, Randomized, Single-Blind, Placebo-controlled, Multi-centre, Parallel Group, Phase IIa Study to Evaluate Efficacy, Safety and Tolerability of Oral AZD5718 After 4- and 12-Weeks of Treatment in Patients with Coronary Artery Disease (CAD)

## Summary

| | |
|---|---|
| EudraCT number | 2017-001582-25 |
| Trial protocol | SE DK FI |
| Global end of trial date | 08 April 2020 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 27 August 2021 |
| First version publication date | 15 April 2021 |
| Version creation reason | • New data added to full data set<br>Update required. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | D7550C00003 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | Forskargatan 18, Södertälje, Sweden, 15185 |
| Public contact | Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, AstraZeneca, +1 887-240-9479, information.center@astrazeneca.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 | 08 April 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 April 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 April 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the PD effect of AZD5718 by assessment of u-LTE4 at 4 weeks in CAD patients

Protection of trial subjects:

Before the start of the clinical study, the clinical study protocol (CSP), informed consent documents (ICDs) and other relevant documents were submitted to the Regulatory Authority for review and approval by AstraZeneca. The study was performed in accordance with ethical principles that had their origin in the Declaration of Helsinki and were consistent with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) and the AstraZeneca policy on Bioethics and Human Biological Samples. The subjects were informed of the nature, significance, implications and risks of the trial before the study. Informed consent was freely given and evidenced in writing. Before signing of the ICD, the subject was given an opportunity to discuss any issues concerning the study with a physician who had suitable knowledge of the study and to have all questions answered openly and honestly.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 30 October 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 | Finland: 17 |
| Country: Number of subjects enrolled | Sweden: 61 |
| Country: Number of subjects enrolled | Denmark: 50 |
| Worldwide total number of subjects | 128 |
| EEA total number of subjects | 128 |

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) | 78 |
| From 65 to 84 years | 50 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted in 3 countries at 9 sites; 3 in Denmark, 2 in Finland and 4 in Sweden.

### Pre-assignment

Screening details:

Participants underwent a screening visit between 2 and 27 days before receiving the first dose of IP.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | AZD5718 (Dose A) |

Arm description:

AZD5718 (Dose A)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | AZD5718 (Dose A) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablets administered once daily

| | |
|---|---|
| **Arm title** | AZD5718 (Dose B) |

Arm description:

AZD5718 (Dose B)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | AZD5718 (Dose B) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablets administered once daily

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

Arm description:

Placebo

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:
Tablets administered once daily

| **Number of subjects in period 1** | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo |
|---|---|---|---|
| Started | 52 | 25 | 51 |
| Completed | 50 | 24 | 51 |
| Not completed | 2 | 1 | 0 |
| Not willing to perform v4b-v4c or take IP | 1 | - | - |
| Randomized by mistake | - | 1 | - |
| Not willing to perform visits or take IP | 1 | - | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | AZD5718 (Dose A) |
| Reporting group description: AZD5718 (Dose A) | |
| Reporting group title | AZD5718 (Dose B) |
| Reporting group description: AZD5718 (Dose B) | |
| Reporting group title | Placebo |
| Reporting group description: Placebo | |

| Reporting group values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo |
|---|---|---|---|
| Number of subjects | 52 | 25 | 51 |
| 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) | 31 | 15 | 32 |
| From 65-84 years | 21 | 10 | 19 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 61.9 | 61.4 | 61.1 |
| standard deviation | ± 8.21 | ± 8.12 | ± 8.51 |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 7 | 0 | 10 |
| Male | 45 | 25 | 41 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |
| White | 52 | 25 | 50 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 0 |
| Not Hispanic or Latino | 51 | 25 | 51 |

| | | | |
|---|---|---|---|
| Unknown or Not Reported | 0 | 0 | 0 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 128 | | |
| 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) | 78 | | |
| From 65-84 years | 50 | | |
| 85 years and over | 0 | | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 17 | | |
| Male | 111 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 1 | | |
| White | 127 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 0 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | | |
| Not Hispanic or Latino | 127 | | |
| Unknown or Not Reported | 0 | | |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | AZD5718 (Dose A) |
| Reporting group description:<br>AZD5718 (Dose A) | |
| Reporting group title | AZD5718 (Dose B) |
| Reporting group description:<br>AZD5718 (Dose B) | |
| Reporting group title | Placebo |
| Reporting group description:<br>Placebo | |

| Primary: Change from baseline in Creatinine-normalized u-LTE4 at Week 4 | |
|---|---|
| End point title | Change from baseline in Creatinine-normalized u-LTE4 at Week 4 |
| End point description: | |
| End point type | Primary |
| End point timeframe:<br>4 weeks | |

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 49 | 24 | 50 | |
| Units: Ratio | | | | |
| geometric mean (geometric coefficient of variation) | 0.04 (± 92.55) | 0.09 (± 84.32) | 1.09 (± 44.38) | |

### Statistical analyses

| Statistical analysis title | Change from baseline in u-LTE4 at Week 4 |
|---|---|
| Statistical analysis description:<br>Change from baseline in Creatinine-normalised u-LTE4 at Week 4. Comparison between AZD5718 (Dose A) and Placebo. | |
| Comparison groups | AZD5718 (Dose A) v Placebo |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Ratio |
| Point estimate | 0.04 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.05 |

| **Statistical analysis title** | Change from baseline in u-LTE4 at Week 4 |
|---|---|

Statistical analysis description:

Change from baseline in Creatinine-normalised u-LTE4 at Week 4. Comparison between AZD5718 (Dose B) and Placebo.

| | |
|---|---|
| Comparison groups | AZD5718 (Dose B) v Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Ratio |
| Point estimate | 0.08 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.1 |

## Secondary: Change from baseline in Creatinine-normalized u-LTE4 at Week 12

| | |
|---|---|
| End point title | Change from baseline in Creatinine-normalized u-LTE4 at Week 12 |

End point description:

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

End point timeframe:

12 weeks

| **End point values** | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 29 | 18 | 36 | |
| Units: Ratio | | | | |
| geometric mean (geometric coefficient of variation) | 0.04 (± 83.69) | 0.10 (± 71.11) | 1.10 (± 49.12) | |

## Statistical analyses

| **Statistical analysis title** | Change from baseline in u-LTE4 at Week 12 |
|---|---|
| Statistical analysis description:<br>Change from baseline in Creatinine-normalised u-LTE4 at Week 12. Comparison between AZD5718 (Dose A) and Placebo | |
| Comparison groups | AZD5718 (Dose A) v Placebo |
| Number of subjects included in analysis | 65 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Ratio |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.05 |

| **Statistical analysis title** | Change from baseline in u-LTE4 at Week 12 |
|---|---|
| Statistical analysis description:<br>Change from baseline in Creatinine-normalised u-LTE4 at Week 12. Comparison between AZD5718 (Dose B) and Placebo. | |
| Comparison groups | AZD5718 (Dose B) v Placebo |
| Number of subjects included in analysis | 54 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | Ratio |
| Point estimate | 0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.12 |

## Secondary: Change from baseline in CFVR at Week 12

| End point title | Change from baseline in CFVR at Week 12 |
|---|---|
| End point description: | |

| End point type | Secondary |
|---|---|
| End point timeframe:<br>12 weeks | |

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 16 | 11 | 24 | |
| Units: Ratio (unitless) | | | | |
| geometric mean (geometric coefficient of variation) | 0.93 (± 23.64) | 0.98 (± 39.53) | 1.16 (± 33.46) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in CFVR at Week 4

| End point title | Change from baseline in CFVR at Week 4 |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 16 | 38 | |
| Units: Ratio (unitless) | | | | |
| geometric mean (geometric coefficient of variation) | 1.03 (± 28.34) | 1.15 (± 31.47) | 1.08 (± 33.16) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of plasma concentrations

| End point title | Summary of plasma concentrations[1] |
|---|---|

End point description:

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

End point timeframe:

13 months

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: There is a typo in the table, it is not a baseline and 1-8 h post dose , it is only 1-8 h post dose. Baseline values all below LOQ.

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 52 | 25 | | |
| Units: nmol/L | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Visit 2: 1-8 Hours Post-Dose | 611.88 (± 234.50) | 47.88 (± 497.86) | | |
| Visit 3: 20-28 Hours Post-Dose | 59.36 (± 90.97) | 16.57 (± 127.80) | | |
| Visit 4: Pre-Dose | 48.00 (± 68.17) | 11.01 (± 60.70) | | |
| Visit 4: 0-2 Hours Post-Dose | 339.28 (± 243.04) | 38.68 (± 159.56) | | |
| Visit 4: 2-4 Hours Post-Dose | 919.22 (± 51.26) | 148.64 (± 71.86) | | |
| Visit 4: 4-8 Hours Post-Dose | 649.09 (± 49.89) | 105.40 (± 52.16) | | |
| Visit 4c: Pre-Dose | 65.39 (± 91.52) | 13.97 (± 88.12) | | |
| Visit 5 - FUP 1 month | 0.51 (± 16.39) | 0.50 (± 0.00) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LAD hyperaemic flow velocity at 4 weeks

| End point title | Change from baseline in LAD hyperaemic flow velocity at 4 weeks |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 16 | 38 | |
| Units: m/sec | | | | |
| arithmetic mean (standard deviation) | 0.02 (± 0.16) | 0.04 (± 0.16) | 0.03 (± 0.17) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LVEF at 4 weeks

| End point title | Change from baseline in LVEF at 4 weeks |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 22 | 45 | |
| Units: Percent (unitless) | | | | |
| arithmetic mean (standard deviation) | -0.23 (± 5.30) | 2.70 (± 6.39) | 0.48 (± 5.00) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LV longitudinal early diastolic strain rate at 4 weeks

| End point title | Change from baseline in LV longitudinal early diastolic strain rate at 4 weeks |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 43 | 19 | 44 | |
| Units: Ratio (unitless) | | | | |
| geometric mean (geometric coefficient of variation) | 1.02 (± 30.61) | 0.98 (± 33.55) | 1.03 (± 30.45) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LV-GLS at rest at Week 4

| End point title | Change from baseline in LV-GLS at rest at Week 4 |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 43 | 17 | 42 | |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | -0.41 (± 3.00) | 0.34 (± 2.47) | -0.63 (± 2.61) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LV-GCS at rest at Week 4

| End point title | Change from baseline in LV-GCS at rest at Week 4 |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| End point values | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 39 | 16 | 34 | |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | 0.34 (± 7.24) | 1.71 (± 5.40) | -1.88 (± 6.78) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in LAD resting mean diastolic flow velocity at 4 Weeks

| End point title | Change from baseline in LAD resting mean diastolic flow velocity at 4 Weeks |
|---|---|

End point description:

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

End point timeframe:

4 weeks

| **End point values** | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 16 | 38 | |
| Units: Ratio | | | | |
| geometric mean (geometric coefficient of variation) | 1.01 (± 23.31) | 0.92 (± 23.68) | 0.99 (± 20.14) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events:<br>Treatment period. | |
| Assessment type | Non-systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |
| **Reporting groups** | |
| Reporting group title | AZD5718 (Dose A) |
| Reporting group description:<br>AZD5718 (Dose A) | |
| Reporting group title | AZD5718 (Dose B) |
| Reporting group description:<br>AZD5718 (Dose B) | |
| Reporting group title | Placebo |
| Reporting group description:<br>Placebo | |

| Serious adverse events | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 3 / 25 (12.00%) | 4 / 51 (7.84%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 25 (0.00%) | 0 / 51 (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 | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 25 (4.00%) | 0 / 51 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 25 (4.00%) | 0 / 51 (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 |

| | | | |
|---|---|---|---|
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 25 (4.00%) | 0 / 51 (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 | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 25 (4.00%) | 0 / 51 (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 |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 1 / 25 (4.00%) | 0 / 51 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| 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 / 52 (0.00%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Post procedural sepsis | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 25 (0.00%) | 0 / 51 (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 |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | AZD5718 (Dose A) | AZD5718 (Dose B) | Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 52 (51.92%) | 12 / 25 (48.00%) | 22 / 51 (43.14%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 0 / 25 (0.00%) | 4 / 51 (7.84%) |
| occurrences (all) | 0 | 0 | 4 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 1 / 25 (4.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 2 | 1 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 2 / 25 (8.00%) | 4 / 51 (7.84%) |
| occurrences (all) | 5 | 2 | 4 |
| Headache | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 25 (4.00%) | 2 / 51 (3.92%) |
| occurrences (all) | 1 | 1 | 2 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | 0 / 25 (0.00%) | 2 / 51 (3.92%) |
| occurrences (all) | 4 | 0 | 2 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 1 / 25 (4.00%) | 3 / 51 (5.88%) |
| occurrences (all) | 3 | 1 | 3 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 1 / 25 (4.00%) | 0 / 51 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 25 (4.00%) | 2 / 51 (3.92%) |
| occurrences (all) | 1 | 1 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 1 / 25 (4.00%) | 4 / 51 (7.84%) |
| occurrences (all) | 2 | 1 | 5 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 52 (11.54%) | 4 / 25 (16.00%) | 7 / 51 (13.73%) |
| occurrences (all) | 6 | 4 | 7 |
| Cough | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 5 | 0 | 1 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 1 / 25 (4.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 2 | 1 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 3 / 52 (5.77%) | 0 / 25 (0.00%) | 1 / 51 (1.96%) |
| occurrences (all) | 3 | 0 | 1 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 52 (11.54%) | 4 / 25 (16.00%) | 7 / 51 (13.73%) |
| occurrences (all) | 6 | 4 | 7 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 10 January 2018 | Version 2.0:<br>• Exploratory objective related to gyrocardiography was removed.<br>• Criterion no 13 updated as follows: NYHA class III-IV heart failure or decompensated heart failure at discharge or hospitalization for exacerbation of chronic heart failure within the previous 3 months from ACS.<br>• Criterion no 16 was updated as follows: Known allergy to adenosine and mannitol, or experience of previous adverse effects of adenosine stress testing.<br>• Criterion no 26 was clarified as follows: Participation in another interventional clinical study with an investigational pharmaceutical product during the last 3 months also including drug eluting stents. |
| 11 April 2018 | Version 3.0:<br>• Treatment period was extended from 4 weeks to 12 weeks and 2 new secondary endpoints were added: u-LTE4 at 12 weeks and CFVR at 12 weeks (Section 9).<br>• The planned total number of patients randomized was increased from 100 to approximately 138 (Section 9.8).<br>• Single futility interim analysis changed to 2 administrative interim analyses for internal decision making. The futility analysis has been removed to be able to evaluate the sustained effect on u-LTE4 at 12 weeks (Section 9.8).<br>• Additional biomarker samples were added at Day 2 after the ACS.<br>• TSH, free T3, free T4 and total T4 were added to the safety laboratory assessments at Visit 2 (baseline at randomization), Visit 4 (4 weeks), Visit 4c (12 weeks) and Visit 5 (Follow-up). |
| 05 September 2018 | Version 4.0:<br>Study sites were provided with the same type of urine dipstick test kits for assessment of glucose, protein, blood and WBC.<br>Urine microscopy was no longer used in the study. |

| | |
|---|---|
| 11 February 2019 | Planned LSLV date changed from Q2 2019 to Q1 2020.<br>Time window for Visit 4 and 4c changed from ±2 days to ±3 days. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported