



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	v1
This version publication date	15 April 2021
First version publication date	15 April 2021

Trial information

Trial identification

Sponsor protocol code	D7550C00003
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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	Denmark: 50
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	Sweden: 61
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, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	AZD5718 (Dose A)
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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)
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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
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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 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 Units: Years			
arithmetic mean	61.9	61.4	61.1
standard deviation	± 8.21	± 8.12	± 8.51
Sex: Female, Male Units: Participants			
Female	7	0	10
Male	45	25	41
Race (NIH/OMB) 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) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	51	25	51

Unknown or Not Reported	0	0	0
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Reporting group values	Total		
Number of subjects	128		
Age categorical			
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			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	17		
Male	111		
Race (NIH/OMB)			
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)			
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:	AZD5718 (Dose A)
Reporting group title	AZD5718 (Dose B)
Reporting group description:	AZD5718 (Dose B)
Reporting group title	Placebo
Reporting group description:	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:	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 (\pm 92.55)	0.09 (\pm 84.32)	1.09 (\pm 44.38)	

Statistical analyses

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 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
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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
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End point description:

End point type	Secondary
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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:	
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:	
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:	
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 (\pm 23.64)	0.98 (\pm 39.53)	1.16 (\pm 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 (\pm 28.34)	1.15 (\pm 31.47)	1.08 (\pm 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: No PK measurements were taken for Placebo arm.

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 (\pm 234.50)	47.88 (\pm 497.86)		
Visit 3: 20-28 Hours Post-Dose	59.36 (\pm 90.97)	16.57 (\pm 127.80)		
Visit 4: Pre-Dose	48.00 (\pm 68.17)	11.01 (\pm 60.70)		
Visit 4: 0-2 Hours Post-Dose	339.28 (\pm 243.04)	38.68 (\pm 159.56)		
Visit 4: 2-4 Hours Post-Dose	919.22 (\pm 51.26)	148.64 (\pm 71.86)		
Visit 4: 4-8 Hours Post-Dose	649.09 (\pm 49.89)	105.40 (\pm 52.16)		
Visit 4c: Pre-Dose	65.39 (\pm 91.52)	13.97 (\pm 88.12)		
Visit 5 - FUP 1 month	0.51 (\pm 16.39)	0.50 (\pm 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 (\pm 0.16)	0.04 (\pm 0.16)	0.03 (\pm 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
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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:

Treatment period.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	AZD5718 (Dose A)
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Reporting group description:

AZD5718 (Dose A)

Reporting group title	AZD5718 (Dose B)
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Reporting group description:

AZD5718 (Dose B)

Reporting group title	Placebo
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Reporting group description:

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2018	<p>Version 2.0:</p> <ul style="list-style-type: none">• Exploratory objective related to gyrocardiography was removed.• 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.• Criterion no 16 was updated as follows: Known allergy to adenosine and mannitol, or experience of previous adverse effects of adenosine stress testing.• 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	<p>Version 3.0:</p> <ul style="list-style-type: none">• 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).• The planned total number of patients randomized was increased from 100 to approximately 138 (Section 9.8).• 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).• Additional biomarker samples were added at Day 2 after the ACS.• 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	<p>Version 4.0:</p> <p>Study sites were provided with the same type of urine dipstick test kits for assessment of glucose, protein, blood and WBC.</p> <p>Urine microscopy was no longer used in the study.</p>

11 February 2019	Planned LSLV date changed from Q2 2019 to Q1 2020. Time window for Visit 4 and 4c changed from ± 2 days to ± 3 days.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported