Clinical trial results:
A randomized, double-blind, placebo-controlled, multi-centre, sequential design, phase IIa study to evaluate safety and tolerability of epicardial injections of AZD8601 during coronary artery bypass grafting surgery

Summary

EudraCT number	2017-002690-19
Trial protocol	FI NL DE
Global end of trial date	23 July 2021

Results information

Result version number	v1
This version publication date	16 July 2022
First version publication date	16 July 2022

Trial information

Trial identification

Sponsor protocol code	D9150C00003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Astraalléen, Södertälje, Sweden,
Public contact	Global Clinical LEad, AstraZeneca, +1 18772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 18772409479, 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	23 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 July 2021
Global end of trial reached?	Yes
Global end of trial date	23 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate safety and tolerability of AZD8601 following epicardial injection in patients undergoing Coronary Artery Bypass Grafting (CABG) surgery with moderately impaired systolic function.

Protection of trial subjects:

This study was performed in compliance with International Council for Harmonisation (ICH) Good Clinical Practice, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 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: 8
Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	3
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 4 clinical research centers in Finland and Germany First subject enrolled (First subject first visit/first consent signed date): 5 February 2017. Last subject last visit: 30 June 2020.

Pre-assignment

Screening details:

This study was performed in compliance with International Council for Harmonisation (ICH) Good Clinical Practice, including the archiving of essential documents.

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	AZD8601 3mg

Arm description:

AZD8601 3mg

Arm type	Experimental
Investigational medicinal product name	AZD8601
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Other use

Dosage and administration details:

Solution for epicardial injection

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection, Injection
Routes of administration	Other use

Dosage and administration details:

Solution for epicardial injection

Number of subjects in period 1	AZD8601 3mg	Placebo
Started	7	4
Completed	7	4

Baseline characteristics

Reporting groups	
Reporting group title	AZD8601 3mg
Reporting group description: AZD8601 3mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	AZD8601 3mg	Placebo	Total
Number of subjects	7	4	11
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)	2	1	3
From 65-84 years	5	3	8
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	68.3	67.8	
standard deviation	± 5.8	± 10.8	-
Sex: Female, Male Units: Participants			
Female	0	2	2
Male	7	2	9
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	0
White	7	4	11
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Subject analysis sets	
Subject analysis set title	AZD8601
Subject analysis set type	Safety analysis
Subject analysis set description: AZD8601	

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Placebo	
Subject analysis set title	AZD8601
Subject analysis set type	Full analysis
Subject analysis set description: AZD8601	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	

Reporting group values	AZD8601	Placebo	AZD8601
Number of subjects	7	4	7
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean	7		
standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Placebo		
Number of subjects	4		
Age categorical Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±		
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	AZD8601 3mg
Reporting group description: AZD8601 3mg	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	AZD8601
Subject analysis set type	Safety analysis
Subject analysis set description: AZD8601	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Placebo	
Subject analysis set title	AZD8601
Subject analysis set type	Full analysis
Subject analysis set description: AZD8601	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	

Primary: Number of subjects with Adverse Events

End point title	Number of subjects with Adverse Events[1]
End point description:	
End point type	Primary
End point timeframe: From dose to end of follow up	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for the primary endpoint Adverse Event are described in the Adverse Event section.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Participants	7	4		

Statistical analyses

No statistical analyses for this end point

Primary: Pulse rate (vital sign)

End point title	Pulse rate (vital sign)[2]

End point description:

End point type	Primary

End point timeframe:

From dosing to end of follow up

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: beats/min				
arithmetic mean (standard deviation)				
Baseline	63.1 (± 10.42)	62.6 (± 6.04)		
Day 1	81.3 (± 7.38)	75.2 (± 4.20)		
Day 2	85.2 (± 6.54)	81.1 (± 7.01)		
Day 3	83.6 (± 8.38)	82.4 (± 6.80)		
Day 4	81.9 (± 14.54)	75.3 (± 7.63)		
Visit 5 (Day 30)	74.3 (± 13.33)	65.5 (± 6.81)		
Visit 6 (Day 91)	66.9 (± 15.05)	70.8 (± 7.18)		
Visit 7 (Day 182)	63.6 (± 15.62)	61.0 (± 2.16)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with an ECG determined to be abnormal and clinically significant

End point title	Number of subjects with an ECG determined to be abnormal and clinically significant[3]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Participants				
Baseline	0	0		
End of treatment	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with high values of Leucocytes, Particle Concentration

End point title	Number of subjects with high values of Leucocytes, Particle Concentration[4]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Oxygen saturation (vital sign)

End point title	Oxygen saturation (vital sign)[5]

End point description:

End point type	Primary

End point timeframe:

From dosing to end of follow up

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Percent				
arithmetic mean (standard deviation)				
Baseline	96.0 (± 0)	100.0 (± 0)		
Day 1	97.6 (± 4.46)	99.3 (± 0.80)		
Day 2	97.7 (± 1.68)	97.4 (± 2.42)		
Day 3	95.6 (± 2.14)	96.6 (± 3.60)		
Day 4	95.7 (± 1.85)	95.8 (± 3.74)		

Statistical analyses

No statistical analyses for this end point

Primary: Systolic blood pressure (vital sign)

End point title	Systolic blood pressure (vital sign)[6]

End point description:

End point type	Primary

End point timeframe:

From baseline to end of follow up

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline	141.4 (± 24.42)	141.7 (± 23.32)		
Day 1	113.5 (± 5.67)	116.8 (± 12.53)		
Day 2	118.1 (± 11.98)	104.8 (± 4.39)		
Day 3	118.5 (± 8.04)	100.8 (± 10.82)		
Day 4	129.1 (± 116.63)	109.0 (± 6.48)		
Visit 5 (Day 30)	135.9 (± 17.56)	134.5 (± 29.49)		
Visit 6 (Day 91)	146.3 (± 11.76)	163.0 (± 35.39)		
Visit 7 (Day 182)	142.3 (± 13.00)	147.3 (± 34.07)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with high values of Erythrocytes, Particle Concentration

End point title	Number of subjects with high values of Erythrocytes, Particle Concentration[7]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

End point values	AZD8601 3mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Diastolic blood pressure (vital sign)

End point title	Diastolic blood pressure (vital sign)[8][9]

End point description:

End point type	Primary

End point timeframe:

From baseline to end of follow up

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[9] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline	74.5 (± 23.57)	82.1 (± 17.95)		
Day 1	62.0 (± 7.63)	59.2 (± 6.52)		
Day 2	58.0 (± 5.12)	59.2 (± 10.62)		
Day 3	56.9 (± 2.83)	63.7 (± 8.64)		
Day 4	66.8 (± 5.91)	73.7 (± 11.07)		
Visit 5 (Day 30)	83.5 (± 14.55)	78.1 (± 10.16)		
Visit 6 (Day 91)	93.8 (± 16.62)	80.0 (± 7.09)		
Visit 7 (Day 182)	83.5 (± 19.60)	79.4 (± 8.06)		

Statistical analyses

No statistical analyses for this end point

Primary: Haemoglobin

End point title	Haemoglobin[10][11]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[11] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Erythrocyte, Volume Fraction

End point title	Erythrocyte, Volume Fraction[12][13]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[13] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Erythrocytes, Mean Cell Volume

End point title	Erythrocytes, Mean Cell Volume[14][15]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[15] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Mean Cell Hemoglobin

End point title	Mean Cell Hemoglobin[16][17]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[17] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	1		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Mean Cell Hemoglobin Conc.

End point title	Mean Cell Hemoglobin Conc.[18][19]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

[19] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Neutrophils

End point title	Neutrophils[20][21]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[21] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Lymphocytes

End point title	Lymphocytes[22][23]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[23] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Monocytes

End point title	Monocytes[24][25]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[25] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Eosinophils

End point title	Eosinophils[26][27]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[27] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Basophils

End point title	Basophils[28][29]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[29] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Platelets

End point title	Platelets[30][31]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[31] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Reticulocytes

End point title	Reticulocytes[32][33]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[33] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	1		
Maximum value during treatment	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Prothrombin Complex INR

End point title	Prothrombin Complex INR[34][35]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[35] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Activated Partial Thromboplastin Time

End point title	Activated Partial Thromboplastin Time[36][37]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[37] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Fibrinogen

End point title	Fibrinogen[38][39]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[38] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[39] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	3	3		

Statistical analyses

No statistical analyses for this end point

Primary: Sodium

End point title	Sodium[40][41]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[41] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Potassium

End point title	Potassium[42][43]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.

[43] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Urea

End point title	Urea[44][45]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[44] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[45] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Creatinine

End point title	Creatinine[46][47]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[47] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	1		
Maximum value during treatment	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Albumin

End point title	Albumin[48][49]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[48] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[49] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Calcium

End point title	Calcium[50][51]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[50] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[51] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Phosphate

End point title	Phosphate[52][53]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[53] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Alkaline Phosphatase

End point title	Alkaline Phosphatase[54][55]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[54] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[55] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	0		
Maximum value during treatment	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Alanine Aminotransferase

End point title	Alanine Aminotransferase[56][57]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[56] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[57] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	0		
Maximum value during treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Aspartate Aminotransferase

End point title	Aspartate Aminotransferase[58][59]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[58] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[59] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	1	1		
Maximum value during treatment	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Bilirubin, Total

End point title	Bilirubin, Total[60][61]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of follow up

Notes:

[60] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical analyses for safety endpoints, only descriptive statistics which are presented here.
[61] - 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: The arms in the baseline period are the same as the arms in the Overall Study.

End point values	Placebo	AZD8601		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	7		
Units: Number of subjects				
Baseline	0	0		
Maximum value during treatment	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events are summarized from the first dose of IP dose throughout the treatment period and including the follow-up period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	AZD8601 3mg
Reporting group description: AZD8601 3mg	

Serious adverse events	Placebo	AZD8601 3mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	3 / 7 (42.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Incision site impaired healing			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site inflammation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Embolic cerebral infarction			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	AZD8601 3mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	7 / 7 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Non-cardiac chest pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Pleural effusion			
subjects affected / exposed	2 / 4 (50.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Investigations			
Liver function test increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 4 (50.00%)	2 / 7 (28.57%)	
occurrences (all)	2	2	
Left ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Sinus bradycardia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Ventricular arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Embolic cerebral infarction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Coagulopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Wound infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2018	Number of countries updated to reflect the current situation where the study initially will be conducted in 1 country but with the possibility to expand to further countries. Change to Lead Investigator and their designation. Correction to Visit 1 time window to earliest 3 months and latest 15 days before surgery (Day -90 to -15). Clarification that Visit 3 is from Day from -1 to 4. Inclusion criterion 4 corrected to "Indication for elective CABG surgery enrolled at least 15 days before the planned surgery." Table 1 updated with assessments that were identified as incorrect or missing in Table compared to text. Table 1 of CSP, Text updated to allow Visit 1 and Visit 2 on the same day except for the PET assessment.
08 May 2018	Table 1 of CSP modification of timepoints for several assessments or sample collections. Removed optional nature of LAD CFVR. Updated text for SAE reporting.
22 January 2019	Adjustment to text regarding number of sites and study timelines in synopsis and Section 1.4. Other administrative changes. Time window between Visit 2 and Visit 3 adjusted. Exploratory gyrocardiography assessment was removed from the study protocol. AZ activity app for the digital 6-min walk test was not applicable for the newly added country Germany but remained optional in other participating countries. Minor adjustments made to urinalysis. CSP adjusted to allow patients to be enrolled at one site and, if needed, to perform the 15O PET assessment at another, named site. Table 1, for blood pressure and pulse oximetry number of assessments on Day 1 corrected from 4 to 3.

27 February 2020	Expected study duration extended to Q1 2022 in the Synopsis. Local ethics committee requested that the safety review procedure included external experts. Study specific stopping criteria added. An unblinded DMG was added. Added that if a patient was referred to another hospital for the 15O PET assessment, CT could also be performed there.	

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported