Clinical trial results:
A double-blind, randomized, placebo-controlled, multicenter, dose escalation study to select and evaluate an oral modified release formulation of omecamtiv mecarbil in subjects with heart failure and left ventricular systolic dysfunction

Summary

EudraCT number	2012-000327-40
Trial protocol	NL GB LT CZ HU IT BG DE BE
Global end of trial date	19 August 2015

Results information

Result version number	v1 (current)
This version publication date	04 September 2016
First version publication date	04 September 2016

Trial information

Trial identification

Sponsor protocol code	20110151

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01786512
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	19 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were (i) to select an oral modified release (MR) formulation and dose of omecamtiv mecarbil (OM) for chronic twice daily (BID) dosing in subjects with heart failure (HF) and left ventricular systolic dysfunction and (ii) to characterize its pharmacokinetics (PK) over 20 weeks of treatment.

Protection of trial subjects:

This study was conducted in accordance with applicable country regulations and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. Essential documents will be retained in accordance with ICH GCP.
All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2013
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	Australia: 5
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Bulgaria: 52
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	Germany: 30
Country: Number of subjects enrolled	Hungary: 48
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Lithuania: 21
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	United States: 146
Country: Number of subjects enrolled	Canada: 53
Country: Number of subjects enrolled	Poland: 92

Worldwide total number of subjects	544
EEA total number of subjects	340

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)	280
From 65 to 84 years	264
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from 26 February 2013 to 05 March 2015 at 86 centers in 13 countries in Europe, Australia, and North America. Subjects with a history of chronic heart failure being treated with stable, optimal pharmacological therapy for ≥ 4 weeks were eligible to participate.

Pre-assignment

Screening details:

The study consisted of a dose-escalation phase to select 1 of 3 OM oral formulations in 2 dose-escalation cohorts, followed by an expansion phase to evaluate 20 weeks of administration of the selected formulation at 2 target dose levels, compared with placebo. Randomization was stratified by presence or absence of atrial fibrillation/flutter.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Escalation Phase Cohort 1: Placebo

Arm description:

Participants received placebo tablets twice a day (BID) for 7 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1

Arm description:

Participants received 25 mg omecamtiv mecarbil (OM) Matrix F1 (M-F1) tablets twice a day for 7 days.

Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Matrix F1
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2

Arm description:

Participants received 25 mg omecamtiv mecarbil (OM) Matrix F2 (M-F2) tablets twice a day for 7 days.

Arm type	Experimental

Investigational medicinal product name	Omecamtiv Mecarbil Matrix F2
Investigational medicinal product code	AMF 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2

Arm description:

Participants received 25 mg omecamtiv mecarbil swellable core technology F2 (SCT-F2) tablets twice a day for 7 days.

Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Swellable Core Technology F2
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 2: Placebo

Arm description:

Participants received placebo tablets twice a day for 7 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1

Arm description:

Participants received 50 mg omecamtiv mecarbil M-F1 tablets twice a day for 7 days.

Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Matrix F1
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally twice a day

Arm title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2

Arm description:

Participants received 50 mg omecamtiv mecarbil M-F2 tablets twice a day for 7 days.

Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Matrix F2
Investigational medicinal product code	AMF 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Administered orally twice a day

Arm title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2
Arm description: Participants received 50 mg omecamtiv mecarbil SCT-F2 tablets twice a day for 7 days.	
Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Swellable Core Technology F2
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally twice a day	
Arm title	Expansion Phase: Placebo
Arm description: Participants received placebo tablets twice a day for 20 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally twice a day	
Arm title	Expansion Phase: Omecamtiv Mecarbil 25 mg
Arm description: Participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day for 20 weeks.	
Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Matrix F1
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally twice a day	
Arm title	Expansion Phase: PK-based Titration
Arm description: All participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day. At week 8 the dose escalated to 50 mg twice a day if the week 2 predose plasma concentration of OM was less than the predefined cutoff of 200 ng/mL.	
Arm type	Experimental
Investigational medicinal product name	Omecamtiv Mecarbil Matrix F1
Investigational medicinal product code	AMG 423
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered orally twice a day	

Number of subjects in period 1	Escalation Phase Cohort 1: Placebo	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Started	11	11	14
Received Study Treatment	11	10	14
Completed	11	10	14
Not completed	0	1	0
Consent withdrawn by subject	-	1	-
Death	-	-	-
Lost to follow-up	-	-	-
Decision by sponsor	-	-	-

Number of subjects in period 1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Placebo	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Started	13	10	11
Received Study Treatment	13	10	11
Completed	13	10	11
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Death	-	-	-
Lost to follow-up	-	-	-
Decision by sponsor	-	-	-

Number of subjects in period 1	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2	Expansion Phase: Placebo
Started	12	14	149
Received Study Treatment	11	14	149
Completed	11	14	145
Not completed	1	0	4
Consent withdrawn by subject	1	-	-
Death	-	-	4
Lost to follow-up	-	-	-
Decision by sponsor	-	-	-

Number of subjects in period 1	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration
Started	150	149
Received Study Treatment	150	146
Completed	145	137
Not completed	5	12

Consent withdrawn by subject	3	7
Death	1	3
Lost to follow-up	1	-
Decision by sponsor	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Escalation Phase Cohort 1: Placebo
Reporting group description:	
Participants received placebo tablets twice a day (BID) for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1
Reporting group description:	
Participants received 25 mg omecamtiv mecarbil (OM) Matrix F1 (M-F1) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Reporting group description:	
Participants received 25 mg omecamtiv mecarbil (OM) Matrix F2 (M-F2) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2
Reporting group description:	
Participants received 25 mg omecamtiv mecarbil swellable core technology F2 (SCT-F2) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Placebo
Reporting group description:	
Participants received placebo tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Reporting group description:	
Participants received 50 mg omecamtiv mecarbil M-F1 tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2
Reporting group description:	
Participants received 50 mg omecamtiv mecarbil M-F2 tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2
Reporting group description:	
Participants received 50 mg omecamtiv mecarbil SCT-F2 tablets twice a day for 7 days.	
Reporting group title	Expansion Phase: Placebo
Reporting group description:	
Participants received placebo tablets twice a day for 20 weeks.	
Reporting group title	Expansion Phase: Omecamtiv Mecarbil 25 mg
Reporting group description:	
Participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day for 20 weeks.	
Reporting group title	Expansion Phase: PK-based Titration
Reporting group description:	
All participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day. At week 8 the dose escalated to 50 mg twice a day if the week 2 predose plasma concentration of OM was less than the predefined cutoff of 200 ng/mL.	

Reporting group values	Escalation Phase Cohort 1: Placebo	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Number of subjects	11	11	14
Age Categorical Units: Subjects			
18 - 64 years	3	4	7
65 - 74 years	8	4	4
75 - 84 years	0	3	3

Age Continuous Units: years			
arithmetic mean	66.5	67.7	65.3
standard deviation	± 4.6	± 11.4	± 8.8
Gender Categorical Units: Subjects			
Female	2	2	3
Male	9	9	11
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black (or African American)	3	1	0
Mixed Race	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	7	10	14
Other	1	0	0
Ethnicity Units: Subjects			
Hispanic/Latino	0	1	0
Not Hispanic/Latino	11	10	14
Stratification Factor - Atrial Fibrillation/Flutter at Randomization Units: Subjects			
Yes	0	0	3
No	11	11	11

Reporting group values	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Placebo	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Number of subjects	13	10	11
Age Categorical Units: Subjects			
18 - 64 years	5	5	6
65 - 74 years	6	5	4
75 - 84 years	2	0	1
Age Continuous Units: years			
arithmetic mean	66.7	62.1	65.1
standard deviation	± 8.7	± 9.3	± 7
Gender Categorical Units: Subjects			
Female	1	3	3
Male	12	7	8
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black (or African American)	0	0	3
Mixed Race	1	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
White	12	10	8
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic/Latino	1	1	0
Not Hispanic/Latino	12	9	11
Stratification Factor - Atrial Fibrillation/Flutter at Randomization Units: Subjects			
Yes	2	0	1
No	11	10	10

Reporting group values	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2	Expansion Phase: Placebo
Number of subjects	12	14	149
Age Categorical Units: Subjects			
18 - 64 years	5	6	82
65 - 74 years	4	5	46
75 - 84 years	3	3	21
Age Continuous Units: years			
arithmetic mean	63.8	64.3	63.7
standard deviation	± 11.6	± 11.5	± 9.7
Gender Categorical Units: Subjects			
Female	4	2	30
Male	8	12	119
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	2
Black (or African American)	1	2	11
Mixed Race	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	11	12	136
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic/Latino	1	0	2
Not Hispanic/Latino	11	14	147
Stratification Factor - Atrial Fibrillation/Flutter at Randomization Units: Subjects			
Yes	2	3	32
No	10	11	117

Reporting group values	Expansion Phase: Omecamtiv Mecarbil	Expansion Phase: PK-based Titration	Total

	25 mg		
Number of subjects	150	149	544
Age Categorical Units: Subjects			
18 - 64 years	81	76	280
65 - 74 years	52	50	188
75 - 84 years	17	23	76
Age Continuous Units: years			
arithmetic mean	62.8	62.7	
standard deviation	± 10.2	± 11.7	-
Gender Categorical Units: Subjects			
Female	23	24	97
Male	127	125	447
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	3
Black (or African American)	5	8	34
Mixed Race	0	0	1
Native Hawaiian or Other Pacific Islander	1	0	1
White	142	140	502
Other	1	1	3
Ethnicity Units: Subjects			
Hispanic/Latino	7	4	17
Not Hispanic/Latino	143	145	527
Stratification Factor - Atrial Fibrillation/Flutter at Randomization Units: Subjects			
Yes	32	32	107
No	118	117	437

End points

End points reporting groups

Reporting group title	Escalation Phase Cohort 1: Placebo
Reporting group description: Participants received placebo tablets twice a day (BID) for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1
Reporting group description: Participants received 25 mg omecamtiv mecarbil (OM) Matrix F1 (M-F1) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Reporting group description: Participants received 25 mg omecamtiv mecarbil (OM) Matrix F2 (M-F2) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2
Reporting group description: Participants received 25 mg omecamtiv mecarbil swellable core technology F2 (SCT-F2) tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Placebo
Reporting group description: Participants received placebo tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Reporting group description: Participants received 50 mg omecamtiv mecarbil M-F1 tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2
Reporting group description: Participants received 50 mg omecamtiv mecarbil M-F2 tablets twice a day for 7 days.	
Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2
Reporting group description: Participants received 50 mg omecamtiv mecarbil SCT-F2 tablets twice a day for 7 days.	
Reporting group title	Expansion Phase: Placebo
Reporting group description: Participants received placebo tablets twice a day for 20 weeks.	
Reporting group title	Expansion Phase: Omecamtiv Mecarbil 25 mg
Reporting group description: Participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day for 20 weeks.	
Reporting group title	Expansion Phase: PK-based Titration
Reporting group description: All participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day. At week 8 the dose escalated to 50 mg twice a day if the week 2 predose plasma concentration of OM was less than the predefined cutoff of 200 ng/mL.	

Primary: Dose Escalation Phase: Maximum Observed Plasma Concentration for Omecamtiv Mecarbil Following the Last Dose (Day 7)

End point title	Dose Escalation Phase: Maximum Observed Plasma Concentration for Omecamtiv Mecarbil Following the Last Dose (Day 7)[1][2]
End point description:	
End point type	Primary
End point timeframe: Day 7	

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: No formal hypothesis testing was performed.

[2] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	13	10
Units: ng/mL				
arithmetic mean (standard deviation)	193 (± 58.8)	201 (± 94.4)	171 (± 53.8)	492 (± 115)

End point values	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: ng/mL				
arithmetic mean (standard deviation)	502 (± 138)	601 (± 204)		

Statistical analyses

No statistical analyses for this end point

Primary: Dose Escalation Phase: Time to Maximum Observed Plasma Concentration for Omecamtiv Mecarbil Following the Last Dose (Day 7)

End point title	Dose Escalation Phase: Time to Maximum Observed Plasma Concentration for Omecamtiv Mecarbil Following the Last Dose (Day 7)[3][4]

End point description:

End point type	Primary

End point timeframe:

Day 7

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: No formal hypothesis testing was performed.

[4] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	13	10
Units: hours				
arithmetic mean (standard deviation)	3.9 (± 4.4)	2 (± 1.2)	4.2 (± 1.9)	2.6 (± 2.4)

End point values	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: hours				
arithmetic mean (standard deviation)	2.2 (± 1.8)	4.6 (± 2.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Dose Escalation Phase: Plasma Concentration of Omecamtiv Mecarbil Prior to Dose on Day 7

End point title	Dose Escalation Phase: Plasma Concentration of Omecamtiv Mecarbil Prior to Dose on Day 7[5][6]

End point description:

End point type	Primary

End point timeframe:

Day 7, predose

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: No formal hypothesis testing was performed.

[6] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	13	10
Units: ng/mL				
arithmetic mean (standard deviation)	157 (± 63.7)	137 (± 56.8)	134 (± 54.7)	376 (± 170)

End point values	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: ng/mL				
arithmetic mean (standard deviation)	395 (± 108)	476 (± 234)		

Statistical analyses

No statistical analyses for this end point

Primary: Dose Escalation Phase: Area Under the Plasma Concentration-time Curve for a Dosing Interval of 12 Hours Post Dose (AUC12) for Omecamtiv Mecarbil

End point title	Dose Escalation Phase: Area Under the Plasma Concentration-time Curve for a Dosing Interval of 12 Hours Post Dose (AUC12) for Omecamtiv Mecarbil[7][8]

End point description:

End point type	Primary

End point timeframe:

Day 7

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: No formal hypothesis testing was performed.

[8] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	13	10
Units: ng*hr/mL				
arithmetic mean (standard deviation)	2030 (± 658)	2000 (± 1020)	1740 (± 586)	5070 (± 1060)

End point values	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: ng*hr/mL				
arithmetic mean (standard deviation)	5010 (± 1160)	6550 (± 2340)		

Statistical analyses

No statistical analyses for this end point

Primary: Expansion Phase: Plasma Concentration of Omecamtiv Mecarbil Prior to Dosing

End point title	Expansion Phase: Plasma Concentration of Omecamtiv Mecarbil Prior to Dosing[9][10]

End point description:

End point type	Primary

End point timeframe:

Weeks 2, 8, 12, 16 and 20

Notes:

[9] - 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: No formal hypothesis testing was performed.

[10] - 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 formal hypothesis testing was performed.

End point values	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	141		
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 2	174 (± 62.2)	179 (± 68.8)		
Week 8	156 (± 69.1)	161 (± 74.4)		
Week 12	165 (± 67.9)	263 (± 116)		
Week 16	155 (± 69)	240 (± 120)		
Week 20	149 (± 71.2)	239 (± 118)		

Statistical analyses

No statistical analyses for this end point

Primary: Expansion Phase: Maximum Observed Plasma Concentration for Omecamtiv Mecarbil

End point title	Expansion Phase: Maximum Observed Plasma Concentration for Omecamtiv Mecarbil[11][12]

End point description:

End point type	Primary

End point timeframe:

Week 2 and week 12

Notes:

[11] - 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: No formal hypothesis testing was performed.

[12] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	141		
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 2	212 (± 70.4)	212 (± 81)		
Week 12	200 (± 71.1)	318 (± 129)		

Statistical analyses

No statistical analyses for this end point

Secondary: Expansion Phase: Change from Baseline in Systolic Ejection Time (SET) at Week 20

End point title	Expansion Phase: Change from Baseline in Systolic Ejection Time (SET) at Week 20[13]

End point description:

Systolic ejection time was measured using echocardiography.
Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: seconds				
least squares mean (standard error)	0 (± 0.0025)	0.0112 (± 0.0024)	0.025 (± 0.0026)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	0.0112
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0047
upper limit	0.0176
Variability estimate	Standard error of the mean
Dispersion value	0.0033

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	0.025
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0184
upper limit	0.0315
Variability estimate	Standard error of the mean
Dispersion value	0.0033

Secondary: Expansion Phase: Change from Baseline in Stroke Volume at Week 20

End point title	Expansion Phase: Change from Baseline in Stroke Volume at

	Week 20[14]

End point description:

Stroke volume was measured using echocardiography.
Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[14] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: mL				
least squares mean (standard error)	-1.05 (± 1.18)	3.53 (± 1.16)	2.58 (± 1.19)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	4.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	7.65
Variability estimate	Standard error of the mean
Dispersion value	1.56

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	6.72
Variability estimate	Standard error of the mean
Dispersion value	1.57

Secondary: Expansion Phase: Change from Baseline in Left Ventricular End Systolic Diameter (LVESD) at Week 20

End point title	Expansion Phase: Change from Baseline in Left Ventricular End Systolic Diameter (LVESD) at Week 20[15]

End point description:

LVESD was measured using echocardiography.Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: cm				
least squares mean (standard error)	-0.242 (± 0.043)	-0.322 (± 0.044)	-0.421 (± 0.045)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-0.079
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.194
upper limit	0.035
Variability estimate	Standard error of the mean
Dispersion value	0.058

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-0.179
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.295
upper limit	-0.062
Variability estimate	Standard error of the mean
Dispersion value	0.059

Secondary: Expansion Phase: Change from Baseline in Left Ventricular End Diastolic Diameter (LVEDD) at Week 20

End point title	Expansion Phase: Change from Baseline in Left Ventricular End Diastolic Diameter (LVEDD) at Week 20[16]

End point description:

LVEDD was measured using echocardiography.
Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[16] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: cm				
least squares mean (standard error)	0.089 (± 0.038)	0.023 (± 0.038)	-0.04 (± 0.04)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-0.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.231
upper limit	-0.028
Variability estimate	Standard error of the mean
Dispersion value	0.052

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-0.067
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.166
upper limit	0.033
Variability estimate	Standard error of the mean
Dispersion value	0.051

Secondary: Expansion Phase: Change from Baseline in Heart Rate at Week 20

End point title	Expansion Phase: Change from Baseline in Heart Rate at Week

	20[17]

End point description:

Heart rate was measured using electrocardiography. Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: beats/minute				
least squares mean (standard error)	0.57 (± 0.79)	-0.77 (± 0.79)	-2.4 (± 0.81)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.47
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	1.09

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-2.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.12
upper limit	-0.81
Variability estimate	Standard error of the mean
Dispersion value	1.09

Secondary: Expansion Phase: Change from Baseline in N-terminal Prohormone B-type Natriuretic Peptide (NT-proBNP) at Week 20

End point title	Expansion Phase: Change from Baseline in N-terminal Prohormone B-type Natriuretic Peptide (NT-proBNP) at Week 20[18]

End point description:

Least squares means are from a repeated measures model including treatment group, stratification factor, scheduled visit, interaction of treatment with scheduled visit and the baseline value as covariates.

End point type	Secondary

End point timeframe:

Baseline and week 20

Notes:

[18] - 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: Dose-escalation phase and expansion phase endpoints are reported separately.

End point values	Expansion Phase: Placebo	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	146	
Units: pg/mL				
least squares mean (standard error)	502 (± 257)	-319 (± 257)	-468 (± 262)	

Statistical analyses

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: PK-based Titration

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-970
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1672
upper limit	-268
Variability estimate	Standard error of the mean
Dispersion value	357

Statistical analysis title	Treatment Difference
Comparison groups	Expansion Phase: Placebo v Expansion Phase: Omecamtiv Mecarbil 25 mg
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment difference
Point estimate	-822
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1516
upper limit	-127
Variability estimate	Standard error of the mean
Dispersion value	353

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until 4 weeks after last dose - treatment duration was 7 days in the dose escalation phase and 20 weeks in the expansion phase.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Escalation Phase Cohort 1: Placebo

Reporting group description:

Participants received placebo tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1

Reporting group description:

Participants received 25 mg omecamtiv mecarbil Matrix F1 (M-F1) tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2

Reporting group description:

Participants received 25 mg omecamtiv mecarbil Matrix F2 (M-F2) tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2

Reporting group description:

Participants received 25 mg omecamtiv mecarbil swellable core technology F2 (SCT-F2) tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 2: Placebo

Reporting group description:

Participants received placebo tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1

Reporting group description:

Participants received 50 mg omecamtiv mecarbil M-F1 tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2

Reporting group description:

Participants received 50 mg omecamtiv mecarbil M-F2 tablets twice a day for 7 days.

Reporting group title	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2

Reporting group description:

Participants received 50 mg omecamtiv mecarbil SCT-F2 tablets twice a day for 7 days.

Reporting group title	Expansion Phase: Placebo

Reporting group description:

Participants received placebo tablets twice a day for 20 weeks.

Reporting group title	Expansion Phase: Omecamtiv Mecarbil 25 mg

Reporting group description:

Participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day for 20 weeks.

Reporting group title	Expansion Phase: PK-based Titration

Reporting group description:

All participants received 25 mg omecamtiv mecarbil M-F1 tablets twice a day. At week 8 the dose escalated to 50 mg twice a day if the week 2 predose plasma concentration of OM was less than the predefined cutoff of 200 ng/mL.

Serious adverse events	Escalation Phase Cohort 1: Placebo	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoma in situ of skin			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsil cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cardiac complication associated with device			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulnar nerve injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	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 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac asthma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory distress			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Inguinal hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Placebo	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 11 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoma in situ of skin			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsil cancer			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cardiac complication associated with device			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulnar nerve injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	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 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac asthma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory distress			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Inguinal hernia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2	Expansion Phase: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	30 / 149 (20.13%)
number of deaths (all causes)	0	0	4
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoma in situ of skin			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tonsil cancer			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cardiac complication associated with device			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
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 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulnar nerve injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	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 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cardiac asthma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	4 / 149 (2.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	3 / 149 (2.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	3 / 149 (2.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory distress			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Inguinal hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 150 (24.00%)	32 / 146 (21.92%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ of skin			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			

subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 150 (0.67%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Cardiac complication associated with device			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 150 (1.33%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin I increased			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	2 / 150 (1.33%)	2 / 146 (1.37%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulnar nerve injury			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	3 / 150 (2.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 150 (0.67%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 150 (1.33%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac asthma			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	3 / 150 (2.00%)	5 / 146 (3.42%)	
occurrences causally related to treatment / all	0 / 4	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			

subjects affected / exposed	3 / 150 (2.00%)	3 / 146 (2.05%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	3 / 150 (2.00%)	3 / 146 (2.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory distress			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	2 / 150 (1.33%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			

subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
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 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inguinal hernia			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic congestion			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			

subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 150 (0.67%)	2 / 146 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			

subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 150 (0.67%)	3 / 146 (2.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate infection			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (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: 5 %

Non-serious adverse events	Escalation Phase Cohort 1: Placebo	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F1	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg M-F2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	2 / 10 (20.00%)	5 / 14 (35.71%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	3 / 14 (21.43%)
occurrences (all)	0	1	3
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nodule			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Mental status changes			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Carotid bruit			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
N-terminal prohormone brain natriuretic peptide increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Troponin I increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Abnormal faeces			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Escalation Phase Cohort 1: Omecamtiv Mecarbil 25 mg SCT-F2	Escalation Phase Cohort 2: Placebo	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	1 / 10 (10.00%)	8 / 11 (72.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Nodule			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Mental status changes			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Carotid bruit			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Troponin I increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 13 (38.46%)	0 / 10 (0.00%)	2 / 11 (18.18%)
occurrences (all)	5	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abnormal faeces			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nausea			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg M-F2	Escalation Phase Cohort 2: Omecamtiv Mecarbil 50 mg SCT-F2	Expansion Phase: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	4 / 14 (28.57%)	48 / 149 (32.21%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences (all)	0	0	3
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	3 / 149 (2.01%)
occurrences (all)	0	1	4
Orthostatic hypotension			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences (all)	1	0	2
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	4 / 149 (2.68%)
occurrences (all)	0	0	5
Feeling hot			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Nodule			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	7 / 149 (4.70%)
occurrences (all)	0	0	10
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences (all)	0	0	2
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	0	1
Mental status changes			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 149 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Carotid bruit			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 149 (0.00%)
occurrences (all)	0	1	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Troponin I increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	9 / 149 (6.04%)
occurrences (all)	0	0	10
Palpitations			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	3 / 149 (2.01%)
occurrences (all)	0	0	3
Sinus bradycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	6 / 149 (4.03%)
occurrences (all)	0	0	7
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	5 / 149 (3.36%)
occurrences (all)	0	0	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	0	1
Abnormal faeces			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 149 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	5 / 149 (3.36%)
occurrences (all)	0	0	5
Dry mouth			

subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	2 / 149 (1.34%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	0 / 149 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	5 / 149 (3.36%)
occurrences (all)	0	0	6
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	0 / 149 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	1 / 149 (0.67%)
occurrences (all)	1	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	5 / 149 (3.36%)
occurrences (all)	0	0	6
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 11 (0.00%)	0 / 14 (0.00%)	6 / 149 (4.03%)
occurrences (all)	0	0	7

Non-serious adverse events	Expansion Phase: Omecamtiv Mecarbil 25 mg	Expansion Phase: PK-based Titration	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 150 (34.00%)	48 / 146 (32.88%)	
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 150 (2.00%)	1 / 146 (0.68%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	1 / 150 (0.67%)	5 / 146 (3.42%)	
occurrences (all)	1	5	
Orthostatic hypotension			
subjects affected / exposed	1 / 150 (0.67%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 150 (1.33%)	2 / 146 (1.37%)	
occurrences (all)	3	2	
Fatigue			
subjects affected / exposed	14 / 150 (9.33%)	9 / 146 (6.16%)	
occurrences (all)	15	10	
Feeling hot			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Nodule			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	9 / 150 (6.00%)	13 / 146 (8.90%)	
occurrences (all)	9	13	
Nasal congestion			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 150 (1.33%)	2 / 146 (1.37%)	
occurrences (all)	2	2	
Pulmonary oedema			

subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 150 (1.33%)	1 / 146 (0.68%)	
occurrences (all)	2	1	
Mental status changes			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 150 (1.33%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Blood bicarbonate decreased			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Carotid bruit			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Heart rate increased			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Troponin I increased			
subjects affected / exposed	1 / 150 (0.67%)	1 / 146 (0.68%)	
occurrences (all)	3	1	
Weight increased			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			

Bundle branch block left			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	2 / 150 (1.33%)	3 / 146 (2.05%)	
occurrences (all)	2	3	
Palpitations			
subjects affected / exposed	3 / 150 (2.00%)	4 / 146 (2.74%)	
occurrences (all)	5	5	
Sinus bradycardia			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 150 (5.33%)	9 / 146 (6.16%)	
occurrences (all)	9	10	
Headache			
subjects affected / exposed	2 / 150 (1.33%)	9 / 146 (6.16%)	
occurrences (all)	2	15	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 150 (0.67%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 150 (0.67%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Abnormal faeces			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	

Constipation			
subjects affected / exposed	2 / 150 (1.33%)	1 / 146 (0.68%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	5 / 150 (3.33%)	4 / 146 (2.74%)	
occurrences (all)	5	4	
Dry mouth			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 150 (0.00%)	0 / 146 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 150 (1.33%)	8 / 146 (5.48%)	
occurrences (all)	2	8	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	2 / 150 (1.33%)	1 / 146 (0.68%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 150 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	3 / 150 (2.00%)	0 / 146 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	2 / 150 (1.33%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 150 (5.33%)	5 / 146 (3.42%)	
occurrences (all)	8	5	
Metabolism and nutrition disorders			
Gout			

subjects affected / exposed occurrences (all)	3 / 150 (2.00%) 4	2 / 146 (1.37%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2012	• Added sample collection for therapeutic drug monitoring assay development • Replaced stratification by region with stratification by presence or absence of atrial fibrillation/flutter • Moved intensive PK from week 4 to week 8 of expansion phase • Clarified adjudication of deaths, all hospitalizations, and selected nonfatal CV events (including possible MI or ischemia) using prespecified criteria • Clarified LVEF eligibility requirements for subjects in the dose-escalation phase and the expansion phase • Simplified the valvular heart disease exclusion • Added daily phone contacts for days without other study contact during the first 7 days after initiation of IP administration for collection of adverse events, including possible ischemic events and for reminding subjects to be compliant with IP administration • Clarified which procedures could be done at a location external to the study site, eg, the subject's home by home healthcare provider or other authorized staff • Added a subject diary for IP administration • Added an inclusion of acceptable echocardiographic image quality of screening echocardiogram per central reader for subjects enrolled in the expansion cohort • Added identity of specific cytochrome P450 3A4 inhibitors and inducers to the exclusion criteria • Extended study follow up to 4 weeks after last dose (day 35 + 5 days for dose-escalation phase; week 16 + 5 days for expansion phase) • Added urinalysis assessments • Added information about the troponin assay used for the study • Clarified that subjects could remain at the site overnight per study protocol on days of intensive PK sampling
30 April 2013	• Revised the IP section to remove the detail of pill count per bottle and refer to the Investigational Product Instruction Manual instead • Updated text on reporting of serious adverse events after end of study • Reduced the window for pregnancy and lactation reporting from 7 days to 24 hours per Amgen's updated processes and protocol template
12 August 2013	• Increased the size of the expansion cohort to 150 subjects per group from 100 subjects per group for a total enrollment of 450 subjects in the expansion cohort, and a maximal study enrollment of up to approximately 570 subjects • Increased the number of study centers to 125 centers from 100 centers • Added collection of digoxin samples for subjects receiving digoxin therapy • Increased the volume of the samples collected for bioanalytical assay development • Updated the status of the ongoing phase 2 study 20100754 ATOMIC-AHF
18 November 2013	• Based on data review at the dose level review meeting 2, added a dose titration step to the OM 50 mg BID group at 25 mg BID with advancement to 50 mg BID gated by the week 2 PK. • Removed month 6 vital status follow-up as the total study duration for expansion phase was 6 months • Modified pregnancy exclusion per Amgen revised standard
07 April 2014	• Clarified exclusion criteria to exclude subjects with acute MIs • Modified contraception requirements to require 2 acceptable methods of effective birth control

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported