Clinical trial results:
Randomized, Double-blind, Placebo-controlled, Two-Part, Adaptive Design Study of Safety, Tolerability, Preliminary Pharmacokinetics, and Pharmacodynamics of Single and Multiple Ascending Oral Doses of MYK-491 in Patients With Stable Heart Failure With Reduced Ejection Fraction

Summary

EudraCT number	2018-002239-11
Trial protocol	DE GB SE NL PL
Global end of trial date	24 October 2019

Results information

Result version number	v1 (current)
This version publication date	26 December 2022
First version publication date	26 December 2022

Trial information

Trial identification

Sponsor protocol code	MYK-491-003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	03 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to establish preliminary safety and tolerability of single-and multiple-ascending oral doses of Danicamtiv in ambulatory patient

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 42
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	52
EEA total number of subjects	9

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)	39

From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

52 participants randomized and treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SAD Cohort 1

Arm description:

Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 175mg and Danicamtiv 350mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days. Some participants received a fourth single dose of Danicamtiv ranging between 350mg-550mg in the optional open-label period D

Arm type	Experimental
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

175mg single-dose

Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

350mg single-dose

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

Dosage and administration details:

Placebo single-dose

Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

450mg single-dose divided to 2 administrations

Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

525mg single-dose

Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

550mg single-dose divided to 2 administrations

Arm title	SAD Cohort 2

Arm description:

Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 400mg and Danicamtiv 500mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days

Arm type	Experimental
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400mg single-dose

Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500mg single-dose

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

Dosage and administration details:

Placebo single-dose

Arm title	MAD Cohort 1

Arm description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (fasting) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.

Arm type	Experimental
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 75mg (fasting) BID for 7 days	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo BID for 2 days	
Arm title	MAD Cohort 2
Arm description: Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 50mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo BID for 2 days	
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50mg (with food) BID for 7 days	
Arm title	MAD Cohort 3
Arm description: Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Arm type	Experimental
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 75mg (with food) BID for 7 days	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo BID for 2 days	
Arm title	MAD Cohort 4
Arm description: Participants received single-blinded placebo twice daily for 2 days. Participants then received double-	

blinded Danicamtiv 100mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.

Arm type	Experimental
Investigational medicinal product name	Danicamtiv
Investigational medicinal product code	MYK-491
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100mg (with food) BID for 7 days

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

Dosage and administration details:

Placebo BID for 2 days

Arm title	MAD Placebo

Arm description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.

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:

Placebo BID for 9 days

Number of subjects in period 1	SAD Cohort 1	SAD Cohort 2	MAD Cohort 1
Started	8	4	6
Completed Treatment Period A	8	4	0 [1]
Completed Treatment Period B	8	4	0 [2]
Completed Treatment Period C	8	4	0 [3]
Completed Treatment Period D	6 [4]	0 [5]	0 [6]
Completed	8	4	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	MAD Cohort 2	MAD Cohort 3	MAD Cohort 4
Started	9	9	6
Completed Treatment Period A	0 [7]	0 [8]	0 [9]
Completed Treatment Period B	0 [10]	0 [11]	0 [12]
Completed Treatment Period C	0 [13]	0 [14]	0 [15]

Completed Treatment Period D	0 [16]	0 [17]	0 [18]
Completed	9	9	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	MAD Placebo
Started	10
Completed Treatment Period A	0 [19]
Completed Treatment Period B	0 [20]
Completed Treatment Period C	0 [21]
Completed Treatment Period D	0 [22]
Completed	9
Not completed	1
Consent withdrawn by subject	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[14] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[15] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[16] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[17] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[18] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[19] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[20] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[21] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

[22] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is for the number of participants completed treatment in period D only

Baseline characteristics

Reporting groups	
Reporting group title	SAD Cohort 1
Reporting group description:	
Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 175mg and Danicamtiv 350mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days. Some participants received a fourth single dose of Danicamtiv ranging between 350mg-550mg in the optional open-label period D	
Reporting group title	SAD Cohort 2
Reporting group description:	
Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 400mg and Danicamtiv 500mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days	
Reporting group title	MAD Cohort 1
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (fasting) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 2
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 50mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 3
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 4
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 100mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Placebo
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	

Reporting group values	SAD Cohort 1	SAD Cohort 2	MAD Cohort 1
Number of subjects	8	4	6
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	57.1	57.5	62.7
standard deviation	± 9.4	± 5.07	± 12.50
Sex: Female, Male Units: Participants			
Female	3	1	3
Male	5	3	3

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	1	3
White	2	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	8	4	6
Unknown or Not Reported	0	0	0

Reporting group values	MAD Cohort 2	MAD Cohort 3	MAD Cohort 4
Number of subjects	9	9	6
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	63.0	56.8	58.5
standard deviation	± 9.86	± 5.09	± 5.36
Sex: Female, Male Units: Participants			
Female	3	2	1
Male	6	7	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	0
White	8	7	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	9	9	6
Unknown or Not Reported	0	0	0

Reporting group values	MAD Placebo	Total	
Number of subjects	10	52	
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	58.6		
standard deviation	± 6.98	-	
Sex: Female, Male Units: Participants			
Female	1	14	
Male	9	38	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	16	
White	7	36	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	9	51	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	SAD Cohort 1
Reporting group description:	
Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 175mg and Danicamtiv 350mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days. Some participants received a fourth single dose of Danicamtiv ranging between 350mg-550mg in the optional open-label period D	
Reporting group title	SAD Cohort 2
Reporting group description:	
Participants received 3 double-blinded single ascending doses in random sequence (1 placebo, Danicamtiv 400mg and Danicamtiv 500mg) in Period A, B, and C with intervals between doses ranging from 3 to 14 days	
Reporting group title	MAD Cohort 1
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (fasting) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 2
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 50mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 3
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Cohort 4
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 100mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Reporting group title	MAD Placebo
Reporting group description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge.	
Subject analysis set title	SAD Cohort 1 Danicamtiv 175mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Danicamtiv 175mg in either period A, B, or C	
Subject analysis set title	SAD Cohort 1 Danicamtiv 350mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Danicamtiv 350mg in either period A, B, C, or D	
Subject analysis set title	SAD Cohort 1 Danicamtiv 350mg Period D
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Danicamtiv 350mg in period D	
Subject analysis set title	SAD Cohort 1 Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Placebo in either period A, B, or C	
Subject analysis set title	SAD Cohort 1 Danicamtiv 450mg

Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received split dose of Danicamtiv 450mg in period D	
Subject analysis set title	SAD Cohort 1 Danicamtiv 525mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Danicamtiv 525mg in period D	
Subject analysis set title	SAD Cohort 1 Danicamtiv 550mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received split dose of Danicamtiv 550mg in period D	
Subject analysis set title	SAD Cohort 2 Danicamtiv 400mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received split dose of Danicamtiv 400mg	
Subject analysis set title	SAD Cohort 2 Danicamtiv 500mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received split dose of Danicamtiv 500mg	
Subject analysis set title	SAD Cohort 2 Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single dose of Placebo	
Subject analysis set title	MAD Cohort 2 Danicamtiv 50mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 50mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge	
Subject analysis set title	MAD Cohort 1+3 Danicamtiv 75mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg twice daily for 7 days, and 2 days of monitoring following the last dose before discharge	
Subject analysis set title	MAD Cohort 4 Danicamtiv 100mg
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 100mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge	
Subject analysis set title	MAD Cohorts Danicamtiv
Subject analysis set type	Per protocol
Subject analysis set description:	
MAD cohorts at doses ranging from 50 mg to 100 mg	
Subject analysis set title	MAD Cohort Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge	
Subject analysis set title	SAD Cohorts Danicamtiv
Subject analysis set type	Per protocol
Subject analysis set description:	
SAD cohorts at doses ranging from 175 mg to 550 mg	

Subject analysis set title	SAD Cohorts Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
SAD cohorts with participants that received placebo	
Subject analysis set title	SAD Cohorts
Subject analysis set type	Per protocol
Subject analysis set description:	
SAD cohorts Placebo and Danicamtiv at doses ranging from 175 mg to 550 mg	
Subject analysis set title	MAD Cohorts
Subject analysis set type	Per protocol
Subject analysis set description:	
MAD cohorts Placebo and Danicamtiv doses ranging from 50 mg to 100 mg	
Subject analysis set title	SAD Cohorts <2000 ng/mL
Subject analysis set type	Per protocol
Subject analysis set description:	
SAD Cohorts with plasma concentration less than 2000 ng/mL	
Subject analysis set title	SAD Cohorts ≥2000 ng/mL
Subject analysis set type	Per protocol
Subject analysis set description:	
SAD Cohorts with plasma concentration greater than or equal to 2000 ng/mL	
Subject analysis set title	MAD Cohorts <2000 ng/mL
Subject analysis set type	Per protocol
Subject analysis set description:	
MAD Cohorts with plasma concentration less than 2000 ng/mL	
Subject analysis set title	MAD Cohorts 2000-<3500 ng/mL
Subject analysis set type	Per protocol
Subject analysis set description:	
MAD Cohorts with plasma concentration between 2000 (inclusive) to 3500 (non-inclusive) ng/mL	
Subject analysis set title	MAD Cohorts ≥3500 ng/mL
Subject analysis set type	Per protocol
Subject analysis set description:	
MAD Cohorts with plasma concentration greater than or equal to 3500 ng/mL	

Primary: Number of Participants with Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)[1]
End point description:	
Number of participants with any grade of treatment-emergent adverse events (TEAEs) and any grade of serious adverse events (SAEs).	
End point type	Primary
End point timeframe:	
From first dose to 30 days post last dose (Up to 2 months)	

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: Only summary statistics planned for this endpoint

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	1
Units: Participants				
TEAEs	2	5	3	0
SAEs	0	0	0	0

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: Participants				
TEAEs	0	1	3	0
SAEs	0	0	0	0

End point values	SAD Cohort 2 Placebo	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	9	15	6
Units: Participants				
TEAEs	0	7	6	4
SAEs	0	0	1	0

End point values	MAD Cohort Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: Participants				
TEAEs	4			
SAEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Change from Baseline in Electrocardiograms (ECG) Intervals - SAD Cohorts

End point title	Number of Participants with Change from Baseline in Electrocardiograms (ECG) Intervals - SAD Cohorts[2]

End point description:

Number of participants with change from baseline in ECGs QTcF, PR, and QRS intervals. Baseline is defined as the last non-missing value prior to the corresponding period.

End point type	Primary

End point timeframe:

Baseline, day 1-16, 2 hours pre-dose and at 3-, 5-, 9-, 12-, 24-, and 36-hours post-dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	1
Units: Participants				
Change in QTcF from Baseline > 30msec	1	1	0	0
Change in QTcF from Baseline > 60msec	0	0	0	0
Change in PR from baseline > 25%	1	0	0	0
Change in QRS from baseline > 25%	1	1	0	0

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: Participants				
Change in QTcF from Baseline > 30msec	0	0	1	1
Change in QTcF from Baseline > 60msec	0	0	0	0
Change in PR from baseline > 25%	0	0	0	0
Change in QRS from baseline > 25%	0	0	0	0

End point values	SAD Cohort 2 Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: Participants				
Change in QTcF from Baseline > 30msec	2			
Change in QTcF from Baseline > 60msec	1			
Change in PR from baseline > 25%	0			
Change in QRS from baseline > 25%	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Change from Baseline in Electrocardiograms (ECG) Intervals - MAD Cohorts

End point title	Number of Participants with Change from Baseline in Electrocardiograms (ECG) Intervals - MAD Cohorts[3]

End point description:

Number of participants with change from baseline in ECGs QTcF, PR, and QRS intervals. Baseline is defined as the last non-missing value prior to first randomized dose.

End point type	Primary

End point timeframe:

Baseline, Day 1-16, 2 hours pre-dose and at 7-, 24-, and 48-hours post final dose

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: Only summary statistics planned for this endpoint

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	MAD Cohort Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	15	6	10
Units: Participants				
Change in QTcF from Baseline > 30msec	2	5	1	3
Change in QTcF from Baseline > 60msec	0	0	1	1
Change in PR from baseline > 25%	0	0	0	1
Change in QRS from baseline > 25%	1	2	0	2

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from Baseline in Vital Signs Part 1 - MAD Cohorts

End point title	Mean Change from Baseline in Vital Signs Part 1 - MAD

End point description:

Mean change from baseline in supine systolic blood pressure (SBP) and supine diastolic blood pressure (DBP) vital signs. Baseline is defined as the last non-missing value prior to first randomized dose

End point type	Primary

End point timeframe:

Baseline and at 6-hours post-dose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint

End point values	MAD Cohorts Danicamtiv	MAD Cohort Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: mmHg				
arithmetic mean (standard deviation)				
Supine SBP	-4.86 (± 7.537)	-6.33 (± 3.215)		
Supine DBP	-3.57 (± 7.323)	-5.67 (± 3.055)		

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from Baseline in Vital Signs Part 2 - MAD Cohorts

End point title	Mean Change from Baseline in Vital Signs Part 2 - MAD

End point description:

Mean change from baseline in heart rate (HR) vital signs. Baseline is defined as the last non-missing value prior to first randomized dose

End point type	Primary

End point timeframe:

Baseline and at 6-hours post-dose

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: Only summary statistics planned for this endpoint

End point values	MAD Cohorts Danicamtiv	MAD Cohort Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: Beats/min				
arithmetic mean (standard deviation)	3.71 (± 2.563)	3.33 (± 2.517)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with a Troponin I Increase - SAD cohorts

End point title	Number of Participants with a Troponin I Increase - SAD cohorts[6]

End point description:

Number of participants with a troponin increase is defined as when one of the following conditions was met (1) if the participant's troponin I value was normal prior to dosing (≤0.03 ng/mL), an elevated level on at least one measurement after start of dosing >2×ULN for the specific assay (>0.06 ng/mL) through Day 16. (2) If the participant's troponin I value was above the ULN for the specific assay prior to dosing, an increase >0.03 ng/mL compared to baseline on at least one measurement after start of dosing through Day 16.

End point type	Primary

End point timeframe:

Baseline, day 1-3, 2 hours pre-dose and at 3-, 5-, 9-, 12-, 24-, and 36-hours post-dose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint

End point values	SAD Cohorts Danicamtiv	SAD Cohorts Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: Participants	3	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with a Troponin I Increase - MAD cohorts

End point title	Number of Participants with a Troponin I Increase - MAD cohorts[7]

End point description:

Number of participants with a troponin increase is defined as when one of the following conditions was met (1) if the participant's troponin I value was normal prior to dosing (≤0.03 ng/mL), an elevated level on at least one measurement after start of dosing >2×ULN for the specific assay (>0.06 ng/mL) through Day 16. (2) If the participant's troponin I value was above the ULN for the specific assay prior to dosing, an increase >0.03 ng/mL compared to baseline on at least one measurement after start of dosing through Day 16.

End point type	Primary

End point timeframe:

Baseline, pre-dose and 7hr post dose on treatment day 1, day 2, day 5 and pre-dose and at 7-, 24-, and 48-hours post final dose

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: Only summary statistics planned for this endpoint

End point values	MAD Cohorts Danicamtiv	MAD Cohort Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	10		
Units: Participants	7	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Clinically Significant Laboratory Abnormalities

End point title	Number of Participants with Clinically Significant Laboratory Abnormalities[8]

End point description:

Number of participants with clinically significant laboratory abnormalities.

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (Up to 2 months)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint

End point values	SAD Cohorts	MAD Cohorts		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	40		
Units: Participants	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Clinically Significant Physical Examinations Abnormalities

End point title	Number of Participants with Clinically Significant Physical Examinations Abnormalities[9]

End point description:

Number of participants with clinically significant physical examinations abnormalities.
No clinically significant abnormal findings were observed.

End point type	Primary

End point timeframe:

From first dose to 30 days post last dose (Up to 2 months)

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: Only summary statistics planned for this endpoint

End point values	SAD Cohorts	MAD Cohorts		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	40		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from Baseline in Vital Signs Part 1 - SAD Cohorts

End point title	Mean Change from Baseline in Vital Signs Part 1 - SAD

End point description:

Mean change from baseline in supine systolic blood pressure (SBP) and supine diastolic blood pressure

(DBP) vital signs. Baseline is defined as the last non-missing value prior to the corresponding period. 99999=Not available

End point type	Primary

End point timeframe:

Baseline and at 6-hours post-dose

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	1
Units: mmHg				
arithmetic mean (standard deviation)				
Supine SBP	-10.13 (± 12.23)	-11.38 (± 9.90)	-1.38 (± 15.02)	16.00 (± 99999)
Supine DBP	-5.50 (± 12.14)	9.50 (± 6.44)	-5.75 (± 13.04)	12.00 (± 99999)

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: mmHg				
arithmetic mean (standard deviation)				
Supine SBP	-7.00 (± 19.80)	-9.50 (± 2.12)	2.50 (± 4.359)	01.75 (± 15.650)
Supine DBP	-1.00 (± 5.66)	-4.00 (± 8.49)	4.00 (± 9.933)	-2.25 (± 17.270)

End point values	SAD Cohort 2 Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: mmHg				
arithmetic mean (standard deviation)				
Supine SBP	0.00 (± 11.633)			
Supine DBP	-3.00 (± 14.674)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from Baseline in Vital Signs Part 2 - SAD Cohorts

End point title	Mean Change from Baseline in Vital Signs Part 2 - SAD

End point description:

Mean change from baseline in heart rate (HR) vital signs. Baseline is defined as the last non-missing value prior to the corresponding period.
99999=Not available

End point type	Primary

End point timeframe:

Baseline and at 6-hours post-dose

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: Only summary statistics planned for this endpoint

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	1
Units: Beats/min				
arithmetic mean (standard deviation)	7.13 (± 6.20)	-1.25 (± 5.75)	3.00 (± 5.50)	5.00 (± 99999)

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: Beats/min				
arithmetic mean (standard deviation)	5.50 (± 0.71)	-1.50 (± 2.12)	3.75 (± 9.743)	-0.50 (± 5.000)

End point values	SAD Cohort 2 Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: Beats/min				
arithmetic mean (standard deviation)	-6.50 (± 13.699)			

Statistical analyses

No statistical analyses for this end point

Secondary: Danicamtiv Maximum Observed Plasma Concentration (Cmax)

End point title	Danicamtiv Maximum Observed Plasma Concentration (Cmax)

End point description:

Maximum observed plasma concentration (Cmax) for Danicamtiv.
Geometric coefficient of variation was not calculated and the arithmetic coefficient of variation (% CV) is being reported.
99999=Not available

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Danicamtiv 350mg Period D	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	1	1
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1476.63 (± 99999)	2655.83 (± 99999)	3590.00 (± 99999)	4420.00 (± 99999)

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)	2718.51 (± 99999)	5263.71 (± 99999)	5337.58 (± 99999)	5740.50 (± 99999)

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	15	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	792.5 (± 99999)	1174.3 (± 99999)	1452.8 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Danicamtiv Time of Maximum Observed Plasma Concentration (Tmax)

End point title	Danicamtiv Time of Maximum Observed Plasma Concentration (Tmax)

End point description:

Time of maximum observed plasma concentration (Tmax) for Danicamtiv.

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Danicamtiv 350mg Period D	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	1	1
Units: hours				
median (full range (min-max))	5.14 (2.0 to 6.3)	6.18 (3.7 to 9.1)	4.1 (4.1 to 4.1)	12.0 (12.0 to 12.0)

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: hours				
median (full range (min-max))	5.74 (5.4 to 6.1)	8.93 (7.9 to 9.9)	9.13 (6.0 to 12.2)	9.08 (6.0 to 10.0)

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	15	6	
Units: hours				
median (full range (min-max))	4.983 (3.00 to 9.00)	4.000 (1.00 to 12.05)	3.500 (2.03 to 9.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve (AUC)

End point title	Area Under the Plasma Concentration-Time Curve (AUC)

End point description:

Area under the plasma concentration-time curve (AUC) for Danicamtiv including the following time points: (AUC(0-12))=from time 0 to 12 hours; (AUC(0-24))=from time 0 to 24 hours; (AUC(0-48))=from time 0 to 48 hours; (AUClast)=from time 0 up to the last measurable concentration; (AUC(0-

=from time 0 to infinity.
Geometric coefficient of variation was not calculated and the arithmetic coefficient of variation (% CV) is being reported.
99999=Not available

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Danicamtiv 350mg Period D	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	1	1
Units: hr x ng/mL				
geometric mean (geometric coefficient of variation)				
(AUC(0-12))	99999 (± 99999)	99999 (± 99999)	99999 (± 999999)	99999 (± 99999)
(AUC(0-24))	26411.97 (± 99999)	48981.93 (± 99999)	70138.66 (± 99999)	79175.02 (± 99999)
(AUC(0-48))	40068.47 (± 99999)	76497.78 (± 99999)	89356.54 (± 99999)	143543.52 (± 99999)
(AUC last)	46750.66 (± 99999)	89216.40 (± 99999)	104060.46 (± 99999)	182804.71 (± 99999)
(AUC(0-∞))	52467.20 (± 99999)	99576.37 (± 99999)	99999 (± 99999)	234888.37 (± 99999)

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: hr x ng/mL				
geometric mean (geometric coefficient of variation)				
(AUC(0-12))	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
(AUC(0-24))	54004.82 (± 99999)	97640.90 (± 99999)	86110.51 (± 99999)	97656.38 (± 99999)
(AUC(0-48))	89341.77 (± 99999)	159193.47 (± 99999)	135385.91 (± 99999)	161073.09 (± 99999)
(AUC last)	106987.30 (± 99999)	188544.49 (± 99999)	99999 (± 99999)	99999 (± 99999)
(AUC(0-∞))	126374.56 (± 99999)	211928.81 (± 99999)	187776.56 (± 99999)	225087.02 (± 99999)

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	15	6	
Units: hr x ng/mL				
geometric mean (geometric coefficient of variation)				
(AUC(0-12))	7169.245 (± 99999)	10310.794 (± 99999)	12728.956 (± 99999)	
(AUC(0-24))	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
(AUC(0-48))	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
(AUC last)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
(AUC(0-∞))	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent First-order Terminal Elimination Half-life (t1/2)

End point title	Apparent First-order Terminal Elimination Half-life (t1/2)

End point description:

Apparent first-order terminal elimination half-life (t1/2).
99999=Not available

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Danicamtiv 350mg Period D	SAD Cohort 1 Danicamtiv 450mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	0[12]	1
Units: hours				
arithmetic mean (standard deviation)	21.96 (± 4.40)	20.95 (± 3.23)	()	30.62 (± 99999)

Notes:

[12] - 0 participants analyzed

End point values	SAD Cohort 1 Danicamtiv 525mg	SAD Cohort 1 Danicamtiv 550mg	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	4	4
Units: hours				
arithmetic mean (standard deviation)	24.73 (± 10.76)	21.45 (± 0.30)	24.45 (± 11.363)	24.30 (± 13.987)

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	13	6	
Units: hours				
arithmetic mean (standard deviation)	24.466 (± 5.8911)	20.573 (± 6.1033)	23.319 (± 3.5903)	

Statistical analyses

No statistical analyses for this end point

Secondary: Danicamtiv Accumulation Ratio for Maximum Observed Plasma Concentration AR(Cmax) - MAD Cohorts

End point title	Danicamtiv Accumulation Ratio for Maximum Observed Plasma Concentration AR(Cmax) - MAD Cohorts

End point description:

Accumulation ratio for maximum observed plasma concentration AR(Cmax) for Danicamtiv.
Geometric coefficient of variation was not calculated and the arithmetic coefficient of variation (% CV) is being reported.
99999=Not available

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	14	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3.451 (± 99999)	3.241 (± 99999)	3.827 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio for Area Under the Plasma Concentration-Time Curve from Time 0 to 12 Hours AR(AUC(0-12)) - MAD Cohorts

End point title	Accumulation Ratio for Area Under the Plasma Concentration-

	Time Curve from Time 0 to 12 Hours AR(AUC(0-12)) - MAD Cohorts

End point description:

Accumulation ratio for area under the plasma concentration-time curve from time 0 to 12 hours AR(AUC(0-12)) for Danicamtiv.
Geometric coefficient of variation was not calculated and the arithmetic coefficient of variation (% CV) is being reported.
99999=Not available

End point type	Secondary

End point timeframe:

1 hour pre-dose and day 1-12 at 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 36, and 48 hours postdose

End point values	MAD Cohort 2 Danicamtiv 50mg	MAD Cohort 1+3 Danicamtiv 75mg	MAD Cohort 4 Danicamtiv 100mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	14	6	
Units: hr x ng/mL				
geometric mean (geometric coefficient of variation)	3.983 (± 99999)	3.696 (± 99999)	4.607 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 1 - SAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 1 - SAD Cohorts

End point description:

Mean change from baseline in TTE parameter systolic ejection time (SET) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to the corresponding period.
Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose and at 3, 6, 9, and 24 hours post dose

End point values	SAD Cohorts <2000 ng/mL	SAD Cohorts ≥2000 ng/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	12		
Units: msec				
arithmetic mean (standard error)	8.04 (± 10.03)	36.3 (± 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 2 - SAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 2 - SAD Cohorts

End point description:

Mean change from baseline in TTE parameter left ventricular stroke volume (LVSV) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to the corresponding period.
Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose and at 3, 6, 9, and 24 hours post dose

End point values	SAD Cohorts <2000 ng/mL	SAD Cohorts ≥2000 ng/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	12		
Units: mL				
arithmetic mean (standard error)	1.01 (± 3.67)	9.01 (± 2.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 3 - SAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 3 - SAD Cohorts

End point description:

Mean change from baseline in TTE parameter left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to the corresponding period. Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose and at 3, 6, 9, and 24 hours post dose

End point values	SAD Cohorts <2000 ng/mL	SAD Cohorts ≥2000 ng/mL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	12		
Units: Percentage of blood pumped from LV				
arithmetic mean (standard error)				
LVEF	4.06 (± 2.27)	4.44 (± 1.86)		
LVFS	3.14 (± 1.36)	2.81 (± 1.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 1 - MAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 1 - MAD Cohorts

End point description:

Mean change from baseline in TTE parameter systolic ejection time (SET) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to first randomized dose.
Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose, and at 7 hours post dose on day 1,2,3, 4, 7, 9, 10, and 11

End point values	MAD Cohorts <2000 ng/mL	MAD Cohorts 2000-<3500 ng/mL	MAD Cohorts ≥3500 ng/mL	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26	13	
Units: msec				
arithmetic mean (standard error)	15.1 (± 3.51)	35.6 (± 3.78)	48.3 (± 4.68)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 2 - MAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 2 - MAD Cohorts

End point description:

Mean change from baseline in TTE parameter left ventricular stroke volume (LVSV) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to first randomized dose.
Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose, and at 7 hours post dose on day 1,2,3, 4, 7, 9, 10, and 11

End point values	MAD Cohorts <2000 ng/mL	MAD Cohorts 2000-<3500 ng/mL	MAD Cohorts ≥3500 ng/mL	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26	13	
Units: mL				
arithmetic mean (standard error)	3.126 (± 1.8348)	7.843 (± 1.9511)	5.685 (± 2.4988)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 3 - MAD Cohorts

End point title	Mean Change from Baseline in Transthoracic Echocardiogram (TTE) Parameter 3 - MAD Cohorts

End point description:

Mean change from baseline in TTE parameter left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) according to Danicamtiv plasma concentration ranges. Baseline is defined as the last non-missing value prior to first randomized dose.
Reporting arms are not mutually exclusive

End point type	Secondary

End point timeframe:

Baseline, predose, and at 7 hours post dose on day 1,2,3, 4, 7, 9, 10, and 11

End point values	MAD Cohorts <2000 ng/mL	MAD Cohorts 2000-<3500 ng/mL	MAD Cohorts ≥3500 ng/mL	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26	13	
Units: Percentage of blood pumped from LV				
arithmetic mean (standard error)				
LVEF	-0.25 (± 0.872)	1.12 (± 0.928)	2.29 (± 1.158)	
LVFS	0.46 (± 0.537)	0.78 (± 0.574)	0.51 (± 0.725)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events were monitored from first dose to 30 days post last dose (Up to 2 months). Participants were assessed for All-cause mortality from their date of randomization to study completion (Up to approximately 20 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	SAD Cohort 1 Danicamtiv 175mg

Reporting group description:

Participants received single dose of Danicamtiv 175mg in either period A, B, or C

Reporting group title	SAD Cohort 1 Danicamtiv 350mg

Reporting group description:

Participants received single dose of Danicamtiv 350mg in either period A, B, C, or D

Reporting group title	SAD Cohort 1 Placebo

Reporting group description:

Participants received single dose of Placebo in either period A, B, or C

Reporting group title	SAD Cohort 1 Danicamtiv Optional Period D

Reporting group description:

Participants received Danicamtiv at either 450mg, 525mg or 550mg in period D

Reporting group title	SAD Cohort 2 Danicamtiv 400mg

Reporting group description:

Participants received split dose of Danicamtiv 400mg

Reporting group title	SAD Cohort 2 Danicamtiv 500mg

Reporting group description:

Participants received split dose of Danicamtiv 500mg

Reporting group title	SAD Cohort 2 Placebo

Reporting group description:

Participants received single dose of Placebo

Reporting group title	MAD Cohort 1 Danicamtiv 75mg

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 2 Danicamtiv 50mg

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 50mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 1 Placebo

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 2 Placebo

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 3 Danicamtiv 75mg

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 75mg twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 4 Danicamtiv 100mg

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Danicamtiv 100mg (with food) twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 3 Placebo

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Reporting group title	MAD Cohort 4 Placebo

Reporting group description:

Participants received single-blinded placebo twice daily for 2 days. Participants then received double-blinded Placebo twice daily for 7 days, and 2 days of monitoring following the last dose before discharge

Serious adverse events	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (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	SAD Cohort 1 Danicamtiv Optional Period D	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (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	SAD Cohort 2 Placebo	MAD Cohort 1 Danicamtiv 75mg	MAD Cohort 2 Danicamtiv 50mg

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MAD Cohort 1 Placebo	MAD Cohort 2 Placebo	MAD Cohort 3 Danicamtiv 75mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (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	MAD Cohort 4 Danicamtiv 100mg	MAD Cohort 3 Placebo	MAD Cohort 4 Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (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

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

Non-serious adverse events	SAD Cohort 1 Danicamtiv 175mg	SAD Cohort 1 Danicamtiv 350mg	SAD Cohort 1 Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	5 / 8 (62.50%)	3 / 8 (37.50%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Application site erosion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Application site irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Infusion site discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infusion site erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac discomfort			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Diverticulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD Cohort 1 Danicamtiv Optional Period D	SAD Cohort 2 Danicamtiv 400mg	SAD Cohort 2 Danicamtiv 500mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	3 / 4 (75.00%)	0 / 4 (0.00%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Application site erosion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Application site irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SAD Cohort 2 Placebo	MAD Cohort 1 Danicamtiv 75mg	MAD Cohort 2 Danicamtiv 50mg
Total subjects affected by non-serious adverse events			

subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	7 / 9 (77.78%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Application site erosion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Application site irritation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Application site rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infusion site discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dry throat			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Cardiac discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Ventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	MAD Cohort 1 Placebo	MAD Cohort 2 Placebo	MAD Cohort 3 Danicamtiv 75mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	4 / 9 (44.44%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Application site erosion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Application site irritation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Infusion site discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Infusion site erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Dry throat			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Troponin increased			

subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Ventricular tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Back pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Bursitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Non-serious adverse events	MAD Cohort 4 Danicamtiv 100mg	MAD Cohort 3 Placebo	MAD Cohort 4 Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	0 / 2 (0.00%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

General disorders and administration site conditions			
Application site erosion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Application site irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Application site rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Troponin increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0

Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rash			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2018	Update inclusion/exclusion criteria and study design
11 July 2018	Update inclusion/exclusion criteria and study design
14 December 2018	Update exclusion/inclusion criteria and clarify study design
19 March 2019	Update inclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported