Clinical trial results:
A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Ranging,
Phase 2b Study of the Safety and Efficacy of Continuous 48-Hour Intravenous Infusions of
BMS-986231 in Hospitalized Patients with Heart Failure and Impaired Systolic Function

Summary

EudraCT number	2016-001685-29
Trial protocol	DE ES CZ NL GB GR IT
Global end of trial date	12 November 2019

Results information

Result version number	v1 (current)
This version publication date	25 November 2020
First version publication date	25 November 2020

Trial information

Trial identification

Sponsor protocol code	CV013-011

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	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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	13 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2019
Global end of trial reached?	Yes
Global end of trial date	12 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the effects of various doses of BMS-986231 compared to placebo on clinically relevant hypotension (defined by systolic blood pressure [SBP] < 90 mmHg or symptoms of hypotension).

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	13 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 58
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czechia: 53
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Greece: 44
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Poland: 42
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 52
Worldwide total number of subjects	329
EEA total number of subjects	194

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)	111
From 65 to 84 years	194
85 years and over	24

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

100 participants in Part I and 222 in Part II were randomized (322 total), of which 97 and 214, respectively, were treated (311 total). Reasons not treated, Part I: 3 other reasons. Reasons not treated, Part II: 2 no longer met study criteria; 1 adverse event (AE); 5 other reasons.
Also, 18 were randomized/treated in Part II Japan-specific cohort.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - Part I

Arm description:

Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

placebo-matching

Arm title	BMS-986231 - Part I

Arm description:

Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

BMS-986231 240 mg/vial; 3-to-6-to-12 µg/kg/min

Arm title	Placebo - Part II

Arm description:

Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours

Arm type	Placebo

Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: placebo-matching	
Arm title	BMS-986231 6 µg/kg/min - Part II
Arm description: BMS-986231 dose of 6 µg/kg/min for 48 hours	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: BMS-986231 240 mg/vial; 6 µg/kg/min	
Arm title	BMS-986231 12 µg/kg/min - Part II
Arm description: BMS-986231 dose of 12 µg/kg/min for 48 hours	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: BMS-986231 240 mg/vial; 12 µg/kg/min	
Arm title	Placebo - Part II (Japan cohort)
Arm description: Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: placebo-matching	
Arm title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Arm description: BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 6 µg/kg/min

Arm title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Arm description: BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 12 µg/kg/min

Number of subjects in period 1	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Started	48	49	71
Completed	48	48	70
Not completed	0	1	1
Adverse event, serious fatal	-	-	-
Participant withdrew consent	-	1	-
Participant refuses assessments	-	-	1

Number of subjects in period 1	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Started	71	72	6
Completed	71	70	6
Not completed	0	2	0
Adverse event, serious fatal	-	2	-
Participant withdrew consent	-	-	-
Participant refuses assessments	-	-	-

Number of subjects in period 1	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Started	6	6
Completed	6	6
Not completed	0	0
Adverse event, serious fatal	-	-
Participant withdrew consent	-	-
Participant refuses assessments	-	-

Period 2

Period 2 title	32-Day Follow-Up Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - Part I

Arm description:

Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

placebo-matching

Arm title	BMS-986231 - Part I

Arm description:

Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

BMS-986231 240 mg/vial; 3-to-6-to-12 µg/kg/min

Arm title	Placebo - Part II

Arm description:

Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

placebo-matching

Arm title	BMS-986231 6 µg/kg/min - Part II

Arm description:

BMS-986231 dose of 6 µg/kg/min for 48 hours

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 6 µg/kg/min

Arm title	BMS-986231 12 µg/kg/min - Part II

Arm description:
BMS-986231 dose of 12 µg/kg/min for 48 hours

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 12 µg/kg/min

Arm title	Placebo - Part II (Japan cohort)

Arm description:
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
placebo-matching

Arm title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)

Arm description:
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 6 µg/kg/min

Arm title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)

Arm description:
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 12 µg/kg/min

Number of subjects in period 2	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Started	48	48	70
Started initial treatment	48	49	71
Completed	44	47	62
Not completed	4	2	9
Adverse event, serious fatal	2	-	5
Participant refused to visit	-	1	2
Participant withdrew consent	-	-	-
withdrew from Day 5, D32 form not done	-	1	-
Family doctor OK'd participant, per call	-	-	1
Lost to follow-up	1	-	1
Poor/non-compliance	1	-	-
Joined	0	1	1
Period timeframe started at treatment	-	1	1

Number of subjects in period 2	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Started	71	70	6
Started initial treatment	71	72	6
Completed	63	64	6
Not completed	8	8	0
Adverse event, serious fatal	6	3	-
Participant refused to visit	-	2	-
Participant withdrew consent	-	2	-
withdrew from Day 5, D32 form not done	-	-	-
Family doctor OK'd participant, per call	-	-	-
Lost to follow-up	1	-	-
Poor/non-compliance	1	1	-
Joined	0	2	0
Period timeframe started at treatment	-	2	-

Number of subjects in period 2	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Started	6	6
Started initial treatment	6	6
Completed	5	6
Not completed	1	0
Adverse event, serious fatal	-	-
Participant refused to visit	-	-
Participant withdrew consent	1	-
withdrew from Day 5, D32 form not done	-	-
Family doctor OK'd participant, per call	-	-
Lost to follow-up	-	-
Poor/non-compliance	-	-
Joined	0	0
Period timeframe started at treatment	-	-

Period 3

Period 3 title	182-Day Follow-Up Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - Part I

Arm description:

Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

placebo-matching

Arm title	BMS-986231 - Part I

Arm description:

Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)

Arm type	Experimental

Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 3-to-6-to-12 µg/kg/min

Arm title	Placebo - Part II

Arm description:
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
placebo-matching

Arm title	BMS-986231 6 µg/kg/min - Part II

Arm description:
BMS-986231 dose of 6 µg/kg/min for 48 hours

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 6 µg/kg/min

Arm title	BMS-986231 12 µg/kg/min - Part II

Arm description:
BMS-986231 dose of 12 µg/kg/min for 48 hours

Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:
BMS-986231 240 mg/vial; 12 µg/kg/min

Arm title	Placebo - Part II (Japan cohort)

Arm description:
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants

Arm type	Placebo
Investigational medicinal product name	Placebo-matching BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details: placebo-matching	

Arm title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Arm description: BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: BMS-986231 240 mg/vial; 6 µg/kg/min	
Arm title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Arm description: BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	
Arm type	Experimental
Investigational medicinal product name	BMS-986231
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details: BMS-986231 240 mg/vial; 12 µg/kg/min	

Number of subjects in period 3	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Started	44	47	62
Started initial treatment	48	49	71
Completed	44	45	60
Not completed	4	4	11
Adverse event, serious fatal	3	3	11
Participant withdrew consent	-	-	-
Alive, per civil unit	-	-	-
Alive, per national insurance system	1	-	-
withdrew from D5, D32/182 forms not done	-	1	-
No cont D182 FU, Sponsor admin reason	-	-	-
Alive, per Family doctor	-	-	-
Vital status collected via EMR	-	-	-
Joined	4	2	9

Period timeframe started at treatment	4	2	9

Number of subjects in period 3	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Started	63	64	6
Started initial treatment	71	72	6
Completed	58	60	1
Not completed	13	12	5
Adverse event, serious fatal	12	9	-
Participant withdrew consent	-	1	-
Alive, per civil unit	-	1	-
Alive, per national insurance system	-	-	-
withdrew from D5, D32/182 forms not done	-	-	-
No cont D182 FU, Sponsor admin reason	-	-	5
Alive, per Family doctor	-	1	-
Vital status collected via EMR	1	-	-
Joined	8	8	0
Period timeframe started at treatment	8	8	-

Number of subjects in period 3	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Started	5	6
Started initial treatment	6	6
Completed	2	1
Not completed	4	5
Adverse event, serious fatal	-	1
Participant withdrew consent	1	-
Alive, per civil unit	-	-
Alive, per national insurance system	-	-
withdrew from D5, D32/182 forms not done	-	-
No cont D182 FU, Sponsor admin reason	3	4
Alive, per Family doctor	-	-
Vital status collected via EMR	-	-
Joined	1	0
Period timeframe started at treatment	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo - Part I
Reporting group description:	
Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	BMS-986231 - Part I
Reporting group description:	
Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	Placebo - Part II
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 6 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 12 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours	
Reporting group title	Placebo - Part II (Japan cohort)
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	

Reporting group values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Number of subjects	48	49	71
Age Categorical			
Age categorical			
Units: Participants			
< 65 years	17	24	21
65 -to <=75 years	22	15	36
>75 years	9	10	14
Age Continuous			
Units: Years			
arithmetic mean	66.0	64.6	67.3
standard deviation	± 12.23	± 12.23	± 11.52
Sex: Female, Male			
Units: Participants			
Female	8	10	18
Male	40	39	53
Race/Ethnicity, Customized			
Race			
Units: Subjects			

White	35	37	63
Black or African American	11	11	4
Asian	0	0	2
Other	2	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	9
Not Hispanic or Latino	44	45	18
Unknown or Not Reported	4	3	44

Reporting group values	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Number of subjects	71	72	6
Age Categorical			
Age categorical			
Units: Participants			
< 65 years	23	19	3
65 -to <=75 years	26	30	0
>75 years	22	23	3
Age Continuous Units: Years			
arithmetic mean	69.2	70.0	65.3
standard deviation	± 11.41	± 11.52	± 17.88
Sex: Female, Male Units: Participants			
Female	20	15	0
Male	51	57	6
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	62	66	0
Black or African American	7	4	0
Asian	2	2	6
Other	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11	11	0
Not Hispanic or Latino	23	20	0
Unknown or Not Reported	37	41	6

Reporting group values	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	Total
Number of subjects	6	6	329
Age Categorical			
Age categorical			
Units: Participants			
< 65 years	3	1	111
65 -to <=75 years	1	2	132
>75 years	2	3	86

Age Continuous Units: Years			
arithmetic mean	69.5	76.7	
standard deviation	± 13.31	± 10.48	-
Sex: Female, Male Units: Participants			
Female	1	2	74
Male	5	4	255
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	0	0	263
Black or African American	0	0	37
Asian	6	6	24
Other	0	0	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	32
Not Hispanic or Latino	0	0	150
Unknown or Not Reported	6	6	147

End points

End points reporting groups

Reporting group title	Placebo - Part I
Reporting group description:	
Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	BMS-986231 - Part I
Reporting group description:	
Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	Placebo - Part II
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 6 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 12 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours	
Reporting group title	Placebo - Part II (Japan cohort)
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	Placebo - Part I
Reporting group description:	
Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	BMS-986231 - Part I
Reporting group description:	
Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	Placebo - Part II
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 6 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 12 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours	
Reporting group title	Placebo - Part II (Japan cohort)
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	

Reporting group title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	Placebo - Part I
Reporting group description:	
Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	BMS-986231 - Part I
Reporting group description:	
Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	Placebo - Part II
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 6 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 12 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours	
Reporting group title	Placebo - Part II (Japan cohort)
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	

Primary: Percentage of participants with clinically relevant hypotension up to 6 hours after the end of study drug infusion

End point title	Percentage of participants with clinically relevant hypotension up to 6 hours after the end of study drug infusion
End point description:	
Percentage of participants with clinically relevant hypotension, defined by systolic blood pressure (SBP) < 90 mm Hg (confirmed by a repeated value < 90 mm Hg) or symptoms of hypotension, up to 6 hours after the end of study drug infusion	
End point type	Primary
End point timeframe:	
From start of infusion up to 6 hours post end of infusion	

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Percentage of participants				
number (confidence interval 95%)				

clinically relevant hypotension	8.3 (2.32 to 19.98)	20.4 (10.24 to 34.34)	18.3 (10.13 to 29.27)	21.1 (12.33 to 32.44)
symptoms of hypotension	2.1 (0.05 to 11.07)	6.1 (1.28 to 16.87)	1.4 (0.04 to 7.60)	2.8 (0.34 to 9.81)
confirmed SBP < 90 mmHg	6.3 (1.31 to 17.20)	20.4 (10.24 to 34.34)	18.3 (10.13 to 29.27)	21.1 (12.33 to 32.44)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Percentage of participants				
number (confidence interval 95%)				
clinically relevant hypotension	34.7 (23.88 to 46.86)	0 (0.00 to 45.93)	33.3 (4.33 to 77.72)	50.0 (11.81 to 88.19)
symptoms of hypotension	8.3 (3.12 to 17.26)	0 (0.00 to 45.93)	0 (0.00 to 45.93)	0 (0.00 to 45.93)
confirmed SBP < 90 mmHg	29.2 (19.05 to 41.07)	0 (0.00 to 45.93)	33.3 (4.33 to 77.72)	50.0 (11.81 to 88.19)

Statistical analyses

Statistical analysis title	Part I, clinically relevant hypotension - risk
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	2.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	14.53

Statistical analysis title	Part I, clinically relevant hypotension - diff.
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.28

Statistical analysis title	Part I, symptoms of hypotension - risk
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	75.47

Statistical analysis title	Part I, symptoms of hypotension - diff.
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.15

Statistical analysis title	Part I, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	14.66

Statistical analysis title	Part I, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.29

Statistical analysis title	Part II-low, clinically relevant hypotension, risk
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.43

Statistical analysis title	Part II-low, clinically relevant hypotension, diff
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.16

Statistical analysis title	Part II-low, symptoms of hypotension - risk

Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	54.35

Statistical analysis title	Part II-low, symptoms of hypotension - diff.
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.09

Statistical analysis title	Part II-low, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.43

Statistical analysis title	Part II-low, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.16

Statistical analysis title	PartII-high, clinically relevant hypotension, risk
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	3.59

Statistical analysis title	PartII-high, clinically relevant hypotension, diff
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.31

Statistical analysis title	Part II-high, symptoms of hypotension - risk
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	5.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	149.72

Statistical analysis title	Part II-high, symptoms of hypotension - diff.
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.16

Statistical analysis title	Part II-high, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	3.21

Statistical analysis title	Part II-high, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.25

Statistical analysis title	Part II J-low, clinically relevant hyp. - diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.78

Statistical analysis title	Part II J-low, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.78

Statistical analysis title	Part II J-high, clinically relevant hyp. - diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 12 µg/kg/min - Part II (Japan cohort)

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.88

Statistical analysis title	Part II J-high, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.88

Secondary: Change in NT-proBNP from baseline to Hour 24, 48, 72, 120 or discharge (whichever comes first), and at Day 32

End point title	Change in NT-proBNP from baseline to Hour 24, 48, 72, 120 or discharge (whichever comes first), and at Day 32

End point description:

Assess the effect of BMS-986231 on NT-proBNP (N-terminal prohormone of brain natriuretic peptide)

End point type	Secondary

End point timeframe:

0, 24, 48, 72, 120 hour or discharge; Day 32

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: pmol/L				
arithmetic mean (standard deviation)				
24 hour	-270.88 (± 400.320)	-364.46 (± 456.158)	-147.96 (± 452.239)	-340.74 (± 430.639)
48 hour	-405.06 (± 591.711)	-510.51 (± 592.734)	-210.87 (± 580.487)	-300.87 (± 725.268)

72 hour	-396.21 (± 675.761)	-373.86 (± 702.530)	-249.26 (± 655.999)	-118.86 (± 900.798)
120 hour	-541.36 (± 773.006)	-409.53 (± 751.624)	-140.60 (± 1358.127)	-76.20 (± 993.110)
Day 32	-202.07 (± 799.169)	-91.61 (± 2254.397)	-321.73 (± 600.297)	-361.73 (± 782.881)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: pmol/L				
arithmetic mean (standard deviation)				
24 hour	-416.91 (± 503.825)	-129.70 (± 255.716)	-165.93 (± 185.910)	-397.60 (± 330.721)
48 hour	-472.32 (± 610.590)	-329.24 (± 646.985)	-251.73 (± 243.794)	-497.35 (± 725.286)
72 hour	-293.94 (± 685.681)	-433.08 (± 761.573)	9.89 (± 523.754)	-229.56 (± 809.850)
120 hour	-390.21 (± 717.114)	-434.36 (± 659.528)	-379.06 (± 244.917)	-552.55 (± 824.009)
Day 32	-476.86 (± 716.072)	-556.69 (± 1288.342)	-343.64 (± 377.590)	-706.11 (± 1111.877)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in participant-reported resting dyspnea from baseline through Hour 72

End point title	Change in participant-reported resting dyspnea from baseline through Hour 72

End point description:

Endpoint was measured by the area under the curve (AUC) of the 11-point Numerical Rating Scale (NRS) obtained at baseline, and Hours 6, 12, 24, 48, and 72.

Participants were asked to report their absolute current severity of dyspnea on an 11-point numerical rating scale (NRS; range 0 to 10).

The numerical rating scale (NRS) was used to assess the degree of dyspnea (breathlessness), measured using an 11-point scale provided by the Sponsor.

A score of 0 represents "I am not breathless at all" and 10 represents "I am the most breathless I can possibly imagine".

End point type	Secondary

End point timeframe:

Hours 6, 12, 24, 48, and 72

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Scores on a scale				
arithmetic mean (standard deviation)				
6 hour	-1.5 (± 1.84)	-1.5 (± 1.64)	-1.1 (± 1.90)	-1.7 (± 1.94)
12 hour	-2.1 (± 2.38)	-2.2 (± 1.73)	-1.7 (± 2.75)	-2.4 (± 2.38)
24 hour	-2.0 (± 2.50)	-2.1 (± 2.19)	-2.1 (± 2.82)	-2.9 (± 2.68)
48 hour	-2.8 (± 2.15)	-2.6 (± 2.51)	-2.8 (± 3.00)	-3.4 (± 2.44)
72 hour	-2.9 (± 2.23)	-3.7 (± 2.22)	-3.2 (± 3.19)	-3.9 (± 2.28)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Scores on a scale				
arithmetic mean (standard deviation)				
6 hour	-1.7 (± 2.13)	-0.3 (± 1.03)	0.0 (± 2.90)	-1.3 (± 3.44)
12 hour	-2.0 (± 2.49)	-1.0 (± 1.79)	-0.2 (± 3.37)	-1.4 (± 4.22)
24 hour	-2.2 (± 2.42)	-0.8 (± 1.72)	-1.5 (± 3.02)	-1.2 (± 2.14)
48 hour	-2.8 (± 2.45)	-1.2 (± 1.47)	-0.8 (± 3.43)	-2.0 (± 1.67)
72 hour	-3.2 (± 2.73)	-1.2 (± 2.14)	-1.2 (± 3.19)	-2.0 (± 2.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with symptomatic hypotension up to 6 hours after the end of study drug infusion

End point title	Percentage of participants with symptomatic hypotension up to 6 hours after the end of study drug infusion

End point description:

The percentage of participants experiencing symptoms of hypotension up to 6 hours post-treatment was reported for each arm.

End point type	Secondary

End point timeframe:

From start of infusion up to 6 hours post end of infusion

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Percentage of participants				
number (confidence interval 95%)	2.1 (0.05 to 11.07)	6.1 (1.28 to 16.87)	1.4 (0.04 to 7.60)	2.8 (0.34 to 9.81)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Percentage of participants				
number (confidence interval 95%)	8.3 (3.12 to 17.26)	0 (0.00 to 45.93)	0 (0.00 to 45.93)	0 (0.00 to 45.93)

Statistical analyses

Statistical analysis title	Part I, symptoms of hypotension - risk
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	75.47

Statistical analysis title	Part I, symptoms of hypotension - diff.
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.15

Statistical analysis title	Part II-low, symptoms of hypotension - risk
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	54.35

Statistical analysis title	Part II-low, symptoms of hypotension - diff.
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.09

Statistical analysis title	Part II-high, symptoms of hypotension - risk
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	5.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	149.72

Statistical analysis title	Part II-high, symptoms of hypotension - diff.

Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.16

Secondary: Percentage of participants with SBP < 90 mm Hg (confirmed by a repeated value)

End point title	Percentage of participants with SBP < 90 mm Hg (confirmed by a repeated value)

End point description:

The percentage of participants experiencing SBP < 90 mm Hg (confirmed by a repeated value) up to 6 hours post-treatment was reported for each arm.

End point type	Secondary

End point timeframe:

From start of infusion up to 6 hours post end of infusion

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Percentage of participants				
number (confidence interval 95%)	6.3 (1.31 to 17.20)	20.4 (10.24 to 34.34)	18.3 (10.13 to 29.27)	21.1 (12.33 to 32.44)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Percentage of participants				
number (confidence interval 95%)	29.2 (19.05 to 41.07)	0 (0.00 to 45.93)	33.3 (4.33 to 77.72)	50.0 (11.81 to 88.19)

Statistical analyses

Statistical analysis title	Part I, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	14.66

Statistical analysis title	Part I, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part I v BMS-986231 - Part I
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.29

Statistical analysis title	Part II-low, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.43

Statistical analysis title	Part II-low, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II v BMS-986231 6 µg/kg/min - Part II

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.16

Statistical analysis title	Part II-high, confirmed SBP < 90 mmHg - risk
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative risk from placebo
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	3.21

Statistical analysis title	Part II-high, confirmed SBP < 90 mmHg - diff.
Comparison groups	Placebo - Part II v BMS-986231 12 µg/kg/min - Part II
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.25

Statistical analysis title	Part II J-low, confirmed SBP < 90 mmHg, diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 6 µg/kg/min - Part II (Japan cohort)

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.78

Statistical analysis title	Part II J-high, confirmed SBP < 90 mmHg, diff.
Comparison groups	Placebo - Part II (Japan cohort) v BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Relative difference from placebo
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.88

Secondary: Number of participants with a Serious Adverse Events (SAE) assessed up to Day 32

End point title	Number of participants with a Serious Adverse Events (SAE) assessed up to Day 32

End point description:

Number of participants who experienced an in-study SAE.

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0
Included serious adverse events with onset time from the start of study treatment, up to and including 32 days after the start of study treatment.

End point type	Secondary

End point timeframe:

32 days

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants	11	14	23	15

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants	15	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued due to hypotension

End point title	Number of participants who discontinued due to hypotension

End point description:

Number of participants who discontinued study treatment due to hypotension.

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

Included nonserious adverse events with onset time from the start of study treatment, up to and including 120 hours after the start of study treatment and serious adverse events with onset time from the start of study treatment, up to and including 32 days after the start of study treatment.

Hypotension defined as systolic blood pressure (SBP) < 90 mmHg.

End point type	Secondary

End point timeframe:

up to 120 hours (for AEs); up to 32 days (for SAEs)

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants	4	8	7	13

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants	16	0	1	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued, experienced a down-titration or dose interruption due to decreased blood pressure

End point title	Number of participants who discontinued, experienced a down-titration or dose interruption due to decreased blood pressure

End point description:

Number of participants who discontinued study treatment, experienced a down-titration (dose reduction) or dose interruption due to decreased blood pressure/hypotension are reported below.

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

Included nonserious adverse events with onset time from the start of study treatment, up to and including 120 hours after the start of study treatment and serious adverse events with onset time from the start of study treatment, up to and including 32 days after the start of study treatment.

If the participant experienced systolic blood pressure (SBP) < 95 mm Hg, without symptoms related to hypotension, the measurement was repeated within 15 minutes. If the SBP remained < 95 mm Hg, the dose reduction occurred.

End point type	Secondary

End point timeframe:

up to 120 hours (for AEs); up to 32 days (for SAEs)

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants				
discontinuation	4	8	7	13
down-titration	3	9	9	10
interruption	3	4	4	12

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants				
discontinuation	15	0	1	3
down-titration	25	0	1	3
interruption	13	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with an Adverse Event (AE) assessed up to 120 hours

End point title	Number of participants with an Adverse Event (AE) assessed up to 120 hours

End point description:

Number of participants who experienced an in-study AE.

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

Included nonserious adverse events with onset time from the start of study treatment, up to and including 120 hours after the start of study treatment.

End point type	Secondary

End point timeframe:

up to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants	31	39	48	48

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants	55	2	6	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who died (all- cause and Cardiovascular-related) through Day 182

End point title	Number of participants who died (all- cause and

	Cardiovascular-related) through Day 182

End point description:

Number of participants who died (all- cause and CV related) through Day 182.

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

CV=Cardiovascular

End point type	Secondary

End point timeframe:

through 182 days

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants				
number (confidence interval 95%)				
All-cause	3 (1.31 to 17.20)	3 (1.28 to 16.87)	11 (8.00 to 26.03)	12 (9.05 to 27.66)
CV-related	3 (1.31 to 17.20)	2 (0.50 to 13.98)	9 (5.96 to 22.70)	10 (6.97 to 24.38)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants				
number (confidence interval 95%)				
All-cause	9 (5.88 to 22.41)	0 (0.00 to 45.93)	0 (0.00 to 45.93)	1 (0.42 to 64.12)
CV-related	4 (1.53 to 13.62)	0 (0.00 to 45.93)	0 (0.00 to 45.93)	0 (0.00 to 45.93)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Troponin T from baseline to Hour 24, 48, and 72

End point title	Change in Troponin T from baseline to Hour 24, 48, and 72

End point description:

Baseline = Last non-missing result with a collection date-time less than or on the date-time of the start of infusion of study drug

End point type	Secondary

End point timeframe:

from baseline to Hour 24, 48, and 72

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: ng/L				
arithmetic mean (standard deviation)				
24 hour	4.11 (± 27.303)	-1.31 (± 12.278)	-1.80 (± 11.266)	-3.45 (± 20.030)
48 hour	-0.93 (± 22.714)	14.56 (± 81.979)	-2.88 (± 16.424)	8.08 (± 71.672)
72 hour	6.07 (± 30.033)	6.76 (± 66.673)	-1.44 (± 16.472)	5.00 (± 65.766)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: ng/L				
arithmetic mean (standard deviation)				
24 hour	-8.09 (± 37.864)	-4.67 (± 3.983)	1.33 (± 5.750)	-7.67 (± 16.669)
48 hour	-11.15 (± 45.495)	-10.67 (± 10.633)	49.50 (± 118.417)	-8.40 (± 25.501)
72 hour	-13.05 (± 68.276)	-10.50 (± 12.145)	248.00 (± 433.581)	-15.00 (± 25.169)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Hematology

End point title	Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Hematology

End point description:

Number of participants who experienced an in-study Hematology marked laboratory abnormality (reported in > 5% of total participants).

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants				
high leukocyte counts	5	2	5	4
low hemoglobin values	4	5	5	6
low platelet values	4	2	2	7
low neutrophils values	0	1	1	1
low leukocyte counts	0	1	2	0
low hematocrit values	1	1	1	3
low erythrocytes values	1	1	1	3

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants				
high leukocyte counts	3	0	0	0
low hemoglobin values	4	1	1	0
low platelet values	1	0	0	0
low neutrophils values	0	0	0	0
low leukocyte counts	0	0	0	0
low hematocrit values	0	0	0	0
low erythrocytes values	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Chemistry

End point title	Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Chemistry

End point description:

Number of participants who experienced an in-study Chemistry marked laboratory abnormality (reported in > 5% of total participants).

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants				
high blood urea nitrogen values	23	16	23	23
high urate values	10	15	10	20
high potassium values	2	5	6	7
high alanine aminotransferase (ALT) values	6	1	5	2
high alkaline phosphatase values	5	0	2	0
low protein values	3	9	3	8
high asparate aminotransferase values	4	0	4	2
high bilirubin values	2	2	0	0
high bicarbonate values	1	2	0	0
low chloride counts	1	2	1	4
high creatine kinase values	0	1	0	0
high protein values	1	0	2	0
high sodium values	0	1	2	0
low bicarbonate values	0	0	2	1
low sodium values	0	0	0	2
low albumin values	0	0	0	1
low calcium values	0	0	2	1

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants				
high blood urea nitrogen values	18	0	1	2
high urate values	8	0	1	1
high potassium values	2	0	1	0
high alanine aminotransferase (ALT) values	2	0	0	0
high alkaline phosphatase values	1	0	0	0
low protein values	4	0	1	0
high asparate aminotransferase values	1	0	0	0
high bilirubin values	0	0	1	0
high bicarbonate values	0	0	0	0
low chloride counts	1	0	0	0
high creatine kinase values	0	0	0	0
high protein values	2	0	0	0
high sodium values	0	0	0	0
low bicarbonate values	1	0	0	0

low sodium values	0	0	0	0
low albumin values	2	0	0	0
low calcium values	2	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Urinalysis

End point title	Number of participants with Marked Laboratory Abnormality assessed to 120 hours - Urinalysis

End point description:

Number of participants who experienced an in-study Urinalysis marked laboratory abnormality (reported in > 5% of total participants).

Medical Dictionary for Regulatory Activities (MedDRA) version: 22.0

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Participants				
high protein values	10	11	16	13
high erythrocyte values	1	1	1	3
high leukocytes values	0	1	0	2

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Participants				
high protein values	17	2	2	2
high erythrocyte values	2	0	0	0
high leukocytes values	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Vital Signs from baseline to 120 hours - blood pressure

End point title	Change in Vital Signs from baseline to 120 hours - blood pressure

End point description:

The change in baseline for vital signs was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	26	50	48
Units: mmHg				
arithmetic mean (standard deviation)				
systolic blood pressure, mmHg	-6.8 (± 16.60)	0.0 (± 17.75)	-4.3 (± 15.23)	-7.9 (± 15.60)
diastolic blood pressure, mmHg	-4.0 (± 12.67)	-1.9 (± 13.53)	-4.4 (± 12.99)	-3.4 (± 14.37)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	6	6	6
Units: mmHg				
arithmetic mean (standard deviation)				
systolic blood pressure, mmHg	-8.8 (± 14.01)	-10.3 (± 15.60)	-17.5 (± 9.14)	-6.2 (± 16.44)
diastolic blood pressure, mmHg	-1.6 (± 10.83)	1.7 (± 16.24)	-15.7 (± 19.08)	-9.3 (± 14.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Vital Signs from baseline to 120 hours - heart rate

End point title	Change in Vital Signs from baseline to 120 hours - heart rate

End point description:

The change in baseline for vital signs was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: beats/min				
arithmetic mean (standard deviation)	-1.8 (± 15.53)	-9.1 (± 17.13)	-8.3 (± 15.55)	-4.6 (± 15.40)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: beats/min				
arithmetic mean (standard deviation)	-6.3 (± 15.60)	-6.7 (± 21.88)	-3.0 (± 13.31)	3.8 (± 11.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Vital Signs from baseline to 120 hours - respiratory rate

End point title	Change in Vital Signs from baseline to 120 hours - respiratory rate
End point description: The change in baseline for vital signs was reported for each arm.	
End point type	Secondary
End point timeframe: to 120 hours	

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: breaths/min				
arithmetic mean (standard deviation)	-2.6 (± 3.93)	-3.0 (± 4.82)	-2.9 (± 3.80)	-2.6 (± 4.33)

End point values	BMS-986231 12 µg/kg/min -	Placebo - Part II (Japan	BMS-986231 6 µg/kg/min -	BMS-986231 12 µg/kg/min -

	Part II	cohort)	Part II (Japan cohort)	Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: breaths/min				
arithmetic mean (standard deviation)	-1.8 (± 3.96)	-2.3 (± 2.88)	0.0 (± 9.98)	-1.4 (± 3.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Vital Signs from baseline to 120 hours - temperature

End point title	Change in Vital Signs from baseline to 120 hours - temperature

End point description:

The change in baseline for vital signs was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: Celsius (C)				
arithmetic mean (standard deviation)	-0.04 (± 0.643)	0.09 (± 0.649)	0.04 (± 0.427)	0.00 (± 0.342)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: Celsius (C)				
arithmetic mean (standard deviation)	-0.05 (± 0.481)	-0.47 (± 0.650)	-0.27 (± 0.535)	0.44 (± 0.541)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Electrocardiograms (ECGs) from baseline to 120 hours - mean heart rate

End point title	Change in Electrocardiograms (ECGs) from baseline to 120 hours - mean heart rate

End point description:

The change in baseline for ECGs was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: beats/min				
arithmetic mean (standard deviation)	-5.3 (± 9.36)	-6.8 (± 21.31)	-7.1 (± 17.46)	-5.1 (± 18.64)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	5	6	6
Units: beats/min				
arithmetic mean (standard deviation)	-6.1 (± 17.33)	2.0 (± 10.72)	-13.0 (± 12.62)	-5.2 (± 14.85)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Electrocardiograms (ECGs) from baseline to 120 hours - PR, QT, QTcF Intervals and QRS Duration

End point title	Change in Electrocardiograms (ECGs) from baseline to 120 hours - PR, QT, QTcF Intervals and QRS Duration

End point description:

The change in baseline for ECGs was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: msec				
arithmetic mean (standard deviation)				
PR Interval, Aggregate, msec	-17.4 (± 66.31)	-2.3 (± 32.11)	-0.1 (± 23.49)	10.9 (± 22.02)
QRS Duration, Aggregate, msec	5.1 (± 22.19)	-0.1 (± 12.46)	1.6 (± 20.29)	-1.6 (± 13.22)
QT Interval, Aggregate, msec	-10.6 (± 49.20)	7.2 (± 48.25)	8.7 (± 53.17)	5.8 (± 42.19)
QTcF Interval, Aggregate, msec	-27.5 (± 41.79)	-13.9 (± 41.56)	-4.0 (± 51.04)	-4.0 (± 33.59)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: msec				
arithmetic mean (standard deviation)				
PR Interval, Aggregate, msec	2.0 (± 25.41)	-1.5 (± 16.50)	10.4 (± 26.32)	6.0 (± 30.10)
QRS Duration, Aggregate, msec	2.7 (± 16.77)	-3.0 (± 4.80)	-2.5 (± 7.20)	3.0 (± 4.38)
QT Interval, Aggregate, msec	-0.3 (± 45.39)	-30.0 (± 28.17)	5.7 (± 24.41)	16.5 (± 50.22)
QTcF Interval, Aggregate, msec	-10.3 (± 37.63)	-24.8 (± 20.00)	-8.8 (± 22.35)	3.2 (± 22.93)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in physical measurements from baseline to 120 hours

End point title	Change in physical measurements from baseline to 120 hours

End point description:

The change in baseline for physical measurements was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: kg				
arithmetic mean (standard deviation)	0.00 (± 0383)	0.10 (± 0.285)	-2.87 (± 4.447)	-2.96 (± 4.231)

End point values	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	6	6	6
Units: kg				
arithmetic mean (standard deviation)	-1.83 (± 5.295)	-3.58 (± 2.182)	-3.97 (± 2.160)	-6.08 (± 4.009)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - x10^9 cells/L

End point title	Change in laboratory assessments from baseline to 120 hours - x10^9 cells/L[1]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	23	41	36
Units: x10^9 cells/L				
arithmetic mean (standard deviation)				
leukocyte, x10^9 c/L	0.12 (± 3.078)	-1.38 (± 1.892)	-0.20 (± 4.370)	0.20 (± 2.549)
platelet, x10^9 c/L	5.63 (± 31.679)	-5.77 (± 34.666)	1.84 (± 40.808)	3.26 (± 37.888)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: x10^9 cells/L				
arithmetic mean (standard deviation)				
leukocyte, x10^9 c/L	-0.09 (± 1.980)			
platelet, x10^9 c/L	1.26 (± 31.135)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - g/L

End point title	Change in laboratory assessments from baseline to 120 hours - g/L[2]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	23	46	42
Units: g/L				
arithmetic mean (standard deviation)				
hemoglobin, g/L	-0.67 (± 11.851)	-0.70 (± 8.573)	1.20 (± 11.487)	0.94 (± 11.684)
protein, g/L	1.10 (± 6.172)	2.77 (± 5.839)	0.57 (± 8.178)	0.38 (± 6.048)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: g/L				

arithmetic mean (standard deviation)				
hemoglobin, g/L	1.38 (± 9.161)			
protein, g/L	-0.05 (± 5.367)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - mmol/L

End point title	Change in laboratory assessments from baseline to 120 hours - mmol/L[3]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: mmol/L				
arithmetic mean (standard deviation)				
blood urea nitrogen, mmol/L	4.01 (± 5.474)	0.32 (± 3.164)	1.96 (± 3.920)	2.15 (± 5.016)
urate, mmol/L	0.06 (± 0.154)	0.01 (± 0.108)	-0.01 (± 0.126)	0.04 (± 0.147)
potassium, mmol/L	0.19 (± 0.697)	0.28 (± 0.513)	0.21 (± 0.692)	0.13 (± 0.558)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: mmol/L				
arithmetic mean (standard deviation)				
blood urea nitrogen, mmol/L	1.24 (± 3.655)			
urate, mmol/L	-0.03 (± 0.111)			
potassium, mmol/L	0.15 (± 0.651)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - U/L

End point title	Change in laboratory assessments from baseline to 120 hours - U/L[4]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: U/L				
arithmetic mean (standard deviation)				
alanine aminotransferase (ALT), U/L	148.13 (± 837.833)	-2.73 (± 11.089)	-3.22 (± 102.038)	30.36 (± 189.310)
alkaline phosphatase, U/L	-1.00 (± 28.018)	1.65 (± 11.052)	-1.31 (± 25.186)	5.43 (± 26.007)
asparate aminotransferase, U/L	214.77 (± 1204.410)	-2.77 (± 10.277)	-11.15 (± 127.903)	10.81 (± 65.009)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: U/L				
arithmetic mean (standard deviation)				
alanine aminotransferase (ALT), U/L	-13.07 (± 76.357)			
alkaline phosphatase, U/L	-0.49 (± 21.474)			
asparate aminotransferase, U/L	-10.00 (± 52.075)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - mg/dL

End point title	Change in laboratory assessments from baseline to 120 hours -

	mg/dL[5]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

Note: 9999 = NA, not available, 120 hour data not collected

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: mg/dL				
arithmetic mean (standard deviation)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: mg/dL				
arithmetic mean (standard deviation)	9999 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours - x10^12 c/L

End point title	Change in laboratory assessments from baseline to 120 hours - x10^12 c/L[6]

End point description:

The change in baseline for laboratory assessments was reported for each arm.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Lab assessments for Japan-cohort reported separately from this endpoint

End point values	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II	BMS-986231 6 µg/kg/min - Part II
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	49	71	71
Units: x10^12 c/L				
arithmetic mean (standard deviation)	-0.02 (± 0.394)	0.02 (± 0.305)	0.04 (± 0.409)	0.04 (± 0.481)

End point values	BMS-986231 12 µg/kg/min - Part II			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: x10^12 c/L				
arithmetic mean (standard deviation)	0.09 (± 0.337)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Protein (nmol/L)

End point title	Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Protein (nmol/L)[7]

End point description:

The change in baseline for laboratory assessments was reported for each arm of the Japan cohort only.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting of lab assessments for this endpoint is in regards to Japan-cohort only

End point values	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	5	
Units: nmol/L				
arithmetic mean (standard deviation)	79.38 (± 192.568)	74.13 (± 110.919)	131.64 (± 407.611)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Creatinine (µmol/L)

End point title	Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Creatinine (µmol/L)[8]

End point description:

The change in baseline for laboratory assessments was reported for each arm of the Japan cohort only.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting of lab assessments for this endpoint is in regards to Japan-cohort only

End point values	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	5	
Units: µmol/L				
arithmetic mean (standard deviation)	4.33 (± 17.728)	-1.50 (± 6.775)	12.40 (± 23.891)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Cystatin (mg/L)

End point title	Change in laboratory assessments from baseline to 120 hours, Japan cohort only - Cystatin (mg/L)[9]

End point description:

The change in baseline for laboratory assessments was reported for each arm of the Japan cohort only.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting of lab assessments for this endpoint is in regards to Japan-cohort only

End point values	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	5	
Units: mg/L				
arithmetic mean (standard deviation)	0.18 (± 0.268)	0.17 (± 0.150)	0.25 (± 0.077)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours, Japan cohort only - percentage Fractional Potassium Excretion

End point title	Change in laboratory assessments from baseline to 120 hours, Japan cohort only - percentage Fractional Potassium Excretion[10]

End point description:

The change in baseline for laboratory assessments was reported for each arm of the Japan cohort only.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Reporting of lab assessments for this endpoint is in regards to Japan-cohort only

End point values	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: Fractional Potassium Excretion percent				
arithmetic mean (standard deviation)	4.88 (± 8.009)	-1.22 (± 4.926)	-12.34 (± 13.316)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in laboratory assessments from baseline to 120 hours, Japan cohort only - percentage Fractional Sodium Excretion

End point title	Change in laboratory assessments from baseline to 120 hours, Japan cohort only - percentage Fractional Sodium Excretion[11]

End point description:

The change in baseline for laboratory assessments was reported for each arm of the Japan cohort only.

End point type	Secondary

End point timeframe:

to 120 hours

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Reporting of lab assessments for this endpoint is in regards to Japan-cohort only

End point values	Placebo - Part II (Japan cohort)	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	5	
Units: Fractional Sodium Excretion percent				
arithmetic mean (standard deviation)	0.02 (± 2.076)	-2.62 (± 4.538)	-5.50 (± 7.984)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs from treatment, up to and including 120 hours after treatment and serious AEs from treatment, up to and including 32 days after treatment.

Mortality data reported through 182 days post-treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo - Part I
Reporting group description:	
Escalating dose of placebo (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	BMS-986231 - Part I
Reporting group description:	
Escalating dose of BMS-986231 (3 µg/kg/min for 4 hours, then 6 µg/kg/min for another 4 hours, then 12 µg/kg/min for the remaining 40 hours)	
Reporting group title	Placebo - Part II
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 6 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours	
Reporting group title	BMS-986231 12 µg/kg/min - Part II
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours	
Reporting group title	Placebo - Part II (Japan cohort)
Reporting group description:	
Matching placebo dose of 6 µg/kg/min or 12 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 6 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 6 µg/kg/min for 48 hours for Japanese participants	
Reporting group title	BMS-986231 12 µg/kg/min - Part II (Japan cohort)
Reporting group description:	
BMS-986231 dose of 12 µg/kg/min for 48 hours for Japanese participants	

Serious adverse events	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 48 (22.92%)	14 / 49 (28.57%)	23 / 71 (32.39%)
number of deaths (all causes)	3	3	11
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

BLADDER CANCER			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ANGIOPATHY			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
HYPOTENSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILIAC ARTERY OCCLUSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			

subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
HYPERCAPNIA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
CONFUSIONAL STATE			

subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ELECTROCARDIOGRAM QRS COMPLEX PROLONGED			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
WRIST FRACTURE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	2 / 48 (4.17%)	6 / 49 (12.24%)	8 / 71 (11.27%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 48 (4.17%)	1 / 49 (2.04%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			

subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOGENIC SHOCK			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	3 / 71 (4.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIORENAL SYNDROME			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
ATRIOVENTRICULAR BLOCK			

subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR ARRHYTHMIA			

subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
HEPATIC CONGESTION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 48 (6.25%)	1 / 49 (2.04%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER MASS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
END STAGE RENAL DISEASE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RENAL FAILURE			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ACINETOBACTER BACTERAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
PNEUMONIA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
BRONCHITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
ENDOCARDITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (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
ERYSIPELAS			

subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPERNATRAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	0 / 71 (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
FLUID OVERLOAD			
subjects affected / exposed	1 / 48 (2.08%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 71 (21.13%)	15 / 72 (20.83%)	1 / 6 (16.67%)
number of deaths (all causes)	12	9	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BLADDER CANCER			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
Vascular disorders			
ANGIOPATHY			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
HYPOTENSION			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
ILIAC ARTERY OCCLUSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
HYPERCAPNIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
SLEEP APNOEA SYNDROME			

subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
DELIRIUM			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

ELECTROCARDIOGRAM QRS COMPLEX PROLONGED			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
WRIST FRACTURE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	2 / 71 (2.82%)	7 / 72 (9.72%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
CARDIOGENIC SHOCK			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIORENAL SYNDROME			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			

subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	2 / 71 (2.82%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
CARDIAC ARREST			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			

subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			

subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
HEPATIC CONGESTION			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
BLADDER MASS			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
END STAGE RENAL DISEASE			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
RENAL FAILURE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ACINETOBACTER BACTERAEMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	2 / 71 (2.82%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

BRONCHITIS			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
CELLULITIS			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 71 (0.00%)	1 / 72 (1.39%)	0 / 6 (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
ENDOCARDITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPERNATRAEMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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
FLUID OVERLOAD			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (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	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BLADDER CANCER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
ANGIOPATHY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILIAC ARTERY OCCLUSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	Additional description: GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCAPNIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASTHMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

PULMONARY OEDEMA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DELIRIUM			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANIC BRAIN SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ELECTROCARDIOGRAM QRS COMPLEX PROLONGED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
WRIST FRACTURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOGENIC SHOCK			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIORENAL SYNDROME			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE ACUTE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATIC CONGESTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER MASS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

END STAGE RENAL DISEASE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ACINETOBACTER BACTERAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENDOCARDITIS			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPERNATRAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FLUID OVERLOAD			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo - Part I	BMS-986231 - Part I	Placebo - Part II
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 48 (37.50%)	40 / 49 (81.63%)	47 / 71 (66.20%)
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	5 / 48 (10.42%)	14 / 49 (28.57%)	15 / 71 (21.13%)
occurrences (all)	7	21	27
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	2 / 48 (4.17%)	2 / 49 (4.08%)	6 / 71 (8.45%)
occurrences (all)	2	2	6
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

CARDIAC FAILURE			
subjects affected / exposed	2 / 48 (4.17%)	6 / 49 (12.24%)	8 / 71 (11.27%)
occurrences (all)	2	6	8
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	3 / 48 (6.25%)	1 / 49 (2.04%)	2 / 71 (2.82%)
occurrences (all)	7	1	2
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	2
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 48 (2.08%)	6 / 49 (12.24%)	5 / 71 (7.04%)
occurrences (all)	1	7	6
DIZZINESS			
subjects affected / exposed	0 / 48 (0.00%)	3 / 49 (6.12%)	0 / 71 (0.00%)
occurrences (all)	0	3	0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
VITREOUS DETACHMENT			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	2 / 48 (4.17%)	0 / 49 (0.00%)	1 / 71 (1.41%)
occurrences (all)	2	0	1
DIARRHOEA			
subjects affected / exposed	0 / 48 (0.00%)	1 / 49 (2.04%)	1 / 71 (1.41%)
occurrences (all)	0	1	1
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
RASH PRURITIC			
subjects affected / exposed	0 / 48 (0.00%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 48 (6.25%)	1 / 49 (2.04%)	1 / 71 (1.41%)
occurrences (all)	3	1	1
RENAL IMPAIRMENT			
subjects affected / exposed	3 / 48 (6.25%)	0 / 49 (0.00%)	3 / 71 (4.23%)
occurrences (all)	3	0	3
Musculoskeletal and connective tissue disorders			
MUSCLE SPASMS			
subjects affected / exposed	2 / 48 (4.17%)	0 / 49 (0.00%)	0 / 71 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 48 (2.08%)	2 / 49 (4.08%)	0 / 71 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
HYPERURICAEMIA			
subjects affected / exposed	1 / 48 (2.08%)	4 / 49 (8.16%)	3 / 71 (4.23%)
occurrences (all)	1	4	3
HYPOKALAEMIA			
subjects affected / exposed	1 / 48 (2.08%)	3 / 49 (6.12%)	7 / 71 (9.86%)
occurrences (all)	1	3	8
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 48 (2.08%)	1 / 49 (2.04%)	0 / 71 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	BMS-986231 6 µg/kg/min - Part II	BMS-986231 12 µg/kg/min - Part II	Placebo - Part II (Japan cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 71 (60.56%)	54 / 72 (75.00%)	2 / 6 (33.33%)
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	20 / 71 (28.17%)	31 / 72 (43.06%)	0 / 6 (0.00%)
occurrences (all)	25	47	0
Psychiatric disorders			

INSOMNIA			
subjects affected / exposed	2 / 71 (2.82%)	1 / 72 (1.39%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	4 / 71 (5.63%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	2 / 71 (2.82%)	7 / 72 (9.72%)	0 / 6 (0.00%)
occurrences (all)	2	7	0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 71 (5.63%)	2 / 72 (2.78%)	0 / 6 (0.00%)
occurrences (all)	4	2	0
DIZZINESS			
subjects affected / exposed	0 / 71 (0.00%)	2 / 72 (2.78%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 71 (0.00%)	2 / 72 (2.78%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
VITREOUS DETACHMENT			
subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
CONSTIPATION			

subjects affected / exposed	1 / 71 (1.41%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	1 / 71 (1.41%)	1 / 72 (1.39%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
RASH PRURITIC			
subjects affected / exposed	0 / 71 (0.00%)	0 / 72 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 71 (1.41%)	1 / 72 (1.39%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
RENAL IMPAIRMENT			
subjects affected / exposed	2 / 71 (2.82%)	1 / 72 (1.39%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
MUSCLE SPASMS			
subjects affected / exposed	2 / 71 (2.82%)	1 / 72 (1.39%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 71 (4.23%)	3 / 72 (4.17%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Metabolism and nutrition disorders			
HYPERURICAEMIA			
subjects affected / exposed	1 / 71 (1.41%)	2 / 72 (2.78%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
HYPOKALAEMIA			
subjects affected / exposed	8 / 71 (11.27%)	8 / 72 (11.11%)	0 / 6 (0.00%)
occurrences (all)	8	8	0
HYPOGLYCAEMIA			

subjects affected / exposed	1 / 71 (1.41%)	2 / 72 (2.78%)	0 / 6 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	BMS-986231 6 µg/kg/min - Part II (Japan cohort)	BMS-986231 12 µg/kg/min - Part II (Japan cohort)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	3 / 6 (50.00%)	4 / 6 (66.67%)	
occurrences (all)	3	5	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
DIZZINESS			

subjects affected / exposed occurrences (all) TRANSIENT ISCHAEMIC ATTACK subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	
Eye disorders VITREOUS DETACHMENT subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1	 0 / 6 (0.00%) 0	
Gastrointestinal disorders CONSTIPATION subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1	 1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	
Hepatobiliary disorders CHOLECYSTITIS subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1	 0 / 6 (0.00%) 0	
Skin and subcutaneous tissue disorders RASH PRURITIC subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0	 0 / 6 (0.00%) 0	
Renal and urinary disorders ACUTE KIDNEY INJURY subjects affected / exposed occurrences (all) RENAL IMPAIRMENT subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	
Musculoskeletal and connective tissue disorders MUSCLE SPASMS subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1	 0 / 6 (0.00%) 0	
Infections and infestations			

URINARY TRACT INFECTION			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
HYPERURICAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
HYPOKALAEMIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2016	Addition of two unblinded interim analysis, addition of Sensory Motor Survey, clarification and updates to Eligibility criteria, and additional edits throughout the document to improve readability.
09 April 2018	Expansion of screening period, addition of Holter Monitoring in a subset of patients, addition of Actigraphy monitoring in a subset of patients, and clarifications throughout the document.
13 March 2019	Clarify the milestone, timing of enrollment and inclusion/exclusion criteria of the Japanese population. While the enrollment in the main study protocol will continue until 210 patients have been randomized globally in Part II (Cohort 2), enrollment in Japan may continue further only in Japan until approximately 18 total Japanese participants are randomized.
30 May 2019	Additional blood pressure and heart rate measurements at 15 minutes, 45 minutes and 1.5 hours. Clarification that blood pressure measurements within 5 min in the first hour, then 15 min of the specified timepoints in Table 5.1-2.
24 September 2019	Advise that Japan participants who were enrolled after the end of global Part II enrollment will be followed for safety and rehospitalization endpoints through Day 32 only. The global study provides adequate safety follow up data and additional Day 182 data from the

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported