

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

| 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 standard deviation | 69.5 ± 13.31 | 76.7 ± 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 |
|-----------------|---|

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 aspartate 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 aspartate 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 (± 0.383) | 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 - x10⁹ 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 - |
|-----------------|---|

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 - $\times 10^{12}$ c/L

| | |
|-----------------|---|
| End point title | Change in laboratory assessments from baseline to 120 hours - $\times 10^{12}$ 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 |
| DYSпноEA | | | |
| 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 BACTERAEEMIA | | | |
| 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 BACTERAEamia | | | |
| 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 occurrences (all) | 2 / 48 (4.17%) 2 | 6 / 49 (12.24%) 6 | 8 / 71 (11.27%) 8 |
| VENTRICULAR TACHYCARDIA subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 7 | 1 / 49 (2.04%) 1 | 2 / 71 (2.82%) 2 |
| ATRIAL FIBRILLATION subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 1 / 71 (1.41%) 2 |
| MYOCARDIAL ISCHAEMIA subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 6 / 49 (12.24%) 7 | 5 / 71 (7.04%) 6 |
| DIZZINESS subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 3 / 49 (6.12%) 3 | 0 / 71 (0.00%) 0 |
| TRANSIENT ISCHAEMIC ATTACK subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Eye disorders VITREOUS DETACHMENT subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Gastrointestinal disorders CONSTIPATION subjects affected / exposed occurrences (all) | 2 / 48 (4.17%) 2 | 0 / 49 (0.00%) 0 | 1 / 71 (1.41%) 1 |
| DIARRHOEA subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 1 / 49 (2.04%) 1 | 1 / 71 (1.41%) 1 |
| Hepatobiliary disorders CHOLECYSTITIS subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Skin and subcutaneous tissue disorders RASH PRURITIC subjects affected / exposed occurrences (all) | 0 / 48 (0.00%) 0 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Renal and urinary disorders ACUTE KIDNEY INJURY subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 1 / 49 (2.04%) 1 | 1 / 71 (1.41%) 1 |
| RENAL IMPAIRMENT subjects affected / exposed occurrences (all) | 3 / 48 (6.25%) 3 | 0 / 49 (0.00%) 0 | 3 / 71 (4.23%) 3 |
| Musculoskeletal and connective tissue disorders MUSCLE SPASMS subjects affected / exposed occurrences (all) | 2 / 48 (4.17%) 2 | 0 / 49 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Infections and infestations URINARY TRACT INFECTION subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 2 / 49 (4.08%) 2 | 0 / 71 (0.00%) 0 |
| Metabolism and nutrition disorders HYPERURICAEMIA subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 4 / 49 (8.16%) 4 | 3 / 71 (4.23%) 3 |
| HYPOKALAEMIA subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 3 / 49 (6.12%) 3 | 7 / 71 (9.86%) 8 |
| HYPOGLYCAEMIA subjects affected / exposed occurrences (all) | 1 / 48 (2.08%) 1 | 1 / 49 (2.04%) 2 | 0 / 71 (0.00%) 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 occurrences (all) | 20 / 71 (28.17%) 25 | 31 / 72 (43.06%) 47 | 0 / 6 (0.00%) 0 |
| Psychiatric disorders | | | |

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

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

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