



Clinical trial results:

A Multicenter, Randomized, Parallel Group, Double Blind, Active and Placebo Controlled Study of BAY 1753011, a Dual V1a/V2 Vasopressin Receptor Antagonist, in Patients with Congestive Heart Failure: AVANTI Study

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2018-004059-18 |
| Trial protocol | DE PT AT PL GR ES BG IT |
| Global end of trial date | 21 May 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 27 April 2022 |
| First version publication date | 27 April 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY1753011/17909 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03901729 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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 | 21 May 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 May 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy of 30 mg of BAY1753011, with or without furosemide, versus furosemide alone in patients with heart failure (HF) and objective evidence of congestion

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 29 May 2019 |
| 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 | Austria: 28 |
| Country: Number of subjects enrolled | Bulgaria: 76 |
| Country: Number of subjects enrolled | Spain: 24 |
| Country: Number of subjects enrolled | Greece: 88 |
| Country: Number of subjects enrolled | Hungary: 63 |
| Country: Number of subjects enrolled | Israel: 47 |
| Country: Number of subjects enrolled | Italy: 36 |
| Country: Number of subjects enrolled | Poland: 108 |
| Country: Number of subjects enrolled | Portugal: 12 |
| Worldwide total number of subjects | 482 |
| EEA total number of subjects | 435 |

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) | 147 |
| From 65 to 84 years | 327 |
| 85 years and over | 8 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 66 study centers in 9 countries from 29 May 2019 (first subject first visit) to 21 May 2021 (last subject last visit).

Pre-assignment

Screening details:

522 subjects signed informed consent; 39 subjects did not complete screening. Most common reasons for not completing screening were screen failure (26 subjects); withdrawal by subject (6 subjects). 483 subjects were randomized, 1 subject withdrew consent before treatment allocation. 482 subjects received treatment.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Part A |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part A: Arm 1 (BAY 1753011 + SoC) |

Arm description:

Subjects were randomized in Part A to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pecavaptan |
| Investigational medicinal product code | BAY 1753011 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30mg once daily in the morning from Day 1 to Day 30

| | |
|------------------|-------------------------------|
| Arm title | Part A: Arm 2 (Placebo + SoC) |
|------------------|-------------------------------|

Arm description:

Subjects were randomized in Part A to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A.

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

Dosage and administration details:

Once daily in the morning from Day 1 to Day 30

| Number of subjects in period 1 | Part A: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) |
|---|-----------------------------------|-------------------------------|
| Started | 242 | 240 |
| Completed | 214 | 206 |
| Not completed | 28 | 34 |
| Consent withdrawn by subject | 5 | 5 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 11 | 6 |
| Other | 6 | 10 |
| Death | 1 | 3 |
| Non-compliance with study drug | - | 7 |
| Physician decision: covid-19 pandemic related | 1 | - |
| Lost to follow-up | 1 | - |
| Protocol deviation | 3 | 1 |
| Subject decision: covid-19 pandemic related | - | 1 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Part B+ Part A extension |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part B: Arm 1 (BAY 1753011 + SoC) |

Arm description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received 30 mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part B.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pecavaptan |
| Investigational medicinal product code | BAY 1753011 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30mg once daily in the morning from Day 30 to Day 60

| | |
|------------------|-------------------------------|
| Arm title | Part B: Arm 1-A (BAY 1753011) |
|------------------|-------------------------------|

Arm description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Pecavaptan (BAY1753011) 30mg in addition

to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pecavaptan |
| Investigational medicinal product code | BAY 1753011 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30mg once daily in the morning from Day 30 to Day 60

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

Dosage and administration details:

Matching placebo, oral tablet, once daily in the morning from Day 30 to Day 60

| | |
|------------------|-------------------------------|
| Arm title | Part B: Arm 2-A (BAY 1753011) |
|------------------|-------------------------------|

Arm description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days.

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

Dosage and administration details:

Matching placebo, oral tablet, once daily in the morning from Day 30 to Day 60

| | |
|--|-------------|
| Investigational medicinal product name | Pecavaptan |
| Investigational medicinal product code | BAY 1753011 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30mg once daily in the morning from Day 30 to Day 60

| | |
|------------------|------------------------------|
| Arm title | Part B: Arm 1-B (Furosemide) |
|------------------|------------------------------|

Arm description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days.

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|---|
| Investigational medicinal product name | Furosemide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 80mg once daily in the morning form Day 30 to Day 60 | |
| Investigational medicinal product name | Placebo BAY1753011 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Matching placebo, oral tablet, once daily in the morning form Day 30 to Day 60 | |
| Arm title | Part B: Arm 2-B (Furosemide) |
| Arm description: | |
| Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo BAY1753011 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Matching placebo, oral tablet, once daily in the morning form Day 30 to Day 60 | |
| Investigational medicinal product name | Furosemide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 80mg once daily in the morning form Day 30 to Day 60 | |
| Arm title | Part B: Arm 2 (Placebo + SoC) |
| Arm description: | |
| Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part B. | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Matching placebo, oral tablet, once daily in the morning from Day 30 to Day 60 | |
| Arm title | Part A Extension: Arm 1 (BAY 1753011 + SoC) |

Arm description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days to continue treatment of part A.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pecavaptan |
| Investigational medicinal product code | BAY 1753011 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

30mg once daily in the morning from Day 30 to Day 60

| | |
|------------------|---|
| Arm title | Part A Extension: Arm 2 (Placebo + SoC) |
|------------------|---|

Arm description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days to continue treatment of part A.

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

Dosage and administration details:

Matching placebo, oral tablet, once daily in the morning from Day 30 to Day 60

| Number of subjects in period 2^[1] | Part B: Arm 1 (BAY 1753011 + SoC) | Part B: Arm 1-A (BAY 1753011) | Part B: Arm 2-A (BAY 1753011) |
|---|-----------------------------------|-------------------------------|-------------------------------|
| Started | 40 | 51 | 52 |
| Completed | 36 | 48 | 48 |
| Not completed | 4 | 3 | 4 |
| Physician decision | 1 | - | - |
| Consent withdrawn by subject | - | 1 | 1 |
| Adverse event, non-fatal | 1 | 2 | 2 |
| Subject decision: covid-19 pandemic | 1 | - | - |
| Physician decision: covid-19 pandemic | - | - | - |
| Lost to follow-up | 1 | - | - |
| Logistic reason: covid-19 pandemic related | - | - | 1 |

| Number of subjects in period 2^[1] | Part B: Arm 1-B (Furosemide) | Part B: Arm 2-B (Furosemide) | Part B: Arm 2 (Placebo + SoC) |
|---|------------------------------|------------------------------|-------------------------------|
| Started | 50 | 51 | 42 |
| Completed | 48 | 46 | 41 |
| Not completed | 2 | 5 | 1 |

| | | | |
|--|---|---|---|
| Physician decision | - | - | - |
| Consent withdrawn by subject | - | 1 | - |
| Adverse event, non-fatal | 2 | 2 | 1 |
| Subject decision: covid-19 pandemic | - | 1 | - |
| Physician decision: covid-19 pandemic | - | 1 | - |
| Lost to follow-up | - | - | - |
| Logistic reason: covid-19 pandemic related | - | - | - |

| Number of subjects in period 2^[1] | Part A Extension: Arm 1 (BAY 1753011 + SoC) | Part A Extension: Arm 2 (Placebo + SoC) |
|---|--|--|
| Started | 63 | 52 |
| Completed | 62 | 52 |
| Not completed | 1 | 0 |
| Physician decision | - | - |
| Consent withdrawn by subject | - | - |
| Adverse event, non-fatal | 1 | - |
| Subject decision: covid-19 pandemic | - | - |
| Physician decision: covid-19 pandemic | - | - |
| Lost to follow-up | - | - |
| Logistic reason: covid-19 pandemic related | - | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 420 subjects completed Part A were screened for eligibility for Part B. A total of 286 subjects who completed Part A were eligible for part B AND were randomized to Part B treatment. In total, 134 subjects were ineligible for Part B, 115 subjects of them continued treatment of Part A for a further 30 days and followed the same schedule as subjects eligible for Part B.

Baseline characteristics

Reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Part A: Arm 1 (BAY 1753011 + SoC) |
| Reporting group description: | |
| Subjects were randomized in Part A to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A. | |
| Reporting group title | Part A: Arm 2 (Placebo + SoC) |
| Reporting group description: | |
| Subjects were randomized in Part A to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A. | |

| Reporting group values | Part A: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) | Total |
|------------------------|-----------------------------------|-------------------------------|-------|
| Number of subjects | 242 | 240 | 482 |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|----------|----------|-----|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 68.7 | 69.4 | |
| standard deviation | ± 10.9 | ± 10.0 | - |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 61 | 57 | 118 |
| Male | 181 | 183 | 364 |
| Body weight at baseline for Part A | | | |
| Units: kilogram (kg) | | | |
| arithmetic mean | 84.33 | 83.31 | |
| standard deviation | ± 16.17 | ± 15.99 | - |
| Serum creatinine at baseline for part A | | | |
| Units: milligram/deciliter (mg/dL) | | | |
| arithmetic mean | 1.31 | 1.33 | |
| standard deviation | ± 0.38 | ± 0.38 | - |
| Augmentation index (AI) at baseline for part A | | | |
| Augmentation index (AI) was determined via pulse wave analysis by the SphygmoCor XCEL System, a non-invasive diagnostic tool for the clinical assessment of pulse wave VELOCITY, and other measures of vascular function. | | | |
| Units: Percentage | | | |
| arithmetic mean | 22.795 | 24.267 | |
| standard deviation | ± 16.584 | ± 18.601 | - |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Part A: Arm 1 (BAY 1753011 + SoC) |
| Reporting group description: Subjects were randomized in Part A to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A. | |
| Reporting group title | Part A: Arm 2 (Placebo + SoC) |
| Reporting group description: Subjects were randomized in Part A to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A. | |
| Reporting group title | Part B: Arm 1 (BAY 1753011 + SoC) |
| Reporting group description: Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received 30 mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part B. | |
| Reporting group title | Part B: Arm 1-A (BAY 1753011) |
| Reporting group description: Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days. | |
| Reporting group title | Part B: Arm 2-A (BAY 1753011) |
| Reporting group description: Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days. | |
| Reporting group title | Part B: Arm 1-B (Furosemide) |
| Reporting group description: Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days. | |
| Reporting group title | Part B: Arm 2-B (Furosemide) |
| Reporting group description: Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days. | |
| Reporting group title | Part B: Arm 2 (Placebo + SoC) |
| Reporting group description: Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects who fulfilled eligibility criteria for Part B received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part B. | |
| Reporting group title | Part A Extension: Arm 1 (BAY 1753011 + SoC) |
| Reporting group description: Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to | |

standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days to continue treatment of part A.

| | |
|-----------------------|---|
| Reporting group title | Part A Extension: Arm 2 (Placebo + SoC) |
|-----------------------|---|

Reporting group description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days to continue treatment of part A.

| | |
|----------------------------|---|
| Subject analysis set title | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

ARM 1-A: Subjects received 30 mg Pecavaptan (BAY1753011) orally once daily in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg once daily for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg once daily for 30 days. ARM 2-A: Subjects received placebo once daily in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg once daily for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg once daily for 30 days.

| | |
|----------------------------|--|
| Subject analysis set title | Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
|----------------------------|--|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

ARM 1-B: Subjects received 30 mg Pecavaptan (BAY1753011) orally once daily in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily for 30 days. ARM 2-B: Subjects received placebo orally once daily in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily for 30 days.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Safety analysis set (SAF) |
|----------------------------|---------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

SAF included all subjects randomly assigned to study drug and who took at least 1 dose of study drug. Subjects were analyzed according to the drug they actually received.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Full analysis set (FAS) |
|----------------------------|-------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

FAS included all subjects randomly assigned to a study drug in PART A. Subjects were analyzed according to the drug they are planned for.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Modified full analysis set (mFAS) |
|----------------------------|-----------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

mFAS included all subjects randomly assigned to a study drug in PART B, and who received at least one dose of study medication during PART B. Subjects were analyzed according to the drug they were planned for.

Primary: Change in body weight between Day 1 and Day 30 (Part A)

| | |
|-----------------|---|
| End point title | Change in body weight between Day 1 and Day 30 (Part A) |
|-----------------|---|

End point description:

Body weight was measured by a member of the investigator's team according TO the clinical study protocol

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:
From Day 1 to Day 30

| End point values | Part A: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) | | |
|--------------------------------------|---|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 ^[1] | 196 ^[2] | | |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | -1.04 (± 3.53) | -0.66 (± 3.58) | | |

Notes:

[1] - FAS

[2] - FAS

Statistical analyses

| Statistical analysis title | Arm1 VS Arm 2 |
|----------------------------|---------------|
|----------------------------|---------------|

Statistical analysis description:

The imputation model used to generate complete data sets was an ANCOVA with treatment, baseline value, and measurement at Visit 3 (Day 7) as covariates. Information from all subjects was used to fit the imputation model. To use the regression method, the pattern of missingness needed to be monotone.

Total of 482 subjects were included into statistical analyses.

| | |
|---|---|
| Comparison groups | Part A: Arm 1 (BAY 1753011 + SoC) v Part A: Arm 2 (Placebo + SoC) |
| Number of subjects included in analysis | 398 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[3] |
| Method | ANCOVA |
| Parameter estimate | least squares means difference |
| Point estimate | -0.26 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | -0.203 |

Notes:

[3] - Point estimates and 95% one-sided confidence intervals were tabulated including the p-value for the one-sided test decision for $\alpha = 5\%$

Primary: Change in body weight between Day 30 and Day 60 (Part B)

| | |
|-----------------|--|
| End point title | Change in body weight between Day 30 and Day 60 (Part B) |
|-----------------|--|

End point description:

Body weight were measured by a member of the investigator's team according TO the clinical study protocol. The values at the time were used for day 30 and 'change from day 30' data were used for day 60.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Day 30 to Day 60

| End point values | Part B: Arm 1 (BAY 1753011 + SoC) | Part B: Arm 1- A (BAY 1753011) | Part B: Arm 2- A (BAY 1753011) | Part B: Arm 1- B (Furosemide) |
|--------------------------------------|---|--------------------------------------|--------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 ^[4] | 51 ^[5] | 52 ^[6] | 50 ^[7] |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 87.47 (± 18.06) | 84.14 (± 16.59) | 83.00 (± 15.34) | 81.51 (± 15.7) |
| Change in Day 60 | 0.16 (± 3.28) | 0.80 (± 3.45) | -0.19 (± 2.28) | 1.40 (± 2.56) |

Notes:

[4] - Change in Day 60: n=33 mFAS

[5] - Change in Day 60: n=45 mFAS

[6] - Change in Day 60: n=46 mFAS

[7] - Change in Day 60: n=46 mFAS

| End point values | Part B: Arm 2- B (Furosemide) | Part B: Arm 2 (Placebo + SoC) | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) | Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
|--------------------------------------|----------------------------------|-------------------------------------|--|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 51 ^[8] | 42 ^[9] | 103 ^[10] | 101 ^[11] |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 82.64 (± 17.59) | 83.41 (± 17.91) | 83.56 (± 15.9) | 82.08 (± 16.6) |
| Change in Day 60 | -0.30 (± 1.93) | 0.52 (± 2.33) | 0.30 (± 2.94) | 0.59 (± 2.42) |

Notes:

[8] - Change in Day 60: n=42 mFAS

[9] - Change in Day 60: n=38 mFAS

[10] - Day 60: n=91 mFAS

[11] - Day 60: n=88 mFAS

Statistical analyses

| Statistical analysis title | BAY 1753011 Monotherapy VS Furosemide Monotherapy |
|---|--|
| Statistical analysis description: | |
| The primary endpoints were analyzed in the mFAS population using ANCOVA. Analysis included covariates Part B treatment (BAY 1753011 monotherapy vs. furosemide monotherapy), Part A treatment and Baseline30 value. The significance level was 20% one-sided, due to the early development phase of this study. The estimated effect on Visit 10 (Day 60) was taken from the model. | |
| Comparison groups | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) v Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
| Number of subjects included in analysis | 204 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[12] |
| P-value | = 0.157 |
| Method | ANCOVA |
| Parameter estimate | least squares means difference |
| Point estimate | 0.687 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 80 % |
| sides | 1-sided |
| upper limit | 0.949 |

Notes:

[12] - For the noninferiority test, the one-sided 80% - confidence interval for treatment difference (BAY 1753011 monotherapy vs. furosemide monotherapy) was derived from the model. For body weight, non-inferiority could be concluded, if the upper bound of the one-sided 80% - confidence interval was below the non-inferiority margin 1kg.

Primary: Change in serum creatinine between Day 1 and Day 30 (Part A)

| | |
|--|--|
| End point title | Change in serum creatinine between Day 1 and Day 30 (Part A) |
| End point description: | |
| Serum creatinine was measured in blood by a central laboratory | |
| End point type | Primary |
| End point timeframe: | |
| From Day 1 to Day 30 | |

| End point values | Part A: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) | | |
|--------------------------------------|--------------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 188 ^[13] | 180 ^[14] | | |
| Units: milligram/deciliter (mg/dL) | | | | |
| arithmetic mean (standard deviation) | 0.06 (± 0.26) | -0.01 (± 0.54) | | |

Notes:

[13] - FAS

[14] - FAS

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Arm 1 VS Arm 2 |
| Statistical analysis description: | |
| The imputation model used to generate complete data sets was an ANCOVA with treatment, baseline value, and measurement at Visit 3 (Day 7) as covariates. Information from all subjects was used to fit the imputation model. To use the regression method, the pattern of missingness needed to be monotone. | |
| Total of 443 subjects were included into statistical analyses. | |
| Comparison groups | Part A: Arm 1 (BAY 1753011 + SoC) v Part A: Arm 2 (Placebo + SoC) |
| Number of subjects included in analysis | 368 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[15] |
| Method | ANCOVA |
| Parameter estimate | least squares means difference |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| upper limit | 0.058 |

Notes:

[15] - Point estimates and 95% one-sided confidence intervals were tabulated including the p-value for the one-sided test decision for $\alpha = 5\%$.

Primary: Change in log transformed blood urea nitrogen (BUN)/creatinine ratio between Day 30 and Day 60 (Part B)

| | |
|-----------------|---|
| End point title | Change in log transformed blood urea nitrogen (BUN)/creatinine ratio between Day 30 and Day 60 (Part B) |
|-----------------|---|

End point description:

Creatinine and blood urea nitrogen (BUN) were measured in blood by a central laboratory. Log transformed BUN/creatinine ratios were calculated

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Day 30 to Day 60

| End point values | Part B: Arm 1 (BAY 1753011 + SoC) | Part B: Arm 1-A (BAY 1753011) | Part B: Arm 2-A (BAY 1753011) | Part B: Arm 1-B (Furosemide) |
|--------------------------------------|-----------------------------------|-------------------------------|-------------------------------|------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 ^[16] | 51 ^[17] | 52 ^[18] | 49 ^[19] |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 2.97 (± 0.31) | 2.97 (± 0.33) | 3.03 (± 0.32) | 2.90 (± 0.35) |
| Change in Day 60 | -0.04 (± 0.37) | -0.08 (± 0.21) | -0.20 (± 0.29) | 0.11 (± 0.29) |

Notes:

[16] - Change in Day 60: n=33 mFAS

[17] - Change in Day 60: n=43 mFAS

[18] - Change in Day 60: n=43 mFAS

[19] - Change in Day 60: n=45 mFAS

| End point values | Part B: Arm 2-B (Furosemide) | Part B: Arm 2 (Placebo + SoC) | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) | Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
|--------------------------------------|------------------------------|-------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 51 ^[20] | 40 ^[21] | 103 ^[22] | 100 ^[23] |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 2.94 (± 0.35) | 3.10 (± 0.25) | 3.00 (± 0.32) | 2.92 (± 0.35) |
| Change in Day 60 | 0.11 (± 0.23) | -0.06 (± 0.27) | -0.14 (± 0.26) | 0.11 (± 0.26) |

Notes:

[20] - Change in Day 60: n=42 mFAS

[21] - Change in Day 60: n=37 mFAS

[22] - Change in Day 60: n=86 mFAS

[23] - Change in Day 60: n=87 mFAS

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | BAY 1753011 Monotherapy vs Furosemide Monotherapy |
|----------------------------|---|

Statistical analysis description:

The primary endpoints were analyzed in the mFAS population using ANCOVA. Analysis included covariates Part B treatment (BAY 1753011 monotherapy vs. furosemide monotherapy), Part A treatment and Baseline30 value. For BUN/creatinine ratio, log transformed values were analyzed and a superiority

test was performed with the treatment effect derived from the model.
Total of 201 subjects were included into statistical analyses

| | |
|---|---|
| Comparison groups | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) v Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
| Number of subjects included in analysis | 203 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[24] |
| Method | ANCOVA |
| Parameter estimate | least squares means difference |
| Point estimate | -0.217 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 1-sided |
| upper limit | -0.191 |

Notes:

[24] - Point estimates and 95% one-sided confidence intervals were tabulated including the p-value for the one-sided test decision for $\alpha = 5\%$

Secondary: Number of Treatment-emergent adverse event (TEAE) (including serious adverse event)

| | |
|-----------------|--|
| End point title | Number of Treatment-emergent adverse event (TEAE) (including serious adverse event) |
|-----------------|--|

End point description:

An Adverse event (AE) was any untoward medical occurrence in a patient or clinical study subject, associated with the use of study drug, whether or not considered related to the study drug. TEAEs are defined as AEs that occurred or worsened after the first dose of study drug up to 7 days after the date of the last dose of study drug. A serious AE (SAE) was defined as any untoward medical occurrence that, at any dose: Resulted in death; Was life-threatening; Required inpatient hospitalization or prolongation of existing hospitalization; Resulted in persistent disability/incapacity; Was a congenital anomaly/birth defect; Other situations such as important medical events that may not have been immediately life-threatening or resulted in death or hospitalization but may have jeopardized the subject or may have required medical or surgical intervention to prevent one of the outcomes listed above.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the time of first study drug administration up to 7 days after the last dose of study drug (Day 60).

| End point values | Part A: Arm 1 (BAY 1753011 + SoC) | Part B: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) | Part B: Arm 1- A (BAY 1753011) |
|-----------------------------|---|---|-------------------------------------|--------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 242 ^[25] | 40 ^[26] | 240 ^[27] | 51 ^[28] |
| Units: count of subjects | | | | |
| TEAE | 141 | 16 | 113 | 30 |
| TESAE | 26 | 8 | 27 | 8 |

Notes:

[25] - SAF

[26] - SAF

[27] - SAF

[28] - SAF

| End point values | Part B: Arm 2- A (BAY 1753011) | Part B: Arm 1- B (Furosemide) | Part B: Arm 2- B (Furosemide) | Part B: Arm 2 (Placebo + SoC) |
|------------------|--------------------------------------|----------------------------------|----------------------------------|-------------------------------------|
|------------------|--------------------------------------|----------------------------------|----------------------------------|-------------------------------------|

| | | | | |
|-----------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 52 ^[29] | 50 ^[30] | 51 ^[31] | 42 ^[32] |
| Units: count of subjects | | | | |
| TEAE | 25 | 21 | 18 | 14 |
| TESAE | 7 | 3 | 5 | 1 |

Notes:

[29] - SAF

[30] - SAF

[31] - SAF

[32] - SAF

| | | | | |
|-----------------------------|---|--|--|--|
| End point values | Part A Extension: Arm 1 (BAY 1753011 + SoC) | Part A Extension: Arm 2 (Placebo + SoC) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 ^[33] | 52 ^[34] | | |
| Units: count of subjects | | | | |
| TEAE | 28 | 18 | | |
| TESAE | 9 | 4 | | |

Notes:

[33] - SAF

[34] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Change in augmentation index (AI) between Day 1 and Day 30 (Part A)

| | |
|---|---|
| End point title | Change in augmentation index (AI) between Day 1 and Day 30 (Part A) |
| End point description: | |
| Augmentation index (AI) was determined via pulse wave analysis by the SphygmoCor XCEL System, a non-invasive diagnostic tool for the clinical assessment of pulse wave VELOCITY, and other measures of vascular function. AI was measured twice for each visit. For the analysis, the mean value of both measurements was used. | |
| End point type | Secondary |
| End point timeframe: | |
| From Day 1 to Day 30 | |

| | | | | |
|--------------------------------------|---|-------------------------------------|--|--|
| End point values | Part A: Arm 1 (BAY 1753011 + SoC) | Part A: Arm 2 (Placebo + SoC) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 ^[35] | 189 ^[36] | | |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | 2.646 (± 15.325) | -0.134 (± 16.661) | | |

Notes:

[35] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Change in augmentation index (AI) between Day 30 and Day 60 (Part B)

| | |
|-----------------|--|
| End point title | Change in augmentation index (AI) between Day 30 and Day 60 (Part B) |
|-----------------|--|

End point description:

Augmentation index (AI) was determined via pulse wave analysis by the SphygmoCor XCEL System, a non-invasive diagnostic tool for the clinical assessment of pulse wave VELOCITY, and other measures of vascular function. AI was measured twice for each visit. For the analysis, the mean value of both measurements was used.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 30 to Day 60

| End point values | Part B: Arm 1 (BAY 1753011 + SoC) | Part B: Arm 1- A (BAY 1753011) | Part B: Arm 2- A (BAY 1753011) | Part B: Arm 1- B (Furosemide) |
|--------------------------------------|---|--------------------------------------|--------------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39 ^[37] | 51 ^[38] | 51 ^[39] | 50 ^[40] |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 22.056 (± 15.435) | 25.234 (± 18.272) | 25.564 (± 15.854) | 25.530 (± 15.697) |
| Change in Day 60 | -2.044 (± 15.885) | -6.157 (± 18.095) | -2.378 (± 16.538) | 2.007 (± 18.001) |

Notes:

[37] - Change in Day 60: n=30 mFAS

[38] - Change in Day 60: n=43 mFAS

[39] - Change in Day 60: n=43 mFAS

[40] - Change in Day 60: n=45 mFAS

| End point values | Part B: Arm 2- B (Furosemide) | Part B: Arm 2 (Placebo + SoC) | BAY 1753011 Monotherapy (ARM 1-A + ARM 2-A) | Furosemide Monotherapy (ARM 1-B + ARM 2-B) |
|--------------------------------------|----------------------------------|-------------------------------------|--|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 48 ^[41] | 41 ^[42] | 102 ^[43] | 98 ^[44] |
| Units: Percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 23.689 (± 16.711) | 22.754 (± 15.543) | 25.399 (± 17.022) | 24.628 (± 16.144) |
| Change in Day 60 | -0.649 (± 11.181) | 1.767 (± 12.822) | -4.267 (± 17.336) | 0.791 (± 15.233) |

Notes:

[41] - Change in Day 60: n=38 mFAS

[42] - Change in Day 60: n=37 mFAS

[43] - Change in Day 60: n=86 mFAS

[44] - Change in Day 60: n=83 mFAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in body weight between Day 30 and Day 60 (Part A extension)

| | |
|-----------------|--|
| End point title | Change in body weight between Day 30 and Day 60 (Part A extension) |
|-----------------|--|

End point description:

Change in body weight between Day 30 and Day 60 were compared. Arithmetic mean and standard deviation were reported. The values at the time were used for day 30 and change from day 30 data were used for day 60.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Day 30 to Day 60

| End point values | Part A Extension: Arm 1 (BAY 1753011 + SoC) | Part A Extension: Arm 2 (Placebo + SoC) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 ^[45] | 52 ^[46] | | |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 82.20 (± 15.94) | 83.27 (± 15.27) | | |
| Change in Day 60 | 0.57 (± 3.13) | 0.46 (± 2.48) | | |

Notes:

[45] - Change in Day 60: n=49 FAS

[46] - Change in Day 60: n=46 FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in serum creatinine between Day 30 and Day 60 (Part A extension)

| | |
|-----------------|---|
| End point title | Change in serum creatinine between Day 30 and Day 60 (Part A extension) |
|-----------------|---|

End point description:

Change in serum creatinine between Day 30 and Day 60 were compared. Arithmetic mean and standard deviation were reported. The values at the time were used for day 30 and change from day 30 data were used for day 60.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:
From Day 30 to Day 60

| End point values | Part A Extension: Arm 1 (BAY 1753011 + SoC) | Part A Extension: Arm 2 (Placebo + SoC) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 ^[47] | 50 ^[48] | | |
| Units: milligram/deciliter (mg/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 30 | 1.35 (± 0.46) | 1.26 (± 0.36) | | |
| Change in Day 60 | -0.06 (± 0.17) | 0.06 (± 0.26) | | |

Notes:

[47] - Change in Day 60: n=47 FAS

[48] - Change in Day 60: n=42 FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of first study drug administration up to 7 days after the date of the last dose of study drug (Day 60).

Adverse event reporting additional description:

The numbers of deaths (all causes) considers all deaths in SAF that occurred from signing of the ICF to end of follow-up.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part A: ARM 2 (Placebo + SoC) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects were randomized in Part A to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Part A: Arm 1 (BAY 1753011 + SoC) |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects were randomized in Part A to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days in Part A.

| | |
|-----------------------|------------------------------------|
| Reporting group title | Part B: ARM 1 (BAY 1753011 + SoC) |
|-----------------------|------------------------------------|

Reporting group description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received 30 mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part B.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part B: ARM 1-A (BAY 1753011) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days.

| | |
|-----------------------|--|
| Reporting group title | Part A Extension: ARM 2 (Placebo + SoC) |
|-----------------------|--|

Reporting group description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Placebo once daily (in the morning) in addition to standard of care (SoC) for 30 days continued treatment of part A.

| | |
|-----------------------|------------------------------|
| Reporting group title | Part B: ARM 1-B (Furosemide) |
|-----------------------|------------------------------|

Reporting group description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days.

| | |
|-----------------------|--|
| Reporting group title | Part A Extension: ARM 1 (BAY 1753011 + SoC) |
|-----------------------|--|

Reporting group description:

Subjects received 30mg Pecavaptan (BAY1753011) orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, subjects who were not eligible for Part B randomization continued to receive Pecavaptan (BAY1753011) 30mg once daily (in the morning) in addition to standard of care (SoC) for 30 days continued treatment of part A.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part B: ARM 2 (Placebo + SoC) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part B.

| | |
|-----------------------|------------------------------|
| Reporting group title | Part B: ARM 2-B (Furosemide) |
|-----------------------|------------------------------|

Reporting group description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Furosemide (80mg) in addition to Placebo BAY1753011 30mg once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Furosemide (40mg) in addition to Placebo BAY1753011 15mg once daily (in the morning) for 30 days.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Part B: ARM 2-A (BAY 1753011) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects received placebo orally once daily (in the morning) in addition to standard of care (SoC) in Part A. Following completion of Part A, a second randomization was conducted. Subjects received Pecavaptan (BAY1753011) 30mg in addition to Placebo Furosemide 80mg orally once daily (in the morning) for 30 days in Part B. In part B, the dose modifications were allowed based on the investigator assessment. Subjects received Pecavaptan (BAY1753011) 15mg in addition to Placebo Furosemide 40mg orally once daily (in the morning) for 30 days.

| Serious adverse events | Part A: ARM 2 (Placebo + SoC) | Part A: Arm 1 (BAY 1753011 + SoC) | Part B: ARM 1 (BAY 1753011 + SoC) |
|---|----------------------------------|--------------------------------------|---------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 240 (11.25%) | 26 / 242 (10.74%) | 8 / 40 (20.00%) |
| number of deaths (all causes) | 5 | 4 | 0 |
| number of deaths resulting from adverse events | 5 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 | | | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Phlebitis | | | |

| | | | |
|--|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 stenosis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Surgical and medical procedures | | | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 1 / 242 (0.41%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |

| | | | |
|---|-----------------|-----------------|----------------|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 240 (0.83%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 8 / 240 (3.33%) | 9 / 242 (3.72%) | 3 / 40 (7.50%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 9 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 congestive | | | |
| subjects affected / exposed | 2 / 240 (0.83%) | 1 / 242 (0.41%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 left ventricular failure | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Brain injury | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 240 (0.83%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|----------------|
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 impairment | | | |
| subjects affected / exposed | 2 / 240 (0.83%) | 1 / 242 (0.41%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 2 / 242 (0.83%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| 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 | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |

| | | | |
|---|-----------------|-----------------|----------------|
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 0 / 242 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| Enterococcal sepsis | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 240 (0.00%) | 1 / 242 (0.41%) | 0 / 40 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 0 / 242 (0.00%) | 0 / 40 (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 | Part B: ARM 1-A (BAY 1753011) | Part A Extension: ARM 2 (Placebo + SoC) | Part B: ARM 1-B (Furosemide) |
|---|----------------------------------|--|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 51 (15.69%) | 4 / 52 (7.69%) | 3 / 50 (6.00%) |
| number of deaths (all causes) | 1 | 0 | 2 |

| | | | |
|---|----------------|----------------|----------------|
| number of deaths resulting from adverse events | 1 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 0 / 50 (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 |
| Vascular disorders | | | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 0 / 50 (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 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | 0 / 50 (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 |
| Peripheral artery stenosis | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | | | |
| Death | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | | | |
| Asthma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 1 / 50 (2.00%) |
| 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 fibrosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Angina unstable | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 52 (1.92%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 0 / 50 (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 |
| Cardiogenic shock | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 coronary syndrome | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 left ventricular failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain injury | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 52 (0.00%) | 0 / 50 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 impairment | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 kidney injury | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | 0 / 50 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Infections and infestations | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 52 (1.92%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 viral | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterococcal sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 52 (0.00%) | 0 / 50 (0.00%) |
| 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 | Part A Extension: ARM 1 (BAY 1753011 + SoC) | Part B: ARM 2 (Placebo + SoC) | Part B: ARM 2-B (Furosemide) |
|--|--|----------------------------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 63 (14.29%) | 1 / 42 (2.38%) | 5 / 51 (9.80%) |
| number of deaths (all causes) | 1 | 0 | 1 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | | | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phlebitis | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 stenosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | | | |
| Death | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 42 (0.00%) | 0 / 51 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 fibrosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 failure | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | | | |
| Fall | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 4 / 63 (6.35%) | 1 / 42 (2.38%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 42 (0.00%) | 0 / 51 (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 congestive | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 42 (0.00%) | 2 / 51 (3.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 coronary syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 left ventricular failure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 1 / 51 (1.96%) |
| 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 | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain injury | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 42 (0.00%) | 0 / 51 (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 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 42 (2.38%) | 0 / 51 (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 | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 42 (2.38%) | 0 / 51 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 1 / 51 (1.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 impairment | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 kidney injury | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 viral | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterococcal sepsis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 42 (0.00%) | 0 / 51 (0.00%) |
| 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 | Part B: ARM 2-A (BAY 1753011) | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 52 (13.46%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from | 0 | | |

| | | | |
|---|----------------|--|--|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral artery stenosis | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Angina unstable | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block complete | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 4 / 52 (7.69%) | | | |
| occurrences causally related to treatment / all | 1 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure acute | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure chronic | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiogenic shock | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute left ventricular failure | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Brain injury | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|----------------------------------|--|--|
| Infections and infestations Clostridium difficile colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia viral subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Wound infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| Enterococcal sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 52 (0.00%) 0 / 0 0 / 0 | | |
| COVID-19 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Part A: ARM 2 (Placebo + SoC) | Part A: Arm 1 (BAY 1753011 + SoC) | Part B: ARM 1 (BAY 1753011 + SoC) |
|---|----------------------------------|--------------------------------------|---------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 240 (13.33%) | 58 / 242 (23.97%) | 7 / 40 (17.50%) |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 7 / 240 (2.92%) | 13 / 242 (5.37%) | 0 / 40 (0.00%) |
| occurrences (all) | 8 | 13 | 0 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 12 / 240 (5.00%) | 8 / 242 (3.31%) | 1 / 40 (2.50%) |
| occurrences (all) | 14 | 9 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 5 / 242 (2.07%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| General disorders and administration site conditions | | | |
| Thirst | | | |
| subjects affected / exposed | 1 / 240 (0.42%) | 13 / 242 (5.37%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 13 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------------|------------------------|---------------------|
| Dry mouth subjects affected / exposed occurrences (all) | 5 / 240 (2.08%) 5 | 21 / 242 (8.68%) 21 | 1 / 40 (2.50%) 1 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 2 / 240 (0.83%) 2 | 8 / 242 (3.31%) 8 | 1 / 40 (2.50%) 1 |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 2 / 240 (0.83%) 2 | 2 / 242 (0.83%) 2 | 2 / 40 (5.00%) 2 |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 4 / 240 (1.67%) 4 | 13 / 242 (5.37%) 13 | 2 / 40 (5.00%) 2 |

| Non-serious adverse events | Part B: ARM 1-A (BAY 1753011) | Part A Extension: ARM 2 (Placebo + SoC) | Part B: ARM 1-B (Furosemide) |
|--|----------------------------------|--|---------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 17 / 51 (33.33%) | 4 / 52 (7.69%) | 6 / 50 (12.00%) |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 52 (1.92%) 1 | 1 / 50 (2.00%) 1 |
| Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all) | 10 / 51 (19.61%) 11 | 1 / 52 (1.92%) 1 | 4 / 50 (8.00%) 4 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 3 | 0 / 52 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| General disorders and administration site conditions Thirst subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 52 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Dry mouth subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 52 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 2 / 52 (3.85%) 2 | 2 / 50 (4.00%) 2 |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 52 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 5 | 1 / 52 (1.92%) 1 | 0 / 50 (0.00%) 0 |

| Non-serious adverse events | Part A Extension: ARM 1 (BAY 1753011 + SoC) | Part B: ARM 2 (Placebo + SoC) | Part B: ARM 2-B (Furosemide) |
|--|--|----------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 11 / 63 (17.46%) | 5 / 42 (11.90%) | 6 / 51 (11.76%) |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 4 / 42 (9.52%) 4 | 2 / 51 (3.92%) 2 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 42 (0.00%) 0 | 2 / 51 (3.92%) 2 |
| General disorders and administration site conditions Thirst subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| Dry mouth subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 6 | 0 / 42 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 0 / 42 (0.00%) 0 | 1 / 51 (1.96%) 1 |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 7 / 63 (11.11%) 7 | 1 / 42 (2.38%) 1 | 0 / 51 (0.00%) 0 |

| | | | |
|--|----------------------------------|--|--|
| Non-serious adverse events | Part B: ARM 2-A (BAY 1753011) | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 16 / 52 (30.77%) | | |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 52 (0.00%) 0 | | |
| Cardiac disorders Cardiac failure subjects affected / exposed occurrences (all) | 6 / 52 (11.54%) 7 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 52 (0.00%) 0 | | |
| General disorders and administration site conditions Thirst subjects affected / exposed occurrences (all) | 1 / 52 (1.92%) 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---------------------|--|--|
| Dry mouth subjects affected / exposed occurrences (all) | 5 / 52 (9.62%) 5 | | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 3 / 52 (5.77%) 6 | | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 52 (0.00%) 0 | | |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 4 / 52 (7.69%) 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 20 May 2019 | 1) Local laboratory samples (chemistry: serum creatinine, eGFR, potassium, sodium) were added for safety reasons, with regard to the investigational medicinal products (IMPs) potential e.g. to change serum electrolytes and for early detection of discontinuation criteria. 2) Local laboratory assessments before and 22-24 hours after the first study drug dose were included for Visit 2 and unscheduled visit as requested by the Data Monitoring Committee (DMC). 3) Additional drug accountability after 1 week of study drug dispensation (Visits 3 and 7) was removed from the protocol to reduce the burden on the sites. 4) Ability to understand and follow study-related instructions as a documented decision of the investigator was added in the inclusion criteria. 5) Exclusion criterion #1 (body weight > 150 kg at screening) was replaced by Body Mass Index (BMI) value < 18.5 kg/m ² or > 35 kg/m ² . |
| 08 November 2019 | 1) Inclusion criterion #8 for lower threshold of loop diuretic doses (average/usual total daily dose of loop diuretic ≥ 40 mg of furosemide or equivalent, within 4 weeks prior to index hospitalization) was added in order to increase the randomization into Part B of the trial. 2) Inclusion criterion #9C for the composite congestion score (CCS) was capped in case approximately 40% of subjects were to be randomized based on this single criterion, to keep a diverse study population. 3) Composite congestion score (CCS) threshold in inclusion criterion #9C was changed from ≥ 2 to ≥ 3, to increase randomization into Part B. 4) The number of replications of the regression method was reduced from 10000 to 100, to reduce the run time of the statistical analyses. |
| 29 June 2020 | 1) Sample size was increased to approximately 640 subjects to be screened and 570 subjects to be randomized in order to achieve 280 completers at the end of Part B, to compensate the increased number of discontinuations during the COVID-19 pandemic. 2) Benefit/risk statement regarding additional risks to trial participants and risk mitigation measures was added to explain the risks associated with the COVID-19 pandemic. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported