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	Investigator, Monitor, Data analyst, Carer, Subject, 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 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 α = 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 α = 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 α = 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 congential 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 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[35]	51[36]	51[37]	50[38]
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:

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

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

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

[38] - 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[39]	41[40]	102[41]	98[42]
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:

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

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

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

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

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[43]	189[44]		
Units: Percentage				
arithmetic mean (standard deviation)	2.646 (± 15.325)	-0.134 (± 16.661)		

Notes:

[43] - FAS

[44] - FAS

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 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	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterococcal sepsis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	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	5 / 240 (2.08%)	21 / 242 (8.68%)	1 / 40 (2.50%)
occurrences (all)	5	21	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 240 (0.83%)	8 / 242 (3.31%)	1 / 40 (2.50%)
occurrences (all)	2	8	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 240 (0.83%)	2 / 242 (0.83%)	2 / 40 (5.00%)
occurrences (all)	2	2	2
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	4 / 240 (1.67%)	13 / 242 (5.37%)	2 / 40 (5.00%)
occurrences (all)	4	13	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	0 / 51 (0.00%)	1 / 52 (1.92%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	10 / 51 (19.61%)	1 / 52 (1.92%)	4 / 50 (8.00%)
occurrences (all)	11	1	4
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 51 (5.88%)	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Thirst			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Dry mouth			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 51 (3.92%)	2 / 52 (3.85%)	2 / 50 (4.00%)
occurrences (all)	2	2	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	5 / 51 (9.80%)	1 / 52 (1.92%)	0 / 50 (0.00%)
occurrences (all)	5	1	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	0 / 63 (0.00%)	0 / 42 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 63 (1.59%)	4 / 42 (9.52%)	2 / 51 (3.92%)
occurrences (all)	1	4	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 63 (0.00%)	0 / 42 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Thirst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 42 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	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