Clinical trial results:
A Randomized, Double-Blinded, Placebo-Controlled, Study to Evaluate the Safety and Tolerability of BMS-986259 in Stabilized Patients Hospitalized for Acute Decompensated Heart Failure

Summary

EudraCT number	2019-004186-40
Trial protocol	GR PL NL GB
Global end of trial date	19 July 2021

Results information

Result version number	v1 (current)
This version publication date	
First version publication date	

Trial information

Trial identification

Sponsor protocol code	CV019-010

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 November 2021
Is this the analysis of the primary	No

completion data?	
Global end of trial reached?	Yes
Global end of trial date	19 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish safety & tolerability of BMS-986259 when initiated in-hospital in participants stabilized after an admission for ADHF

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Poland: 13
Worldwide total number of subjects	25
EEA total number of subjects	19

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)	10
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

25 participants were randomized and treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo matching BMS-986259

Arm type	Placebo
Investigational medicinal product name	Placebo matching BMS-986259
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mL QD for 14 days

Arm title	BMS-986259 3 mg

Arm description:

BMS-986259 administered subcutaneously QD for 14 days

Arm type	Experimental
Investigational medicinal product name	BMS-986259
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 mg QD for 14 days

Number of subjects in period 1	Placebo	BMS-986259 3 mg
Started	13	12
Completed	10	9
Not completed	3	3
Participant withdrew consent	1	-
Adverse event, non-fatal	2	2

Other reasons	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo matching BMS-986259	
Reporting group title	BMS-986259 3 mg
Reporting group description: BMS-986259 administered subcutaneously QD for 14 days	

Reporting group values	Placebo	BMS-986259 3 mg	Total
Number of subjects	13	12	25
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	4	6	10
>=65 years	9	6	15
Age Continuous Units: Years			
arithmetic mean	65.1	63.1	
standard deviation	± 12.18	± 15.65	-
Sex: Female, Male Units: Participants			
Female	4	3	7
Male	9	9	18
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	13	12	25
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo matching BMS-986259	
Reporting group title	BMS-986259 3 mg
Reporting group description: BMS-986259 administered subcutaneously QD for 14 days	

Primary: Percentage of Participants Experiencing Clinically Relevant Hypotension

End point title	Percentage of Participants Experiencing Clinically Relevant Hypotension[1]
End point description: Clinically Relevant Hypotension is defined as any of the following: - Supine Systolic Blood Pressure (SBP) <85 mmHg (confirmed by repeat measurement within 30 minutes), regardless of symptoms of hypotension - Supine SBP <90 mmHg (confirmed by repeat measurement within 30 minutes) AND symptoms of hypotension (eg, dizziness, lightheadedness, etc).	
End point type	Primary
End point timeframe: From first dose to 30 days following first dose	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed for this endpoint.

End point values	Placebo	BMS-986259 3 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: Percent of participants				
number (not applicable)	15.4	16.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax)

End point title	Maximum Observed Serum Concentration (Cmax)[2]
End point description:	
End point type	Secondary
End point timeframe: Day 1 and Day 5 of study treatment	

Notes:

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

Justification: Values can be reported only for participants who received study drug.

End point values	BMS-986259 3 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	105 (± 49)			
Day 5	268 (± 31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Observed Serum Concentration (Tmax)

End point title	Time of Maximum Observed Serum Concentration (Tmax)[3]

End point description:

End point type	Secondary

End point timeframe:

Day 1 and Day 5 of study treatment

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Values can be reported only for participants who received study drug.

End point values	BMS-986259 3 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Hours				
median (full range (min-max))				
Day 1	11.0 (7.00 to 23.3)			
Day 5	7.97 (5.00 to 24.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve Within a Dosing Interval (AUC(TAU))

End point title	Area Under the Concentration-Time Curve Within a Dosing Interval (AUC(TAU))[4]

End point description:

End point type	Secondary

End point timeframe:

Day 1 and Day 5 of study treatment

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Values can be reported only for participants who received study drug.

End point values	BMS-986259 3 mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	1778 (± 40)			
Day 5	5156 (± 36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (Ctrough)

End point title	Trough Concentration (Ctrough)[5]

End point description:

End point type	Secondary

End point timeframe:

Day 2 through Day 14 of study treatment

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Values can be reported only for participants who received study drug.

End point values	BMS-986259 3 mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 2	79.9 (± 36.0)			
Day 3	145 (± 32.3)			
Day 4	181 (± 28.9)			
Day 5	185 (± 32.4)			
Day 6	210 (± 27.3)			
Day 7	260 (± 41.3)			
Day 8	226 (± 69.4)			
Day 9	252 (± 48.1)			

Day 10	259 (± 49.7)			
Day 12	229 (± 22.9)			
Day 13	248 (± 50.5)			
Day 14	246 (± 7.53)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from first dose to study completion date (up to approximately 8 months).
SAEs and NSAEs were assessed from first dose to 30 days following first dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	BMS986259 3 mg

Reporting group description:

BMS-986259 administered subcutaneously QD for 14 days

Reporting group title	Placebo

Reporting group description:

Placebo matching BMS-986259

Serious adverse events	BMS986259 3 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	5 / 13 (38.46%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	BMS986259 3 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 12 (66.67%)	3 / 13 (23.08%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 12 (25.00%)	1 / 13 (7.69%)	
occurrences (all)	3	2	
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 13 (7.69%) 1	
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0	
Blood and lymphatic system disorders Haemoconcentration subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 13 (7.69%) 1	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 13 (7.69%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 13 (7.69%) 1	
Reproductive system and breast disorders Genital haemorrhage subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0	
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 13 (0.00%) 0	
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0	

Infections and infestations Pneumonia subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0	 1 / 13 (7.69%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2020	Added safety measures in response to the Coronavirus disease 2019 (COVID-19) pandemic

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported