Clinical trial results:
A multicenter, open-label, randomized, active-controlled, Phase 2 study to evaluate the pharmacokinetics, efficacy, and safety of intravenous BV100 combined with polymyxin B versus best available therapy in adult patients with ventilator-associated bacterial pneumonia suspected or confirmed to be due to carbapenem-resistant Acinetobacter baumannii

Summary

EudraCT number	2022-002856-37
Trial protocol	HU
Global end of trial date	26 September 2024

Results information

Result version number	v1 (current)
This version publication date	28 February 2026
First version publication date	28 February 2026

Trial information

Trial identification

Sponsor protocol code	BV100-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	NCT number: NCT05685615

Notes:

Sponsors

Sponsor organisation name	BioVersys SAS
Sponsor organisation address	1 rue du Pr Calmette/3 rue du Pr Laguesse, Lille, France, 59000
Public contact	Lead Project Manager, PSI CRO Hungary LLc, +36 15556755, tamas.szirak@psi-cro.com
Scientific contact	Lead Project Manager, PSI CRO Hungary LLc, +36 15556755, tamas.szirak@psi-cro.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	24 March 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the PK properties of BV100 co-administered with polymyxin B during 7 to 14 days of treatment in patients with ventilator-associated bacterial pneumonia (VABP) due to suspected or documented CRAB infection.

Protection of trial subjects:

This trial was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki, the Council for International Organizations of Medical Sciences international ethical guidelines, and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) E6(R2) Guidelines. In addition, all local laws and regulatory requirements were followed, in particular, those affording greater protection to the safety of trial patients.

A DSMB was appointed to this trial to make recommendations to the Sponsor regarding the modification, continuance, or stopping of the trial based on assessments of safety or for efficacy based futility.

Background therapy:

None.

Evidence for comparator:

Polymyxin B is not a substrate of any important hepatic drug metabolizing enzymes or transporters and is unlikely to be associated with any drug-drug interactions with BV100. Thus, the combination of polymyxin B and BV100 was not expected to result in AEs not directly attributable to either polymyxin B or BV100. The dose of polymyxin B used in this trial followed the international consensus guidelines for the optimal use of polymyxins.

The anti-Acinetobacter antibiotics that represent BAT in the control group depended on the local susceptibility pattern of CRAB isolates. These antibiotics correspond to the commonly used antibiotics with anti-Acinetobacter activity. For patients in Part A randomized to best available therapy (BAT) and for patients in Part B, the BATs were to be determined according to country and individual sites. The authorized anti-Acinetobacter antibiotic was to be administered according to the local site practice.

Actual start date of recruitment	27 April 2023
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	Georgia: 28
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Hungary: 2
Worldwide total number of subjects	41
EEA total number of subjects	13

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)	15
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 72 patients were screened and 41 were enrolled across 11 sites in Georgia, Greece, and Hungary. Of the 41 patients enrolled, 2 patients were not treated (1 patient in the BAT group and 1 patient in the BV100 300 mg + BAT [Part B] group were randomized by mistake). First Patient First Visit (date of informed consent) was on 27 April 2023.

Pre-assignment

Screening details:

Male and female patients ≥ 18 and ≤ 80 years of age diagnosed with VABP suspected/confirmed due to CRAB. Patients were eligible if they had BMI of < 40 kg/m2, were hospitalized ≥ 48 hours, intubated and receiving mechanical ventilation ≥ 48 hours at the time of randomization, and had clinical and radiological findings to support diagnosis of VABP.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BV100 200 mg + Polymyxin B (Part A)

Arm description:

Patients received multiple IV doses of BV100 200 mg + polymyxin B on Day 1 up to Day 14.

Arm type	Experimental
Investigational medicinal product name	BV100
Investigational medicinal product code	
Other name	Rifabutin
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

BV100 200 mg administered every 12 hours (± 1 hour) from Day 1 up to Day 14 (120-minute infusions [± 10 min]).

In Part A, the polymyxin B infusion was to be administered first (60 min ± 10 min), followed immediately with the BV100 infusion (120 min ± 10 min).

Investigational medicinal product name	Polymyxin B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Polymyxin B administered every 12 hours (± 1 hour) from Day 1 up to Day 14 (60-minute infusions [± 10 min]).

The recommended dose of polymyxin B used in this trial followed the International Consensus Guidelines for the optimal use of polymyxins (Tsuji et al; 2019):
Loading dose (Day 1) = 2.0-2.5 mg/kg* (equivalent to 20 000-25 000 IU/kg).
Maintenance doses (q12h) = 1.25-1.5 mg/kg* (equivalent to 12 500-15 000 IU/kg).

In Part A, the polymyxin B infusion was to be administered first (60 min ± 10 min), followed immediately with the BV100 infusion (120 min ± 10 min).

*Based on total body weight (TBW). Maximum dose was 2.5 mg/kg/day (25 000 IU/kg). The total daily dose was not to exceed 200 mg/day given as 100 mg q12h, 1h infusions.

Arm title	BV100 300 mg + Polymyxin B (Part A)

Arm description:

Patients received multiple IV doses of BV100 300 mg + polymyxin B on Day 1 up to Day 14.

Arm type	Experimental
Investigational medicinal product name	BV100
Investigational medicinal product code	
Other name	Rifabutin
Pharmaceutical forms	Powder and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

BV100 300 mg administered every 12 hours (± 1 hour) from Day 1 up to Day 14 (120-minute infusions [± 10 min]).

In Part A, the polymyxin B infusion was to be administered first (60 min ± 10 min), followed immediately with the BV100 infusion (120 min ± 10 min).

Investigational medicinal product name	Polymyxin B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Polymyxin B administered every 12 hours (± 1 hour) from Day 1 up to Day 14 (60-minute infusions [± 10 min]).

The recommended dose of polymyxin B used in this trial followed the International Consensus Guidelines for the optimal use of polymyxins (Tsuji et al; 2019):
Loading dose (Day 1) = 2.0-2.5 mg/kg [1] (equivalent to 20 000-25 000 IU/kg).
Maintenance doses (q12h) = 1.25-1.5 mg/kg [1] (equivalent to 12 500-15 000 IU/kg).

In Part A, the polymyxin B infusion was to be administered first (60 min ± 10 min), followed immediately with the BV100 infusion (120 min ± 10 min).

[1] Based on total body weight (TBW). Maximum dose was 2.5 mg/kg/day (25 000 IU/kg). The total daily dose was not to exceed 200 mg/day given as 100 mg q12h, 1h infusions.

Arm title	BAT (Part A)

Arm description:

Patients received multiple doses of BAT on Day 1 up to Day 14.

Arm type	Active comparator
Investigational medicinal product name	BAT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Infusion

Dosage and administration details:

The BATs were to be determined according to country and individual sites and administered according to the local site practice.

Arm title	BV100 300 mg + BAT (Part B)

Arm description:

Patients received multiple IV doses of BV100 300 mg + BAT on Day 1 up to Day 14.

Arm type	Experimental

Investigational medicinal product name	BV100
Investigational medicinal product code	
Other name	Rifabutin
Pharmaceutical forms	Powder and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

BV100 300 mg administered every 12 hours (± 1 hour) from Day 1 up to Day 14 (120-minute infusions [± 10 min]).

In Part B, the BAT was to be administered first, followed immediately with the BV100 infusion.

Investigational medicinal product name	BAT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Infusion , Inhalation use

Dosage and administration details:

The BATs were determined according to country and individual sites and were to be the same treatment received as before entering the trial but could change with treatment failure, at the discretion of the Investigator.

In Part B, the BAT was to be administered first, followed immediately with the BV100 infusion.

Number of subjects in period 1	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)
Started	10	11	11
Treated	10	11	10
Completed	9	6	4
Not completed	1	5	7
Death	1	5	6
Protocol deviation	-	-	1

Number of subjects in period 1	BV100 300 mg + BAT (Part B)
Started	9
Treated	8
Completed	4
Not completed	5
Death	4
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	BV100 200 mg + Polymyxin B (Part A)
Reporting group description:	
Patients received multiple IV doses of BV100 200 mg + polymyxin B on Day 1 up to Day 14.	
Reporting group title	BV100 300 mg + Polymyxin B (Part A)
Reporting group description:	
Patients received multiple IV doses of BV100 300 mg + polymyxin B on Day 1 up to Day 14.	
Reporting group title	BAT (Part A)
Reporting group description:	
Patients received multiple doses of BAT on Day 1 up to Day 14.	
Reporting group title	BV100 300 mg + BAT (Part B)
Reporting group description:	
Patients received multiple IV doses of BV100 300 mg + BAT on Day 1 up to Day 14.	

Reporting group values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)
Number of subjects	10	11	11
Age categorical			
Units: Subjects			
Age continuous			
Age data are presented for the ITT population. Patients were between 31 and 79 years of age (mean 65.6 years).			
Units: years			
arithmetic mean	67.9	63.6	62.9
standard deviation	± 8.62	± 10.44	± 16.10
Gender categorical			
Gender data are presented for the ITT population. Most patients (65.9%) were male.			
Units: Subjects			
Female	5	3	4
Male	5	8	7
Race			
Race data are presented for the ITT population. All patients (100%) were White.			
Units: Subjects			
White	10	11	11
American Indian or Alaska Native	0	0	0
Black or African American	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Not Reported	0	0	0
Other	0	0	0
Ethnicity			
Ethnicity data are presented for the ITT population.			

All patients (100%) were not Hispanic or Latino.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	10	11	11
Not Reported	0	0	0
Country			
Country data are presented for the ITT population. Twenty-eight patients (68.3%) were enrolled from Georgia, 11 patients (26.8%) from Greece, and 2 patients (4.9%) from Hungary. All patients (100%) in the BAT group were from Georgia.			
Units: Subjects			
Georgia	7	10	11
Greece	2	0	0
Hungary	1	1	0
Childbearing Potential			
Childbearing potential percentages are based on the number of female patients. Childbearing data are presented for the ITT population. All female patients (100%) were post-menopausal and not of childbearing potential.			
Units: Subjects			
Yes	0	0	0
No	5	3	4
Not counted (male)	5	8	7
Days in the ICU prior to randomization			
ICU data are presented for the ITT population. Prior to randomization, more than half of patients (26 patients; 63.4%) had been in the ICU for 5 to 14 days.			
Units: Subjects			
<5	1	2	5
5-14	8	8	4
>14	1	1	2
eGFR (mL/min/1.73m2) at Screening			
eGFR data are presented for the ITT population. Two patients were randomized and/or enrolled by mistake, did not receive treatment, and did not have the eGFR assessment done by the central laboratory. The eGFR values at Screening were similar across all ranges: 24.4% had an eGFR < 60 mL/min/1.73m2, 24.4% had an eGFR ≥ 60 and < 90 mL/min/1.73m2, 19.5% had an eGFR ≥ 90 and ≤ 120 mL/min/1.73m2, and 24.4% had an eGFR > 120 mL/min/1.73m2.			
Units: Subjects			
<60	3	2	2
≥60 and <90	1	5	2
≥90 and ≤120	2	3	3
>120	4	1	3
Not done	0	0	1
Glasgow Coma Score (GCS) Neurologic Score			
GCS data are presented for the micro-ITT population. Most patients had a GCS score of ≤ 7. Four patients (10.3%) had a GCS score of 12.			
Units: Subjects			
0 points	1	0	0
1 point	0	1	0
4 points	1	2	1
5 points	0	0	4
6 points	1	2	3

7 points	5	2	1
8 points	1	0	1
9 points	0	0	0
10 points	0	1	0
11 points	1	0	0
12 points	0	3	0
Excluded from population	0	0	1
VABP Diagnosis Details: Time Since VABP Diagnosis			
VABP diagnosis details are presented for the micro-ITT population. The mean (standard deviation [SD]) time since VABP diagnosis: 2.4 (3.68) days.			
Units: Days			
arithmetic mean	1.4	2.5	1.1
standard deviation	± 0.52	± 2.54	± 0.32
Total APACHE II Score			
Total APACHE II score data are presented for the micro-ITT population. The mean (SD) total APACHE II score was 16.1 (4.36).			
Units: Score			
arithmetic mean	15.7	17.4	15.1
standard deviation	± 2.58	± 5.20	± 3.60

Reporting group values	BV100 300 mg + BAT (Part B)	Total	
Number of subjects	9	41	
Age categorical Units: Subjects			
Age continuous			
Age data are presented for the ITT population. Patients were between 31 and 79 years of age (mean 65.6 years).			
Units: years			
arithmetic mean	68.7		
standard deviation	± 10.17	-	
Gender categorical			
Gender data are presented for the ITT population. Most patients (65.9%) were male.			
Units: Subjects			
Female	2	14	
Male	7	27	
Race			
Race data are presented for the ITT population. All patients (100%) were White.			
Units: Subjects			
White	9	41	
American Indian or Alaska Native	0	0	
Black or African American	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Not Reported	0	0	
Other	0	0	

Ethnicity			
Ethnicity data are presented for the ITT population. All patients (100%) were not Hispanic or Latino.			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	9	41	
Not Reported	0	0	
Country			
Country data are presented for the ITT population. Twenty-eight patients (68.3%) were enrolled from Georgia, 11 patients (26.8%) from Greece, and 2 patients (4.9%) from Hungary. All patients (100%) in the BAT group were from Georgia.			
Units: Subjects			
Georgia	0	28	
Greece	9	11	
Hungary	0	2	
Childbearing Potential			
Childbearing potential percentages are based on the number of female patients. Childbearing data are presented for the ITT population. All female patients (100%) were post-menopausal and not of childbearing potential.			
Units: Subjects			
Yes	0	0	
No	2	14	
Not counted (male)	7	27	
Days in the ICU prior to randomization			
ICU data are presented for the ITT population. Prior to randomization, more than half of patients (26 patients; 63.4%) had been in the ICU for 5 to 14 days.			
Units: Subjects			
<5	0	8	
5-14	6	26	
>14	3	7	
eGFR (mL/min/1.73m2) at Screening			
eGFR data are presented for the ITT population. Two patients were randomized and/or enrolled by mistake, did not receive treatment, and did not have the eGFR assessment done by the central laboratory. The eGFR values at Screening were similar across all ranges: 24.4% had an eGFR < 60 mL/min/1.73m2, 24.4% had an eGFR ≥ 60 and < 90 mL/min/1.73m2, 19.5% had an eGFR ≥ 90 and ≤ 120 mL/min/1.73m2, and 24.4% had an eGFR > 120 mL/min/1.73m2.			
Units: Subjects			
<60	3	10	
≥60 and <90	2	10	
≥90 and ≤120	0	8	
>120	2	10	
Not done	2	3	
Glasgow Coma Score (GCS) Neurologic Score			
GCS data are presented for the micro-ITT population. Most patients had a GCS score of ≤ 7. Four patients (10.3%) had a GCS score of 12.			
Units: Subjects			
0 points	2	3	
1 point	2	3	

4 points	1	5	
5 points	1	5	
6 points	0	6	
7 points	0	8	
8 points	0	2	
9 points	1	1	
10 points	0	1	
11 points	0	1	
12 points	1	4	
Excluded from population	1	2	
VABP Diagnosis Details: Time Since VABP Diagnosis			
VABP diagnosis details are presented for the micro-ITT population. The mean (standard deviation [SD]) time since VABP diagnosis: 2.4 (3.68) days.			
Units: Days			
arithmetic mean	5.1		
standard deviation	± 7.16	-	
Total APACHE II Score			
Total APACHE II score data are presented for the micro-ITT population. The mean (SD) total APACHE II score was 16.1 (4.36).			
Units: Score			
arithmetic mean	15.9		
standard deviation	± 5.94	-	

End points

End points reporting groups

Reporting group title	BV100 200 mg + Polymyxin B (Part A)
Reporting group description:	
Patients received multiple IV doses of BV100 200 mg + polymyxin B on Day 1 up to Day 14.	
Reporting group title	BV100 300 mg + Polymyxin B (Part A)
Reporting group description:	
Patients received multiple IV doses of BV100 300 mg + polymyxin B on Day 1 up to Day 14.	
Reporting group title	BAT (Part A)
Reporting group description:	
Patients received multiple doses of BAT on Day 1 up to Day 14.	
Reporting group title	BV100 300 mg + BAT (Part B)
Reporting group description:	
Patients received multiple IV doses of BV100 300 mg + BAT on Day 1 up to Day 14.	
Subject analysis set title	Intention-to-Treat (ITT) Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Population includes all patients randomized (Part A) and assigned (Part B), even if the patient did not take the assigned treatment, did not receive the correct treatment, or otherwise did not follow the protocol. The ITT analyses used the treatment as randomized/assigned.

The ITT population included all 41 (100%) enrolled patients (10 patients in the BV100 200 mg + polymyxin B group, 11 patients in the BV100 300 mg + polymyxin B group, 11 patients in the BAT group, and 9 patients in the BV100 300 mg + BAT [Part B] group).

Subject analysis set title	Microbiological ITT (micro-ITT) Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The micro-ITT Population includes all patients in the ITT Population with (i) a Baseline RDT positive for A. baumannii, irrespective of the culture result, (ii) surveillance culture positive for A. baumannii, or (iii) a quantitative culture from a respiratory specimen or blood culture obtained within up to 36 hours prior to randomization (Part A) or assignment (Part B), positive for A. baumannii, regardless of its susceptibility to trial drug and who received at least 1 dose of trial treatment. Patients were analyzed according to the treatment as randomized/assigned.

The micro-ITT and Safety populations were identical and each comprised a total of 39 patients (95.1%) overall, with 2 patients excluded from these populations (1 patient in the BAT group and 1 patient in the BV100 300 mg + BAT [Part B] group) due to not receiving at least 1 dose of trial treatment.

Subject analysis set title	Carbapenem-resistant MITT (micro-CRMITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The micro-CRMITT population includes all patients in the micro-ITT population with a quantitative culture from a respiratory specimen or blood culture obtained within up to 36 hours prior to randomization (Part A) or assignment (Part B), positive for CRAB, regardless of susceptibility to trial drug. Patients were analyzed according to the treatment as randomized/assigned.

All patients with a suitable respiratory specimen who met the criteria for inclusion in the micro-CRMITT population had CRAB.
The micro-CRMITT population comprised a total of 26 patients (63.4%) overall, including 9 patients (90.0%) in the BV100 200 mg + polymyxin B group, 7 patients (63.6%) in the BV100 300 mg + polymyxin B group, and 10 patients (90.9%) in the BAT group. No patients from the BV100 300 mg + BAT [Part B] group were included in the micro-CRMITT population.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population includes all patients from the ITT Population who received at least 1 dose of trial treatment (not counting BAT received prior to randomization) and had at least 1 post-baseline safety assessment. Patients were analyzed according to the actual treatment received.

The Safety and micro-ITT populations were identical and each comprised a total of 39 patients (95.1%) overall, with 2 patients excluded from these populations (1 patient in the BAT group and 1 patient in the BV100 300 mg + BAT [Part B] group) due to not receiving at least 1 dose of trial treatment.

Subject analysis set title	Pharmacokinetic (PK) Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK Population includes all patients in the Safety Population for whom at least 1 BV100 post-dose sample for PK analysis was available.

The PK population comprised a total of 29 patients (70.7%) overall, including 10 patients (100%) in the BV100 200 mg + polymyxin B group, 11 patients (100%) in the BV100 300 mg + polymyxin B group, and 8 patients (88.9%) in the BV100 300 mg + BAT (Part B) group. Two patients were excluded due to not receiving at least 1 dose of trial treatment.

Primary: Rifabutin Cmax

End point title	Rifabutin Cmax[1]

End point description:

Maximum observed plasma concentration (Cmax) for rifabutin.

Plasma concentrations: Rifabutin and DMI concentrations above the lower limit of quantification (LLOQ) were quantified for most patients around 5 minutes post-infusion on Day 1 and pre-dose on Day 4. 25-O-desacetyl-rifabutin concentrations above the LLOQ were quantified for most patients around 1-2 hours post-infusion on Day 1 and pre-dose on Day 4.

All PK data are presented for the PK population.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[2]	11[3]	0[4]	7[5]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	689.0 (± 79.6)	1099 (± 108.0)	()	705.5 (± 43.9)
Day 4	1187 (± 71.9)	1306 (± 98.2)	()	1431 (± 34.0)

Notes:

[2] - Patients analyzed: Day 1 = 10; Day 4 = 9

[3] - Patients analyzed: Day 1 = 11; Day 4 = 11

[4] - Patients did not receive BV100

[5] - Patients analyzed: Day 1 = 7; Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: Rifabutin tmax

End point title	Rifabutin tmax[6]

End point description:

Time of occurrence of Cmax (tmax) for rifabutin.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[6] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[7]	11[8]	0[9]	7[10]
Units: hours				
median (full range (min-max))				
Day 1	1.58 (0.08 to 4.02)	1.00 (0.10 to 12.00)	(to)	1.00 (0.08 to 2.02)
Day 4	2.00 (0.50 to 12.00)	1.00 (0.08 to 12.00)	(to)	1.00 (0.07 to 2.00)

Notes:

[7] - Patients analyzed: Day 1 = 10; Day 4 = 9

[8] - Patients analyzed: Day 1 = 11; Day 4 = 11

[9] - Patients did not receive BV100

[10] - Patients analyzed: Day 1 = 7 Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: Rifabutin AUC0-12

End point title	Rifabutin AUC0-12[11]

End point description:

Area under the concentration-time curve from dosing (time 0) to 12h (AUC0-12) for rifabutin.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[11] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[12]	9[13]	0[14]	4[15]
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	2857 (± 45.3)	3791 (± 64.3)	()	4565 (± 21.3)
Day 4	6012 (± 44.2)	5921 (± 43.6)	()	8357 (± 50.8)

Notes:

[12] - Patients analyzed: Day 1 = 6; Day 4 = 9

[13] - Patients analyzed: Day 1 = 9; Day 4 = 8

[14] - Patients did not receive BV100

[15] - Patients analyzed: Day 1 = 4; Day 4 = 4

Statistical analyses

No statistical analyses for this end point

Primary: 25-O-desacetyl-rifabutin Cmax

End point title	25-O-desacetyl-rifabutin Cmax[16]

End point description:

Maximum observed plasma concentration (Cmax) for 25-O-desacetyl-rifabutin.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[16] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[17]	9[18]	0[19]	7[20]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	17.71 (± 78.3)	20.50 (± 97.9)	()	22.94 (± 39.7)
Day 4	25.33 (± 128.6)	28.03 (± 93.8)	()	28.33 (± 80.0)

Notes:

[17] - Patients analyzed: Day 1 = 9; Day 4 = 10

[18] - Patients analyzed: Day 1 = 9; Day 4 = 10

[19] - Patients did not receive BV100

[20] - Patients analyzed: Day 1 = 7; Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: 25-O-desacetyl-rifabutin tmax

End point title	25-O-desacetyl-rifabutin tmax[21]

End point description:

Time of occurrence of Cmax (tmax) for 25-O-desacetyl-rifabutin.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[21] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[22]	9[23]	0[24]	7[25]
Units: hours				
median (full range (min-max))				
Day 1	4.00 (1.00 to 11.92)	2.02 (1.00 to 11.95)	(to)	4.00 (1.03 to 11.98)
Day 4	2.02 (0.50 to 12.00)	2.00 (0.00 to 12.00)	(to)	2.01 (0.98 to 4.08)

Notes:

[22] - Patients analyzed: Day 1 = 9; Day 4 = 10

[23] - Patients analyzed: Day 1 = 9; Day 4 = 10

[24] - Patients did not receive BV100

[25] - Patients analyzed: Day 1 = 7; Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: 25-O-desacetyl-rifabutin: AUC0-12

End point title	25-O-desacetyl-rifabutin: AUC0-12[26]

End point description:

Area under the concentration-time curve from dosing (time 0) to 12h (AUC0-12) for 25-O-desacetyl-rifabutin.

End point type	Primary

End point timeframe:

Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[26] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[27]	4[28]	0[29]	1[30]
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	198.3 (± 35.4)	232.6 (± 56.7)	()	142.6 (± 99999)
Day 4	220.9 (± 106.5)	178.8 (± 81.5)	()	292.8 (± 60.5)

Notes:

[27] - Patients analyzed: Day 1 = 4; Day 4 = 8

[28] - Patients analyzed: Day 1 = 4; Day 4 = 7

[29] - Patients did not receive BV100

[30] - Patients analyzed: Day 1 = 1; Day 4 = 4. '99999' = CV not calculated as only 1 patient was evaluable

Statistical analyses

No statistical analyses for this end point

Primary: DMI Cmax

End point title	DMI Cmax[31]

End point description:

Maximum observed plasma concentration (Cmax) for DMI.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[31] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[32]	11[33]	0[34]	7[35]
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Day 1	12.62 (± 29.7)	14.32 (± 49.9)	()	20.51 (± 37.7)
Day 4	21.70 (± 40.2)	22.19 (± 36.5)	()	48.74 (± 23.7)

Notes:

[32] - Patients analyzed: Day 1 = 10; Day 4 = 9

[33] - Patients analyzed: Day 1 = 11; Day 4 = 11

[34] - Patients did not receive BV100

[35] - Patients analyzed: Day 1 = 7; Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: DMI tmax

End point title	DMI tmax[36]

End point description:

Time of occurrence of Cmax (tmax) for DMI.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[36] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[37]	11[38]	0[39]	7[40]
Units: hours				
median (full range (min-max))				
Day 1	2.00 (0.47 to 4.02)	2.00 (0.10 to 12.00)	(to)	2.00 (0.08 to 4.00)
Day 4	2.00 (0.10 to 12.00)	2.00 (0.50 to 12.00)	(to)	1.51 (0.98 to 2.08)

Notes:

[37] - Patients analyzed: Day 1 = 10; Day 4 = 9

[38] - Patients analyzed: Day 1 = 11; Day 4 = 11

[39] - Patients did not receive BV100

[40] - Patients analyzed: Day 1 = 7; Day 4 = 6

Statistical analyses

No statistical analyses for this end point

Primary: DMI AUC0-12

End point title	DMI AUC0-12[41]

End point description:

Area under the concentration-time curve from dosing (time 0) to 12h (AUC0-12) for DMI.

End point type	Primary

End point timeframe:

PK blood sampling:
Days 1 and 4: prior to first BV100 infusion, 5 min, 30 min, and 1, 2, 4, 8, and 12 hours post-infusion.
Day 2: prior to first BV100 infusion.
Days 5 and 9: prior to first BV100 infusion, 5 min post-infusion (if still on trial drugs).

Notes:

[41] - 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: All analyses were descriptive in nature and no formal statistical comparisons of data from different arms or trial parts were done.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[42]	9[43]	0[44]	4[45]
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)				
Day 1	89.48 (± 39.3)	99.96 (± 38.6)	()	162.6 (± 15.6)
Day 4	181.0 (± 50.5)	178.7 (± 48.9)	()	460.8 (± 36.8)

Notes:

[42] - Patients analyzed: Day 1 = 6; Day 4 = 9

[43] - Patients analyzed: Day 1 = 9; Day 4 = 8

[44] - Patients did not receive BV100

[45] - Patients analyzed: Day 1 = 4; Day 4 = 4

Statistical analyses

No statistical analyses for this end point

Secondary: ACM rates 14 and 28 days after randomization

End point title	ACM rates 14 and 28 days after randomization[46]

End point description:

The incidence of ACM within 14 and 28 days after randomization was obtained by collecting the survival status through 23:59 (24-hour clock) on Day 14 and Day 28 (EoS Visit) as either alive or dead.

ACM rates are presented for the micro-CRMITT population.

In Part A, the BV100 200 mg + polymyxin B group had the lowest ACM rates at both Day 14 (11.1%) and Day 28 (11.1%). A low ACM rate at Day 14 also occurred in the BV100 300 mg + polymyxin B group (14.3%) but was notably increased at Day 28 (42.9%). The BAT group had the highest ACM rates at both Day 14 (40.0%) and Day 28 (60.0%). Overall, ACM rates increased across all treatment groups from Day 14 (23.1%) to Day 28 (38.5%). There were no deaths attributed to trial treatment.

End point type	Secondary

End point timeframe:

All-cause mortality (ACM) rates at 14 and 28 days, counted as the calendar days from first exposure to treatment.

Notes:

[46] - 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: There were no patients in the BV100 300 mg + BAT (Part B) group for the population being reported for this endpoint (micro-CRMITT population).

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9[47]	7[48]	10[49]	
Units: percentage				
number (confidence interval 95%)				
ACM rate at Day 14	11.1 (0.28 to 48.25)	14.3 (0.36 to 57.87)	40.0 (12.16 to 73.76)	
ACM rate at Day 28	11.1 (0.28 to 48.25)	42.9 (9.90 to 81.59)	60.0 (26.24 to 87.84)	

Notes:

[47] - Number of deaths: Day 14 = 1, Day 28 = 1

[48] - Number of deaths: Day 14 = 1, Day 28 = 3

[49] - Number of deaths: Day 14 = 4, Day 28 = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure status at EoT

End point title	Clinical cure status at EoT[50]

End point description:

Clinical Cure data at EoT are presented for the micro-CRMITT population.

At EoT, clinical cure was achieved in 18 patients (69.2%) overall. Clinical cure rates were greater in the BV100 300 mg + polymyxin B group (6 patients; 85.7%) and the BV100 200 mg + polymyxin B group (7 patients; 77.8%), compared to the BAT group (5 patients; 50.0%). The highest rate of clinical failure at EoT occurred in the BAT group (5 patients; 50.0%).

End point type	Secondary

End point timeframe:

Clinical cure status (cure, failure, indeterminate) assessed by the Investigator at the End of Treatment (EoT) and Test of Cure (ToC) Visits.

Notes:

[50] - 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: There were no patients in the BV100 300 mg + BAT group for the population being reported for this endpoint (micro-CRMITT population).

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9[51]	7[52]	10[53]	
Units: subjects				
Clinical cure	7	6	5	
Clinical failure	2	1	5	
Indeterminate	0	0	0	

Notes:

[51] - Percentages: Clinical cure = 77.8%; Clinical failure = 22.2%; Indeterminate = 0%

[52] - Percentages: Clinical cure = 85.7%; Clinical failure = 14.3%; Indeterminate = 0%

[53] - Percentages: Clinical cure = 50.0%; Clinical failure = 50.0%; Indeterminate = 0%

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure status at ToC

End point title	Clinical cure status at ToC[54]

End point description:

Clinical Cure data at ToC are presented for the micro-CRMITT population.

At ToC, clinical cure was achieved in 15 patients (57.7%) overall. Clinical cure rates remained high and unchanged (from EoT) for the BV100 300 mg + polymyxin B group (6 patients; 85.7%). For the BV100 200 mg + polymyxin B group, a slight decrease in clinical cure rate occurred (6 patients; 66.7%), and

the BAT group had a notable decrease (3 patients; 30.0%). The clinical cure rate in the combined BV100 + polymyxin B treatment groups was 75.0% (12 patients). The highest rate of clinical failure at ToC occurred in the BAT group (7 patients; 70.0%).

End point type	Secondary

End point timeframe:

Clinical cure status (cure, failure, indeterminate) assessed by the Investigator at the EoT and ToC Visits.

Notes:

[54] - 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: There were no patients in the BV100 300 mg + BAT B (Part B) group for the population being reported for this endpoint (micro-CRMITT population).

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9[55]	7[56]	10[57]	
Units: subjects				
Clinical cure	6	6	3	
Clinical failure	3	1	7	
Indeterminate	0	0	0	

Notes:

[55] - Percentages: Clinical cure = 66.7%; Clinical failure = 33.3%; Indeterminate = 0%

[56] - Percentages: Clinical cure = 85.7%; Clinical failure = 14.3%; Indeterminate = 0%

[57] - Percentages: Clinical cure = 30.0%; Clinical failure = 70.0%; Indeterminate = 0%

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in PaO2/FiO2 Ratio

End point title	Change from Baseline in PaO2/FiO2 Ratio

End point description:

Changes from Baseline in PaO2/FiO2 ratio are presented for the micro-ITT population.

At Baseline, most patients (74.4%) had a PaO2/FiO2 ratio of ≤ 240 and the overall mean (SD) ratio was 208.1 (60.62), with a range of 115.0 to 423.0. The overall mean (SD) change from Baseline was 22.5 (73.17) at EoT and 55.2 (121.1) at ToC.

End point type	Other pre-specified

End point timeframe:

PaO2/FiO2 ratio and the change from Baseline by treatment group and over time on Days 3, 5, 7, 10, EoT, ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[58]	11[59]	10[60]	8[61]
Units: change from Baseline				
arithmetic mean (standard deviation)				
Baseline	187.40 (± 45.206)	224.45 (± 53.097)	187.30 (± 31.380)	237.70 (± 96.833)

Day 3	29.45 (± 64.515)	-15.45 (± 84.131)	4.87 (± 51.212)	-24.33 (± 57.015)
Day 5	18.70 (± 54.928)	-7.80 (± 48.641)	-0.70 (± 27.272)	11.33 (± 110.937)
Day 7	43.60 (± 60.645)	18.13 (± 64.146)	2.44 (± 53.247)	5.80 (± 105.493)
Day 10	55.25 (± 79.874)	19.00 (± 78.042)	1.89 (± 70.988)	63.33 (± 173.463)
EoT	53.10 (± 71.482)	28.27 (± 69.078)	16.00 (± 75.584)	-15.38 (± 72.419)
ToC	81.89 (± 139.050)	54.10 (± 90.235)	74.20 (± 156.126)	-9.60 (± 118.473)

Notes:

[58] - Patients assessed: Baseline to Day 7, EoT (n=10); Day 10 (n=8); ToC (n=9)

[59] - Patients assessed: Baseline, Day 3, EoT (n=11); Day 5, ToC (n=10); Day 7 (n=8); Day 10 (n=5)

[60] - Patients assessed: Baseline, Day 3, EoT (n=10); Days 5, 7, 10 (n=9); ToC (n=5)

[61] - Patients assessed: Baseline, EoT (n=8); Days 3, 5 (n=6); Day 7, ToC (n=5); Day 10 (n=3)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in mCPIS

End point title	Change from Baseline in mCPIS

End point description:

Changes from Baseline in mCPIS are presented for the micro-ITT population.

The mean (SD) mCPIS at Baseline was similar across all treatment groups. The overall mean (SD) change from Baseline at ToC was -5.5 (2.57).

End point type	Other pre-specified

End point timeframe:

Overall scores and the change from Baseline in modified Clinical Pulmonary Infection Score (mCPIS) on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[62]	11[63]	10[64]	8[65]
Units: Change from Baseline				
arithmetic mean (standard deviation)				
Baseline	8.7 (± 2.31)	9.0 (± 2.61)	9.5 (± 1.51)	8.3 (± 1.39)
Day 3	-2.3 (± 1.95)	-3.7 (± 3.00)	-3.0 (± 2.54)	-1.7 (± 1.86)
Day 5	-2.9 (± 1.60)	-5.1 (± 2.51)	-3.7 (± 2.35)	-2.3 (± 1.21)
Day 7	-3.3 (± 2.06)	-5.0 (± 2.93)	-3.9 (± 2.93)	-3.2 (± 1.64)
Day 10	-3.8 (± 2.43)	-4.8 (± 2.59)	-3.9 (± 2.71)	-4.0 (± 3.61)
EoT	-5.3 (± 2.06)	-4.9 (± 3.39)	-4.9 (± 2.77)	-3.6 (± 2.67)
ToC	-5.3 (± 2.60)	-5.4 (± 2.76)	-6.0 (± 3.61)	-5.6 (± 1.52)

Notes:

[62] - Patients assessed: Baseline to Day 7 (n=10); Day 10 (n=8); EoT (n=10); ToC (n=9)

[63] - Patients assessed: Baseline, Day 3, EoT (n=11); Day 5, ToC (n=10); Day 7 (n=8); Day 10 (n=5)

[64] - Patients assessed: Baseline, Day 3, EoT (n=10); Days 5, 7, 10 (n=9); ToC (n=5)

[65] - Patients assessed: Baseline, EoT (n=8); Days 3, 5 (n=6); Day 7, ToC (n=5); Day 10 (n=3)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in SOFA Scores

End point title	Change from Baseline in SOFA Scores

End point description:

Change from Baseline in SOFA scores are presented for the micro-ITT population.

The mean (SD) SOFA score at Baseline was similar across all treatment groups. The overall mean (SD) change from Baseline at ToC was -0.9 (2.53).

End point type	Other pre-specified

End point timeframe:

Overall scores and the change from Baseline in Sequential Organ Failure Assessment (SOFA) scores on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[66]	11[67]	10[68]	8[69]
Units: Change from Baseline				
arithmetic mean (standard deviation)				
Baseline	5.8 (± 1.87)	6.1 (± 1.04)	6.8 (± 1.87)	6.8 (± 3.37)
Day 3	0.7 (± 2.54)	0.6 (± 1.57)	-0.3 (± 1.34)	0.3 (± 1.63)
Day 5	0.3 (± 2.95)	-0.2 (± 1.48)	-1.0 (± 1.87)	1.7 (± 2.94)
Day 7	0.2 (± 3.29)	-0.1 (± 1.96)	-1.7 (± 3.04)	3.0 (± 3.67)
Day 10	-0.1 (± 2.23)	0.6 (± 1.34)	-1.2 (± 2.17)	1.3 (± 3.51)
EoT	0.2 (± 1.62)	-0.8 (± 2.75)	-1.3 (± 2.16)	2.4 (± 4.14)
ToC	-0.1 (± 2.62)	-2.0 (± 2.62)	-1.6 (± 1.52)	0.8 (± 2.17)

Notes:

[66] - Patients assessed: Baseline to Day 7 (n=10); Day 10 (n=8); EoT (n=10); ToC (n=9)

[67] - Patients assessed: Baseline, Day 3, EoT (n=11); Day 5, ToC (n=10); Day 7 (n=8); Day 10 (n=5)

[68] - Patients assessed: Baseline, Day 3, EoT (n=10); Days 5, 7, 10 (n=9); ToC (n=5)

[69] - Patients assessed: Baseline, EoT (n=8); Days 3, 5 (n=6); Day 7, ToC (n=5); Day 10 (n=3)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Days Spent in ICU

End point title	Days Spent in ICU

End point description:

The number of days in the ICU are presented for the micro-ITT population.

The overall mean (SD) number of days in ICU over a 28-day period was 25.5 (3.97) days and up to hospital discharge was 25.7 (4.14) days. In a sensitivity analysis, the overall mean (SD) number of days in ICU over a 28-day period was 25.5 (3.97) days.

End point type	Other pre-specified

End point timeframe:

The number of calendar days in the Intensive Care Unit (ICU) from randomization up to and including Day 28.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: Days				
arithmetic mean (standard deviation)				
Days in ICU over 28-day Period	26.5 (± 2.59)	24.6 (± 4.01)	24.2 (± 5.69)	26.9 (± 2.23)
Days in ICU up to Hospital Discharge	26.7 (± 2.75)	25.0 (± 4.43)	24.2 (± 5.69)	27.1 (± 2.42)
Days in ICU over 28-day Period (sensitivity)	26.5 (± 2.59)	24.6 (± 4.01)	24.2 (± 5.69)	26.9 (± 2.23)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Hospital Stay

End point title	Hospital Stay

End point description:

The number of hospital days are presented for the micro-ITT population.

The overall mean (SD) number of hospital days over a 28-day period was 26.9 (2.33) days and up to hospital discharge was 27.2 (2.51) days.

End point type	Other pre-specified

End point timeframe:

The number of calendar days in the hospital from randomization up to and including Day 28.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: Days				
arithmetic mean (standard deviation)				
Hospital days over a 28-day Period	27.4 (± 1.26)	26.0 (± 2.72)	26.6 (± 3.27)	28.0 (± 0.00)
Hospital days up to Hospital Discharge	27.6 (± 1.43)	26.4 (± 3.14)	26.7 (± 3.33)	28.33 (± 0.46)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of VFDs

End point title	Number of VFDs

End point description:

The number of VFDs are presented for the micro-ITT population.

The overall mean (SD) number of VFDs over a 28-day period was 5.6 (8.67) days. In a sensitivity analysis, the overall mean (SD) number of VFDs over a 28-day period was 6.6 (8.79) days.

End point type	Other pre-specified

End point timeframe:

The number of ventilator-free days (VFDs) from randomization over a 28-day period.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: Days				
arithmetic mean (standard deviation)				
VFDs over a 28-day Period	8.2 (± 9.45)	6.8 (± 9.73)	3.9 (± 7.46)	2.8 (± 7.78)
VFDs over a 28-day Period (sensitivity)	8.2 (± 9.45)	8.8 (± 9.87)	5.2 (± 7.83)	3.3 (± 7.70)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Clinical Response at ToC - Change in Fever

End point title	Clinical Response at ToC - Change in Fever

End point description:

Assessment of clinical response (improved, worsened, stable, or unchanged) included the evaluation of signs and symptoms of pneumonia.

Clinical response data are presented for the micro-ITT population.

In general, the majority of clinical response parameters improved or remained unchanged from Baseline to ToC, except for variations in oxygenation (PaO2/FiO2 ratio) across several timepoints. Respiratory secretions and ventilator settings showed an increase in the percentage of patients with worsened values at ToC, compared to Baseline.

End point type	Other pre-specified

End point timeframe:

Clinical response was assessed on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: subjects				
Improved	6	6	5	0
Worsened	1	1	5	4
Stable	2	2	0	3
Unchanged	1	2	0	1
Not assessed	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Clinical Response at ToC - Presence or absence of respiratory secretions

End point title	Clinical Response at ToC - Presence or absence of respiratory secretions

End point description:

Clinical response data are presented for the micro-ITT population.

End point type	Other pre-specified

End point timeframe:

Clinical response was assessed on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: subjects				
Improved	7	4	4	5
Worsened	1	1	5	3
Stable	0	1	1	0
Unchanged	2	5	0	0
Not assessed	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Clinical Response at ToC - Changes in purulence of respiratory secretions

End point title	Clinical Response at ToC - Changes in purulence of respiratory secretions

End point description:

Clinical response data are presented for the micro-ITT population.

End point type	Other pre-specified

End point timeframe:

Clinical response was assessed on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: subjects				
Improved	4	3	1	5
Worsened	1	1	5	3
Stable	0	0	1	0
Unchanged	5	7	3	0
Not assessed	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Clinical Response at ToC - Changes in oxygenation parameters (PaO2/FiO2)

End point title	Clinical Response at ToC - Changes in oxygenation parameters (PaO2/FiO2)

End point description:

Clinical response data are presented for the micro-ITT population.

End point type	Other pre-specified

End point timeframe:

Clinical response was assessed on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: subjects				
Improved	5	6	2	3
Worsened	4	3	7	5
Stable	1	0	0	0
Unchanged	0	2	1	0
Not assessed	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Clinical Response at ToC - Changes in ventilator settings

End point title	Clinical Response at ToC - Changes in ventilator settings

End point description:

Clinical response data are presented for the micro-ITT population.

End point type	Other pre-specified

End point timeframe:

Clinical response was assessed on Days 3, 5, 7, 10, EoT, and ToC.

End point values	BV100 200 mg + Polymyxin B (Part A)	BV100 300 mg + Polymyxin B (Part A)	BAT (Part A)	BV100 300 mg + BAT (Part B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	8
Units: subjects				
Improved	5	6	3	5
Worsened	1	1	5	3
Stable	0	0	1	0
Unchanged	4	4	1	0
Not assessed	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs and SAEs were to be collected at every visit (from the signing of the ICF until End of Study).

All SAEs and AESIs were to be followed until resolution, stabilization, the event was otherwise explained, or the patient was lost to follow-up.

Adverse event reporting additional description:

AEs were analyzed in the Safety Population.

TEAEs occurred in 34 patients (87.2%) overall, with a total of 108 events.

Values provided are for TEAEs, defined as those that first occurred or worsened following the start of trial treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Polymyxin B + BV100 (200) - Part A
Reporting group description: -	
Reporting group title	Polymyxin B + BV100 (300) - Part A
Reporting group description: -	
Reporting group title	BAT - Part A
Reporting group description: -	
Reporting group title	BAT + BV100 (300) - Part B

Reporting group description:

All data reported are treatment-emergent events.

Serious adverse events	Polymyxin B + BV100 (200) - Part A	Polymyxin B + BV100 (300) - Part A	BAT - Part A
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	5 / 11 (45.45%)	6 / 10 (60.00%)
number of deaths (all causes)	1	5	6
number of deaths resulting from adverse events	1	5	6
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
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			
Shock			

subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (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			
Cardiac arrest			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Cardiogenic shock			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Cerebrovascular accident			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration			

site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
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 acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Septic shock			
subjects affected / exposed	2 / 10 (20.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0

Serious adverse events	BAT + BV100 (300) - Part B		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Injury, poisoning and procedural complications			
Intestinal anastomosis complication			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Shock				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac arrest				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain oedema				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Liver injury			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Polymyxin B + BV100 (200) - Part A	Polymyxin B + BV100 (300) - Part A	BAT - Part A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	9 / 11 (81.82%)	6 / 10 (60.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 10 (20.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Platelet count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhythm idioventricular			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Intraventricular haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	2 / 10 (20.00%)	3 / 11 (27.27%)	0 / 10 (0.00%)
occurrences (all)	2	3	0
Thrombocytopenia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastric haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	3 / 10 (30.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	3	1	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Renal impairment			
subjects affected / exposed	5 / 10 (50.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	5	2	2
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematological infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Klebsiella infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pseudomonas infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Septic shock			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Systemic candida			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Hypocalcaemia			

subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	2	1	3
Hypomagnesaemia			
subjects affected / exposed	2 / 10 (20.00%)	5 / 11 (45.45%)	2 / 10 (20.00%)
occurrences (all)	2	5	2

Non-serious adverse events	BAT + BV100 (300) - Part B		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Platelet count decreased			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) Bradycardia subjects affected / exposed occurrences (all) Rhythm idioventricular subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0		
Nervous system disorders Intraventricular haemorrhage subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 2 / 8 (25.00%) 2 1 / 8 (12.50%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastric haemorrhage subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0		
Hepatobiliary disorders			

Hepatic function abnormal subjects affected / exposed occurrences (all) Hyperbilirubinaemia subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Skin and subcutaneous tissue disorders Skin ulcer subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all) Renal impairment subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Infections and infestations Abdominal infection subjects affected / exposed occurrences (all) Clostridium difficile infection subjects affected / exposed occurrences (all) Haematological infection subjects affected / exposed occurrences (all) Klebsiella infection subjects affected / exposed occurrences (all) Pseudomonas infection subjects affected / exposed occurrences (all) Septic shock	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Systemic candida			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypernatraemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 May 2024	All patients in the trial were randomized/enrolled under Protocol Version 1 (03 October 2022). Protocol Version 2/Amendment 1 (28 May 2024) was approved after patient enrollment was completed; therefore, no patients were enrolled or treated under Version 2. However, all patient data were included to the analysis under Protocol Version 2. As a result, Protocol Version 1 served as the reference version for the CSR. Errors, omissions, or changes implemented in Protocol Version 2 were noted in the CSR where applicable. The overall rationale for Protocol Version 2 (Amendment 1) was to add the following substantial changes: • Clarify Acinetobacter baumannii vs CRAB • Add ToC Visit to Protocol text, where needed • Add when a patient can be switched from Part A to Part B • Clarify polymyxin B references • Clarify when to collect VIP scoring • Clarify timing between Acinetobacter baumannii diagnosis and SARS CoV-2 • Revise upper age limit to be included in the trial • Clarify patients have to be mechanically ventilated continuously to be included in the trial • Clarify for SOFA and mCPIS that if a local laboratory value is not available on the date of a visit, the most recent local laboratory value should be used • Revise frequency of vital signs to once per day • Clarify inclusion criteria regarding what qualifies as documented infection • Clarify exclusion criteria regarding evidence of infection outside the respiratory tract • Revise exclusion criteria regarding QTcF parameter from electrocardiogram

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This phase 2 study was primarily designed to assess PK and was not powered to draw definitive conclusions on efficacy. The study was conducted in a rare, critically ill population with limited sample size. The data should be interpreted with caution.

Notes: