Clinical trial results:
A prospective, randomized, open-label, comparative study to assess the efficacy, safety and tolerability of aztreonam-avibactam (ATM-AVI) and best available therapy for the treatment of serious infections due to multi-drug resistant gram-negative bacteria producing metallo--lactamase (MBL)

Summary

EudraCT number	2017-004544-38
Trial protocol	GR RO
Global end of trial date	23 January 2023

Results information

Result version number	v1 (current)
This version publication date	28 January 2024
First version publication date	28 January 2024

Trial information

Trial identification

Sponsor protocol code	C3601009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03580044
WHO universal trial number (UTN)	-
Other trial identifiers	Assemble: Other study ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	30 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, of aztreonam- avibactam (ATM- AVI) and best available therapy (BAT) at the Test of Cure (TOC) visit in the microbiological Intent- To-Treat (micro-ITT) population for the treatment of selected serious infections that are due to MBL-producing Gram-negative bacteria.

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 Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 December 2020
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	China: 2
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	India: 1
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Philippines: 1
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Thailand: 1
Worldwide total number of subjects	15
EEA total number of subjects	5

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	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects hospitalized with a diagnosis of complicated intra-abdominal infection (cIAI), nosocomial pneumonia (NP) including hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), complicated urinary tract infection (cUTI), or bloodstream infections (BSI) due to producing Gram-negative bacteria were enrolled.

Pre-assignment

Screening details:

A total of 15 subjects signed the informed consent form and were randomized in the study. This study was conducted across 9 countries from 25 Dec-2020 to 23-Jan-2023. The study was terminated as recruitment of subjects with serious infections caused by gram-negative bacteria producing MBL was challenging.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Aztreonam- Avibactam (ATM- AVI)

Arm description:

Subjects were administered a loading dose of aztreonam- avibactam (ATM-AVI) by intravenous (IV) infusion over 30 minutes immediately followed by an extended loading dose of ATM-AVI by infusion over 3 hours, and then started a maintenance dose of ATM-AVI by IV infusion over 3 hours on Day 1. Subjects with creatinine clearance >50 milliliters per minute (mL/min) and >30 to 50 mL per minute were administered maintenance dose once every 6 hours for maximum of 14 days. Subjects with creatinine clearance >15 to 30 mL/min were administered maintenance dose once every 8 hours for maximum of 14 days. Subjects with cIAI also received metronidazole (MTZ) 500 milligram (mg) every 8 hours by IV infusion over 60 minutes.

Arm type	Experimental
Investigational medicinal product name	Aztreonam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Aztreonam 2 gram powder concentrate for infusion.

Investigational medicinal product name	Metronidazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Metronidazole 500 mg/100 millilitre (mL) solution for infusion.

Investigational medicinal product name	Avibactam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avibactam 600 milligrams (mg) powder concentrate for infusion.

Arm title	Best Available Therapy (BAT)

Arm description:

Subjects who were hospitalized with a diagnosis of cIAI, NP, HAP, VAP, cUTI or BSI received Best Available Therapy (BAT) based upon site practice and local epidemiology for a maximum of 14 days. Subjects with cIAI in the BAT arm received metronidazole if BAT did not provide adequate anaerobic coverage.

Arm type	Active comparator
Investigational medicinal product name	BAT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Based on investigative site practice and local epidemiology.

Number of subjects in period 1	Aztreonam-Avibactam (ATM-AVI)	Best Available Therapy (BAT)
Started	12	3
Treated	12	2
Completed	9	1
Not completed	3	2
Consent withdrawn by subject	1	1
Death	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Aztreonam- Avibactam (ATM- AVI)
Reporting group description:	
Subjects were administered a loading dose of aztreonam- avibactam (ATM-AVI) by intravenous (IV) infusion over 30 minutes immediately followed by an extended loading dose of ATM-AVI by infusion over 3 hours, and then started a maintenance dose of ATM-AVI by IV infusion over 3 hours on Day 1. Subjects with creatinine clearance >50 milliliters per minute (mL/min) and >30 to 50 mL per minute were administered maintenance dose once every 6 hours for maximum of 14 days. Subjects with creatinine clearance >15 to 30 mL/min were administered maintenance dose once every 8 hours for maximum of 14 days. Subjects with cIAI also received metronidazole (MTZ) 500 milligram (mg) every 8 hours by IV infusion over 60 minutes.	
Reporting group title	Best Available Therapy (BAT)
Reporting group description:	
Subjects who were hospitalized with a diagnosis of cIAI, NP, HAP, VAP, cUTI or BSI received Best Available Therapy (BAT) based upon site practice and local epidemiology for a maximum of 14 days. Subjects with cIAI in the BAT arm received metronidazole if BAT did not provide adequate anaerobic coverage.	

Reporting group values	Aztreonam-Avibactam (ATM-AVI)	Best Available Therapy (BAT)	Total
Number of subjects	12	3	15
Age Categorical Units: Subjects			
<65 years	8	2	10
65-74 years	3	1	4
75-84 years	1	0	1
Age Continuous Units: Years			
arithmetic mean	56.6	65.7	
standard deviation	± 17.14	± 6.66	-
Sex: Female, Male Units: Subjects			
Female	4	2	6
Male	8	1	9
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	6	1	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	2	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	11	3	14
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Aztreonam- Avibactam (ATM- AVI)

Reporting group description:

Subjects were administered a loading dose of aztreonam- avibactam (ATM-AVI) by intravenous (IV) infusion over 30 minutes immediately followed by an extended loading dose of ATM-AVI by infusion over 3 hours, and then started a maintenance dose of ATM-AVI by IV infusion over 3 hours on Day 1. Subjects with creatinine clearance >50 milliliters per minute (mL/min) and >30 to 50 mL per minute were administered maintenance dose once every 6 hours for maximum of 14 days. Subjects with creatinine clearance >15 to 30 mL/min were administered maintenance dose once every 8 hours for maximum of 14 days. Subjects with cIAI also received metronidazole (MTZ) 500 milligram (mg) every 8 hours by IV infusion over 60 minutes.

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

Subjects who were hospitalized with a diagnosis of cIAI, NP, HAP, VAP, cUTI or BSI received Best Available Therapy (BAT) based upon site practice and local epidemiology for a maximum of 14 days. Subjects with cIAI in the BAT arm received metronidazole if BAT did not provide adequate anaerobic coverage.

Primary: Percentage of Subjects With Clinical Cure at the Test of Cure (TOC) Visit - Microbiological Intent to Treat (Micro-ITT) Analysis Set

End point title	Percentage of Subjects With Clinical Cure at the Test of Cure (TOC) Visit -Microbiological Intent to Treat (Micro-ITT) Analysis Set[1]

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that no further antimicrobial treatment was required for the index infection (i.e., cIAI, cUTI, HAP/VAP or BSI) after study treatment. Also for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. The clinical response assessment was determined by a blinded independent adjudication committee. 95% confidence interval (CI) was calculated using Jeffrey's method. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. 99999 indicates data could not be calculated due to insufficient number of subjects.

End point type	Primary

End point timeframe:

Day 28

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 analysis was planned for this endpoint

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of subjects				
number (confidence interval 95%)	41.7 (18.0 to 68.8)	0.0 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Cure at the End of Treatment (EOT) Visit- Micro-ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure at the End of Treatment (EOT) Visit- Micro-ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that no further antimicrobial treatment was required for the index infection (i.e., cIAI, cUTI, HAP/VAP or BSI) after study treatment. Also for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. The clinical response assessment was determined by a blinded independent adjudication committee. 95% CI was calculated using Jeffrey's method. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. 99999 indicates data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of subjects				
number (confidence interval 95%)	58.3 (31.2 to 82.0)	0.0 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Cure at the TOC Visit- Microbiologically Evaluable (ME) Analysis Set

End point title	Percentage of Subjects With Clinical Cure at the TOC Visit- Microbiologically Evaluable (ME) Analysis Set

End point description:

Clinical cure = improvement in baseline signs and symptoms such that no further antimicrobial treatment was required for the index infection (i.e., cIAI, cUTI, HAP/VAP or BSI) after study treatment. Also, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. The clinical response assessment was determined by a blinded independent adjudication committee. 95% CI calculated using Jeffrey's method. ME analysis set: Subjects from micro-ITT who received at least 48 hours of study therapy or <48 hours before discontinuation due to an adverse event, no concomitant antibiotics against baseline MBL positive pathogens between 1st dose and TOC (excluding subjects with failed study therapy requiring additional antibiotics), had baseline organisms confirmed by central microbiological testing (except when locally confirmed) and no indeterminate clinical outcomes at TOC. 99999= data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of subjects				
number (confidence interval 95%)	55.6 (25.4 to 82.7)	0.0 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Cure at the EOT Visit- ME Analysis Set

End point title	Percentage of Subjects With Clinical Cure at the EOT Visit- ME Analysis Set

End point description:

Clinical cure: improvement in baseline signs and symptoms such that no further antimicrobial treatment was required for index infection (i.e. cIAI,cUTI,HAP/VAP or BSI)after study treatment.For cIAI subjects,no unplanned drainage or surgical intervention was necessary since the initial procedure.The clinical response assessment was determined by a blinded independent adjudication committee.95% CI was calculated using Jeffrey’s method.ME analysis set:Subjects from micro-ITT who received at least 48 hours of study therapy or <48 hours before discontinuation due to an adverse event, no concomitant antibiotics against baseline MBL positive pathogens between first dose of study therapy and TOC(excluding subjects with failed study therapy requiring additional antibiotics)had baseline organisms confirmed by central microbiological testing (except when locally confirmed) and no indeterminate clinical outcomes at TOC.99999=data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of subjects				
number (confidence interval 95%)	66.7 (34.8 to 89.6)	0.0 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Favorable Per Subject Microbiological Response at EOT Visit-Micro-ITT Analysis Set

End point title	Percentage of Subjects With a Favorable Per Subject Microbiological Response at EOT Visit-Micro-ITT Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication was defined as absence (or urine quantification <10^3 colony forming units per milliliter [CFU/mL] for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. Subjects with a per subject response of Indeterminate were excluded from this analysis. Here 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	1		
Units: Percentage of subjects				
number (not applicable)	81.82	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Favorable Per Subject Microbiological Response at TOC Visit-Micro-ITT Analysis Set

End point title	Percentage of Subjects With a Favorable Per Subject Microbiological Response at TOC Visit-Micro-ITT Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication was defined as absence (or urine quantification <10^3 colony forming units per milliliter [CFU/mL] for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. Subjects with a per subject response of Indeterminate were excluded from this analysis. Here 'Number of Subjects Analyzed' signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	1		
Units: Percentage of subjects				
number (not applicable)	60.00	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Favorable Per Subject Microbiological Response at EOT Visit-ME Analysis Set

End point title	Percentage of Subjects With a Favorable Per Subject Microbiological Response at EOT Visit-ME Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication was defined as absence (or urine quantification <10^3 CFU/mL for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). ME analysis set: Subjects from micro-ITT who received at least 48 hours of study therapy or <48 hours before discontinuation due to an adverse event; no concomitant antibiotics against baseline MBL positive pathogens between first dose of study therapy and TOC (excluding subjects with failed study therapy requiring additional antibiotics), had baseline organisms confirmed by central microbiological testing (except when locally confirmed) and no indeterminate clinical outcomes at TOC.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of subjects				
number (not applicable)	66.67	0.00		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Favorable Per Subject Microbiological Response at TOC Visit-ME Analysis Set

End point title	Percentage of Subjects With a Favorable Per Subject Microbiological Response at TOC Visit-ME Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication was defined as absence (or urine quantification <10^3 CFU/mL for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). ME analysis set: Subjects from micro-ITT who received at least 48 hours of study therapy or <48 hours before discontinuation due to an adverse event, no concomitant antibiotics against baseline MBL positive pathogens between first dose of study therapy and TOC (excluding subjects with failed study therapy requiring additional antibiotics), had baseline organisms confirmed by central microbiological testing (except when locally confirmed) and no indeterminate clinical outcomes at TOC.

End point type	Secondary

End point timeframe:

Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of subjects				
number (not applicable)	66.7	0.00		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the EOT Visit-Micro-ITT Analysis Set

End point title	Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the EOT Visit-Micro-ITT Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication: absence (or urine quantification <10^3 CFU/mL for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. Here, n= pathogens evaluable for specified rows. 99999 indicates data could not be calculated due to insufficient pathogen.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of pathogens				
number (not applicable)				
Enterobacterales (n=12,3)	75.0	0.0		
Pseudomonas aeruginosa (n=2,0)	50.0	99999		
Stenotrophomonas maltophilia (n=3,0)	66.7	99999		
Enterococcus faecium (n=1,0)	100.0	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the TOC Visit-Micro-ITT Analysis Set

End point title	Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the TOC Visit-Micro-ITT Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication: absence (or urine quantification <10^3 CFU/mL for cUTI subjects) of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication was defined as repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subject).Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment. n= pathogens evaluable for specified rows. 99999 indicates data could not be calculated due to insufficient pathogen.

End point type	Secondary

End point timeframe:

Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of pathogens				
number (not applicable)				
Enterobacterales (n=12,3)	50.0	0.00		
Pseudomonas aeruginosa (n=2,0)	0.0	99999		
Stenotrophomonas maltophilia (n=3,0)	33.3	99999		
Enterococcus faecium (n=1,0)	0.0	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the EOT Visit-ME Analysis Set

End point title	Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the EOT Visit-ME Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication: absence (or urine quantification <10^3 CFU/mL for cUTI subjects)of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication: repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). ME analysis set: Subjects from micro-ITT who received at least 48 hours or <48 hours of study therapy before discontinuation due to AE,no concomitant antibiotics against baseline MBL positive pathogens between 1st dose and TOC (excluding those with failed study therapy requiring additional antibiotics),had baseline organisms confirmed by central microbiological testing (except when locally confirmed);no indeterminate clinical outcomes at TOC. n= pathogens evaluable for specified rows. 99999= data could not be calculated due to insufficient pathogens.

End point type	Secondary

End point timeframe:

Up to 24 hours after the last infusion on Day 14

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of pathogens				
number (not applicable)				
Enterobacterales (n=10,1)	80.0	0.0		
Stenotrophomonas maltophilia (n=2,0)	100.0	99999		
Enterococcus faecium (n=1,0)	100.0	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the TOC Visit-ME Analysis Set

End point title	Percentage of Pathogens According to Favourable Per-Pathogen Microbiological Response at the TOC Visit-ME Analysis Set

End point description:

Favorable microbiological response was defined as eradication or presumed eradication. Eradication:absence (or urine quantification <10^3 CFU/mL for cUTI subjects)of causative pathogen from an appropriately obtained specimen at the site of infection. Presumed eradication: repeat culture of specimens were not performed/clinically indicated in a subject who had a clinical response of cure (specific to cIAI and HAP/VAP subjects). ME analysis set: Subjects from micro-ITT who received at least 48 hours or <48 hours of study therapy before discontinuation due to AE,no concomitant antibiotics against baseline MBL positive pathogens between 1st dose and TOC (excluding those with failed study therapy requiring additional antibiotics),had baseline organisms confirmed by central microbiological testing (except when locally confirmed);no indeterminate clinical outcomes at TOC. n= pathogens evaluable for specified rows. 99999= data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	1		
Units: Percentage of pathogens				
number (not applicable)				
Enterobacterales (n= 10,1)	60.0	0.0		
Stenotrophomonas maltophilia (n=2,0)	50.0	99999		
Enterococcus faecium (n=1,0)	0.0	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Died Within 28 Days From Randomisation- Micro ITT Analysis Set

End point title	Percentage of Subjects who Died Within 28 Days From Randomisation- Micro ITT Analysis Set

End point description:

Percentage of subjects who died due to any cause on or before 28 days after randomisation were reported in this this endpoint. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least 1 MBL-positive Gram-negative baseline pathogen from an adequate specimen at the start of study treatment.

End point type	Secondary

End point timeframe:

From randomisation up to Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of subjects				
number (not applicable)	8.3	33.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Died Within 28 Days From Randomisation-ITT Analysis Set

End point title	Percentage of Subjects who Died Within 28 Days From Randomisation-ITT Analysis Set

End point description:

Percentage of subjects who died due to any cause on or before 28 days after randomisation were reported in this endpoint. ITT analysis set included all randomized subjects regardless of receipt of study drug.

End point type	Secondary

End point timeframe:

From randomisation up to Day 28

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	3		
Units: Percentage of subjects				
number (not applicable)	8.3	33.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events and Serious Adverse Events

End point title	Number of Subjects With Treatment Emergent Adverse Events and Serious Adverse Events

End point description:

An adverse event (AE) was any untoward medical occurrence in a study subject administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. A serious adverse event (SAE) was any untoward medical occurrence at any dose that: resulted in death; was life-threatening (immediate risk of death); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/ incapacity; resulted in congenital anomaly/birth defect; considered an important medical event. Treatment-emergent adverse event (TEAE) was any AE that started after the study medication start date and time. Safety analysis set included all subjects who received any amount of study treatment. Subjects were analysed according to the treatment they received.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) until late follow-up visit (Up to Day 45)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	2		
Units: Subjects				
TEAEs	11	2		
SAEs	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Sign Abnormalities

End point title	Number of Subjects With Vital Sign Abnormalities

End point description:

Vital signs included blood pressure and heart rate and were measured in a supine position after at least 10 minutes of rest for the subjects. Criteria for vital sign abnormalities included: systolic blood pressure (SBP): value >150 millimeters of mercury (mmHg) and increase from baseline >=30 mmHg and value <90 and decrease from baseline >=30. Diastolic BP (DBP) (mm Hg) Value >100 and increase from baseline >= 20 and Value <50 and decrease from baseline >=20. Heart Rate (beats per minute [BPM]) Value <40 or >120. Safety analysis set included all subjects who received any amount of study treatment. Subjects were analyzed according to the treatment they received. Here 'Number of Subjects Analysed' signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) until TOC (Up to Day 28)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	2		
Units: Subjects				
SBP: Value >150 and increase from baseline >=30	3	0		
SBP: Value <90 and decrease from baseline >=30	0	1		
DBP: Value >100 and increase from baseline >=20	0	0		
DBP: Value <50 and decrease from baseline >=20	0	0		
Heart Rate (BPM): <40 or >120	6	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Physical Examination Findings

End point title	Number of Subjects With Abnormal Physical Examination Findings

End point description:

Physical examination included assessment of the following: abdomen, cardiovascular, ears, eyes, general appearance, head, lungs, lymph nodes, musculoskeletal, neurological, nose, skin and throat. Number of subjects with abnormal physical examination findings for each body system is reported in this outcome measure. Safety analysis set included all subjects who received any amount of study treatment. Subjects were analyzed according to the treatment they received. Here, 'Number Analyzed'= subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Baseline (last non-missing value observed before start of treatment on Day 1), EOT (Up to 24 hours after the last infusion on Day 14), TOC (Day 28)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	2		
Units: Subjects				
Abdomen - Baseline (n=12,2)	3	0		
Abdomen - End of Treatment (11,1)	4	0		
Abdomen -Test of cure (8,1)	2	0		
Cardiovascular - Baseline (n=12,2)	1	2		
Cardiovascular - End of Treatment (11,1)	1	1		
Cardiovascular -Test of cure (8,1)	0	1		
Ears- Baseline (n=12,2)	0	0		
Ears - End of Treatment (11,1)	0	0		
Ears-Test of cure (8,1)	0	0		
Eyes - Baseline (n=12,2)	2	0		
Eyes - End of Treatment (11,1)	3	0		
Eyes -Test of cure (8,1)	1	0		
General Appearance- Baseline (n=12,2)	5	1		
General Appearance - End of Treatment (11,1)	3	0		
General Appearance-Test of cure (8,1)	0	0		
Head- Baseline (n=12,2)	2	0		
Head- End of Treatment (11,1)	2	0		
Head- Test of cure (8,1)	0	0		
Lungs- Baseline (n=12,2)	4	1		
Lungs-End of Treatment (11,1)	2	0		
Lungs-Test of cure (8,1)	1	0		
Lymph Nodes-Baseline (n=12,2)	0	0		
Lymph Nodes-End of Treatment (11,1)	0	0		
Lymph Nodes-Test of cure (8,1)	0	0		
Musculoskeletal-Baseline (n=12,2)	3	2		
Musculoskeletal-End of Treatment (11,1)	1	1		
Musculoskeletal-Test of cure (8,1)	1	1		
Neurological-Baseline (n=12,2)	8	1		

Neurological-End of Treatment (11,1)	5	0		
Neurological-Test of cure (8,1)	3	0		
Nose-Baseline (n=12,2)	1	0		
Nose-End of Treatment (11,1)	0	0		
Nose-Test of cure (8,1)	0	0		
Skin-Baseline (n=12,2)	5	0		
Skin-End of Treatment (11,1)	3	0		
Skin-Test of cure (8,1)	1	0		
Throat-Baseline (n=11,2)	0	1		
Throat-End of Treatment (11,1)	1	0		
Throat-Test of cure (8,1)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Hematology Assessments

End point title	Number of Subjects With Clinically Significant Abnormalities in Hematology Assessments

End point description:

Potential clinically significant criteria included: Hematocrit, hemoglobin and erythrocytes <0.7*lower limit of normal (LLN) and >30% Decrease from Baseline (DFB) or >1.3*upper limit of normal (ULN) and >30% Increase from Baseline (IFB); Leukocytes:<0.65*LLN and >60% DFB or >1.5*ULN and >100% DFB; Basophils/Leukocytes, Eosinophils/Leukocytes and Monocytes/Leukocytes:>4.0*ULN and >300% Increase from Baseline; Lymphocytes/Leukocytes <0.25*LLN and >75% DFB and >1.5* ULN and >100% IFB; Neutrophils/Leukocytes: <0.65*LLN and >75% DFB or >1.6*ULN and >100% IFB; Platelets<0.65*LLN and >50% DFB or >1.5*ULN and >100% IFB. Safety analysis set- all subjects who received any amount of study treatment. Subjects were analyzed according to the treatment received. All subjects reported under 'N' contributed data to the table but may not have evaluable data for every row. 'n'= subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) until TOC (Up to Day 28)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	2		
Units: Subjects				
Hematocrit: <0.7*LLN & >30% DFB (n=11,1)	0	0		
Hematocrit: >1.3*ULN & >30% IFB (n=11,1)	0	0		
Hemoglobin: <0.7*LLN & >30% DFB (n=11,1)	0	0		
Hemoglobin: >1.3*ULN & >30% IFB (n=11,1)	0	0		
Erythrocytes: <0.7*LLN & >30% DFB (n=11,1)	0	0		

Erythrocytes: >1.3*ULN & >30% IFB (n=11,1)	0	0		
Leukocytes: <0.65*LLN & >60% DFB (n=11,1)	0	0		
Leukocytes:>1.5*ULN & >100% IFB (n=11,1)	0	0		
Basophils/Leukocytes: >4.0*ULN & >300% IFB(n=11,1)	0	0		
Eosinophils/Leukocytes:>4.0*ULN& >300% IFB(n=11,1)	0	0		
Lymphocytes/Leukocytes: <0.25*LLN& >75%DFB(n=11,1)	0	0		
Lymphocytes/Leukocytes: >1.5*ULN&>100% IFB(n=11,1)	0	0		
Monocytes/Leukocytes:>4.0*ULN & >300% IFB (n=11,1)	0	0		
Neutrophils/Leukocytes:<0.65*LLN& >75% DFB(n=11,1)	0	0		
Neutrophils/Leukocytes: >1.6*ULN&>100% IFB(n=11,1)	0	0		
Platelets: <0.65*LLN & >50% DFB (n=11,1)	0	0		
Platelets: >1.5 *ULN & >100% IFB (n=11,1)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Clinical Chemistry Assessments

End point title	Number of Subjects With Clinically Significant Abnormalities in Clinical Chemistry Assessments

End point description:

Potential clinically significant criteria included: Aspartate Aminotransferase(AST) and Alanine Aminotransferase (ALT): >3.0*ULN and >100% IFB; Bilirubin: >1.5*ULN and >100% IFB;Direct Bilirubin: >2.0*ULN and >150% IFB; Alkaline Phosphatase (ALP): 80% decrease from baseline (DFB) and >3.0*ULN and >100% IFB; Urea Nitrogen:100% DFB and >3.0*ULN and >200% IFB; Creatinine >2.0*ULN and >100% IFB; Sodium :10% DFB or >1.1*ULN and >10% IFB; Potassium: 20% DFB or >1.2*ULN and >20% IFB; Chloride: 20% DFB or >1.2*ULN and >20% IFB; Bicarbonate: 40% DFB or >1.3*ULN and >40% IFB; Calcium: 30% DFB or >1.3*ULN and >30% IFB; Albumin: 50% DFB or >1.5* ULN and >50% IFB; Glucose: 40% DFB or >3.0*ULN and >200% IFB. Safety analysis set- all subjects who received any amount of study treatment. Subject were analysed according to the treatment received. All subjects reported under 'N' contributed data to the table but may not have evaluable data for every row. Here,'n'= subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) until TOC (Up to Day 28)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	2		
Units: Subjects				
AST: >3.0* ULN & >100% IFB (n=11,1)	1	0		
ALT: >3.0* ULN & >100% IFB (n=11,1)	0	0		
Bilirubin: >1.5* ULN & >100% IFB (n=11,1)	1	0		
Direct Bilirubin: >2.0* ULN & >150% IFB (n=11,1)	1	0		
ALP:80% DFB (n=11,1)	0	0		
ALP:>3.0*ULN & >100% IFB (n=11,1)	1	0		
Urea Nitrogen:100% DFB (n=11,1)	0	0		
Urea Nitrogen:>3.0* ULN & >200% IFB (n=11,1)	0	0		
Creatinine:>2.0* ULN & >100% IFB (n=11,2)	0	0		
Sodium:10% DFB (n=11,1)	0	0		
Sodium:>1.1* ULN & >10% IFB (n=11,1)	0	0		
Potassium:20% DFB (n=11,1)	1	0		
Potassium:>1.2* ULN & >20% IFB (n=11,1)	0	0		
Chloride:20% DFB (n=11,1)	0	0		
Chloride:>1.2*ULN & >20% IFB (n=11,1)	0	0		
Bicarbonate:40% DFB (n=11,1)	0	0		
Bicarbonate:>1.3* ULN & >40% IFB (n=11,1)	0	0		
Calcium:30% DFB (n=11,1)	0	0		
Calcium:>1.3* ULN & >30% IFB (n=11,1)	0	0		
Albumin:50% DFB (n=11,1)	0	0		
Albumin:>1.5* ULN & >50% IFB (n=11,1)	0	0		
Glucose:40% DFB (n=11,1)	0	0		
Glucose:>3.0*ULN & >200% IFB (n=11,1)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG)

End point title	Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG)

End point description:

A standard 12-lead ECG was recorded with the subject in a supine position after at least 10 minutes of rest. The following ECG parameters were recorded: heart rate, PR-interval, QRS-duration, QT-interval, QTc-interval, RR interval. Clinical significance of ECG abnormalities were judged by Investigator. Safety analysis set included all subjects who received any amount of study treatment. Subjects were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) until TOC (Up to Day 28)

End point values	Aztreonam-Avibactam (ATM- AVI)	Best Available Therapy (BAT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	2		
Units: Subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to the Last follow up visit (up to maximum of 45 days)

Adverse event reporting additional description:

Same event may appear as non-SAE and SAE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Analysis was performed on safety population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Best Available Therapy (BAT)

Reporting group description:

Subjects who were hospitalized with a diagnosis of cIAI, NP, HAP, VAP, cUTI or BSI received Best Available Therapy (BAT) based upon site practice and local epidemiology for a maximum of 14 days. Subjects with cIAI in the BAT arm received metronidazole if BAT did not provide adequate anaerobic coverage.

Reporting group title	Aztreonam- Avibactam (ATM- AVI)

Reporting group description:

Subjects were administered a loading dose of aztreonam- avibactam (ATM-AVI) by intravenous (IV) infusion over 30 minutes immediately followed by an extended loading dose of ATM-AVI by infusion over 3 hours, and then started a maintenance dose of ATM-AVI by IV infusion over 3 hours on Day 1. Subjects with creatinine clearance >50 milliliters per minute (mL/min) and >30 to 50 mL per minute were administered maintenance dose once every 6 hours for maximum of 14 days. Subjects with creatinine clearance >15 to 30 mL/min were administered maintenance dose once every 8 hours for maximum of 14 days. Subjects with cIAI also received metronidazole (MTZ) 500 milligram (mg) every 8 hours by IV infusion over 60 minutes.

Serious adverse events	Best Available Therapy (BAT)	Aztreonam-Avibactam (ATM-AVI)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	5 / 12 (41.67%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	1	2	
Investigations			
Bacterial test positive			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcus test positive			

subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 2 (50.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 2 (50.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			

subjects affected / exposed	1 / 2 (50.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 2 (50.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Best Available Therapy (BAT)	Aztreonam-Avibactam (ATM-AVI)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	9 / 12 (75.00%)	
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pyrexia			

subjects affected / exposed	1 / 2 (50.00%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Intensive care unit delirium			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Product issues			
Device occlusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Catheter culture positive			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Platelet count increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Staphylococcus test positive			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Injury, poisoning and procedural			

complications			
Stoma prolapse			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal wound dehiscence			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Eye disorders			
Ocular hypertension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Frequent bowel movements			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin maceration			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Intervertebral discitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 12 (8.33%) 1	
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 12 (16.67%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2022	Amendment 2.0: Updated section 4: Study eligibility criteria to better reflect the target patient population in clinical practice.

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.

Total number of deaths is reported for safety set under Adverse Events section. Actual number of deaths were 2 for Aztreonam-Avibactam and 1 for Best Available Therapy for ITT population as well.

Notes: