Clinical trial results:
A Phase 3 Prospective, Randomized, Multicenter, Open-Label, Central Assessor-Blinded, Parallel Group, Comparative Study To Determine The Efficacy, Safety And Tolerability Of Aztreonam-Avibactam (ATM-AVI) ± Metronidazole (MTZ) Versus Meropenem± Colistin (MER±COL) For The Treatment Of Serious Infections Due To Gram Negative Bacteria, Including Metallo--Lactamase (MBL) – Producing Multidrug Resistant Pathogens, For Which There Are Limited Or No Treatment Options

Summary

EudraCT number	2017-002742-68
Trial protocol	HU CZ ES BG GR HR IT RO
Global end of trial date	23 February 2023

Results information

Result version number	v2 (current)
This version publication date	06 December 2024
First version publication date	06 March 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	C3601002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03329092
WHO universal trial number (UTN)	-
Other trial identifiers	D4910C00004: 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 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of ATM-AVI MTZ and MER COL at the Test of Cure (TOC) visit for the treatment of serious infections due to Gram-negative bacteria, including those due to MBL-producing MDR pathogens.

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	05 April 2018
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	Argentina: 2
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	China: 120
Country: Number of subjects enrolled	Croatia: 6
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	India: 27
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 11
Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	Mexico: 14
Country: Number of subjects enrolled	Philippines: 5
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	Taiwan: 4

Country: Number of subjects enrolled	Türkiye: 25
Country: Number of subjects enrolled	Ukraine: 65
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	422
EEA total number of subjects	98

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)	283
From 65 to 84 years	131
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

Subjects who were hospitalized with a diagnosis of complicated intra-abdominal infection (cIAI) or nosocomial pneumonia (NP) including hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were enrolled. This study was conducted across 20 countries from 05-Apr-2018 to 23-Feb-2023.

Pre-assignment

Screening details:

A total of 461 subjects were screened of which 38 failed screening and 1 subject was not randomized due to lack of study drug at the site. A total of 422 subjects were randomized in the study.

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 ± Metronidazole

Arm description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 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 IV infusion over 3 hours on Day 1. Subjects were administered a maintenance dose of ATM-AVI by IV infusion over 3 hours on Days 2 to 14. Subjects with cIAI also received metronidazole (MTZ) 500 milligrams (mg) IV every 8 hours.

Arm type	Experimental
Investigational medicinal product name	Azetronam
Investigational medicinal product code	PF-06947387
Other name	
Pharmaceutical forms	Powder for concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Aztreonam 2 gm powder for concentrate for solution 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 mL solution for infusion.

Investigational medicinal product name	Avibactam
Investigational medicinal product code	PF-06947387
Other name	
Pharmaceutical forms	Powder for concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avibactam 600 mg powder for concentrate for solution for infusion

Arm title	Meropenem± colistimethate

Arm description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 1000 mg meropenem every 8 hours by IV infusion. A higher dose of 2000 mg was given by IV infusion over 180 minutes if carbapenem resistant pathogen was strongly suspected. Subjects were administered colistimethate sodium at investigator's discretion.

Arm type	Active comparator
Investigational medicinal product name	Colistimethate sodium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Colistin 2 million International Units (IU) powder for solution for infusion. Colistimethate sodium equivalent to 150 mg colistin base activity per vial.

Investigational medicinal product name	Meropenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravesical use

Dosage and administration details:

Meropenem 1 g powder for solution for infusion

Number of subjects in period 1	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate
Started	282	140
Subjects with cIAI	208 [1]	104 [2]
Subjects with HAP/VAP	74 [3]	36 [4]
Completed	242	122
Not completed	40	18
Consent withdrawn by subject	16	3
Physician decision	1	-
Adverse event, non-fatal	3	1
Death	17	11
Unspecified	2	2
Lost to follow-up	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone includes only subjects with HAP/VAP.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone includes only subjects with HAP/VAP.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: This milestone includes only subjects with HAP/VAP.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone includes only subjects with HAP/VAP.

Baseline characteristics

Reporting groups	
Reporting group title	Aztreonam-avibactam ± Metronidazole
Reporting group description:	
Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 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 IV infusion over 3 hours on Day 1. Subjects were administered a maintenance dose of ATM-AVI by IV infusion over 3 hours on Days 2 to 14. Subjects with cIAI also received metronidazole (MTZ) 500 milligrams (mg) IV every 8 hours.	
Reporting group title	Meropenem± colistimethate
Reporting group description:	
Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 1000 mg meropenem every 8 hours by IV infusion. A higher dose of 2000 mg was given by IV infusion over 180 minutes if carbapenem resistant pathogen was strongly suspected. Subjects were administered colistimethate sodium at investigator's discretion.	

Reporting group values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate	Total
Number of subjects	282	140	422
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	186	97	283
From 65-84 years	90	41	131
85 years and over	6	2	8
Age Continuous Units: Years			
arithmetic mean	55.2	54.0	
standard deviation	± 17.84	± 16.30	-
Sex: Female, Male Units: Subjects			
Female	96	39	135
Male	186	101	287
Ethnicity Units: Subjects			
Hispanic or Latino	58	21	79
Not Hispanic or Latino	213	113	326
Unknown or Not Reported	11	6	17
Race Units: Subjects			
American Indian or Alaska Native	7	2	9
Asian	107	69	176
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	1	1	2
White	164	64	228
More than one race	2	1	3
Unknown or Not Reported	1	3	4

End points

End points reporting groups

Reporting group title	Aztreonam-avibactam ± Metronidazole

Reporting group description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 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 IV infusion over 3 hours on Day 1. Subjects were administered a maintenance dose of ATM-AVI by IV infusion over 3 hours on Days 2 to 14. Subjects with cIAI also received metronidazole (MTZ) 500 milligrams (mg) IV every 8 hours.

Reporting group title	Meropenem± colistimethate

Reporting group description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 1000 mg meropenem every 8 hours by IV infusion. A higher dose of 2000 mg was given by IV infusion over 180 minutes if carbapenem resistant pathogen was strongly suspected. Subjects were administered colistimethate sodium at investigator's discretion.

Subject analysis set title	Aztreonam- Avibactam
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received aztreonam-avibactam in studies C3601002 (NCT03329092) and C3601009 (NCT03580044) were included in the analysis.

Subject analysis set title	Aztreonam- Avibactam
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received aztreonam-avibactam in studies C3601002 (NCT03329092) and C3601009 (NCT03580044) were included in the analysis.

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

End point title	Percentage of Subjects With Clinical Cure at Test of Cure (TOC) Visit: Intent-To-Treat (ITT) Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% confidence interval (CI) was based on Jeffrey's method. The ITT analysis set included all randomized subjects regardless of receipt of study drug.

End point type	Primary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of Subjects				
number (confidence interval 95%)	68.4 (62.8 to 73.7)	65.7 (57.6 to 73.2)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	12.4

Primary: Percentage of Subjects With Clinical Cure at TOC Visit: Clinically Evaluable (CE) Analysis Set

End point title	Percentage of Subjects With Clinical Cure at TOC Visit: Clinically Evaluable (CE) Analysis Set

End point description:

Clinical cure = improvement in baseline signs and symptoms after the study treatment, no further antimicrobial treatment for index infection (i.e., cIAI or HAP/VAP) was required. Additionally for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. It was determined by Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens.

End point type	Primary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Percentage of subjects				
number (confidence interval 95%)	77.0 (71.0 to 82.3)	74.3 (65.3 to 81.9)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	13.2

Secondary: Percentage of Subjects With Clinical Cure at TOC Visit: Microbiological Intent-To-Treat (Micro-ITT) Analysis Set

End point title	Percentage of Subjects With Clinical Cure at TOC Visit: Microbiological Intent-To-Treat (Micro-ITT) Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. The microbiological Intent-To-Treat (micro-ITT) analysis set was a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (confidence interval 95%)	72.9 (66.0 to 79.0)	72.3 (62.7 to 80.6)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	12.1

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

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

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (confidence interval 95%)	78.5 (71.4 to 84.5)	75.9 (65.7 to 84.3)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	14.7

Secondary: Percentage of Subjects With Clinical Cure at TOC Visit by Type of Infection: ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure at TOC Visit by Type of Infection: ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. ITT analysis set included all randomized subjects regardless of receipt of study drug. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. Here, n=signifies number of subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of subjects				
number (confidence interval 95%)				
cIAI; n=208,104	76.4 (70.3 to 81.8)	74.0 (65.0 to 81.7)		
HAP/VAP; n=74,36	45.9 (34.9 to 57.3)	41.7 (26.7 to 57.9)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL

Statistical analysis description:

HAP/VAP

Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	23.1

Statistical analysis title	ATM± AVI and MER± COL
Statistical analysis description:	
cIAI	
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	13

Secondary: Percentage of Subjects With Clinical Cure at TOC Visit by Type of Infection: CE Analysis Set

End point title	Percentage of Subjects With Clinical Cure at TOC Visit by Type of Infection: CE Analysis Set

End point description:

Clinical cure = improvement in baseline signs and symptoms after treatment, no antimicrobial treatment for index infection was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary in initial. CI based on Jeffrey’s method. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have Gram-positive pathogens. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every row. Here, ‘n=number of subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Percentage of subjects				
number (confidence interval 95%)				
cIAI: n=168,83	85.1 (79.2 to 89.9)	79.5 (69.9 to 87.1)		
HAP/VAP:n=45,22	46.7 (32.7 to 61.1)	54.5 (34.3 to 73.7)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Statistical analysis description: HAP/VAP	
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.9
upper limit	17.3

Statistical analysis title	ATM± AVI and MER± COL
Statistical analysis description: cIAI	
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	16.6

Secondary: Percentage of Subjects With Clinical Cure in Subjects With Metallo-beta-lactamase (MBL) Positive Pathogen at TOC Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure in Subjects With Metallo-beta-lactamase (MBL) Positive Pathogen at TOC Visit: Micro-ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. Micro-ITT analysis set was a subset of the ITT analysis and included all subjects who had at least 1 Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. Here, 'Number of Subjects Analyzed' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: Percentage of subjects				
number (not applicable)	28.6	66.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Cure in Subjects With MBL Positive Pathogen at TOC Visit: ME Analysis Set

End point title	Percentage of Subjects With Clinical Cure in Subjects With MBL Positive Pathogen at TOC Visit: ME Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. Here, 'Number of Subjects Analyzed' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: Percentage of subjects				
number (not applicable)	50.0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents.

End point type	Secondary

End point timeframe:

At TOC Visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)	77.2	75.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Died on or Before 28 Days After Randomization: ITT Analysis Set

End point title	Percentage of Subjects who Died on or Before 28 Days After Randomization: ITT Analysis Set

End point description:

Percentage of subjects who died on or before 28 days after randomization is reported in this endpoint. The ITT analysis set included all randomized subjects regardless of receipt of study drug.

End point type	Secondary

End point timeframe:

From randomization up to 28 days

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of subjects				
number (not applicable)	4.3	7.1		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. Micro-ITT analysis set was a subset of the ITT analysis and included all subjects who had at least 1 Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. Subjects with a per subject response of indeterminate were excluded from this analysis. Here, 'Number of Subjects Analyzed' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At TOC visit day (28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	92		
Units: Percentage of subjects				
number (not applicable)	75.7	73.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Died on or Before 28 Days After Randomization: Micro-ITT Analysis Set

End point title	Percentage of Subjects who Died on or Before 28 Days After Randomization: Micro-ITT Analysis Set

End point description:

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

End point type	Secondary

End point timeframe:

From randomization up to 28 days

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)	2.8	6.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Aztreonam

End point title	Plasma Concentration of Aztreonam[1]

End point description:

Plasma concentration for aztreonam according to renal function (augmented, normal and mild, moderate and severe) is presented in this endpoint. Augmented = Creatinine clearance (CrCL) > 150 milliliters per minute (mL/min); Normal & Mild = CrCL > 50 to <=150 mL/min; Moderate = CrCL > 30 to ≤ 50 mL/min; Severe = CrCL > 15 to ≤ 30 mL/min. Pharmacokinetic (PK) analysis set included all subjects who had at least 1 plasma concentration data assessment available for ATM or AVI. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n= subjects evaluable for the specified category. 99999 signifies data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Anytime between 25 to 30 minutes, 3.25 to 3.5 hours, 5.5 to 6.5 hours, 7.5 to 8.5 hours post start of infusion on Day 1; 2.75 to 3 hours, 3.5 to 4.5 hours, 5 to 6 and 7 to 8 hours post start of infusion on Day 4

Notes:

[1] - 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: This endpoint is specific to Aztreonam.

End point values	Aztreonam-avibactam ± Metronidazole			
Subject group type	Reporting group			
Number of subjects analysed	253			
Units: Milligram/Liter				
geometric mean (geometric coefficient of variation)				
Augmented: 25 to 30 minutes on Day 1; n=36	43.3 (± 339.08)			
Augmented:3.25 to 3.5 hours on Day 1; n= 34	55.99 (± 287.36)			
Augmented: 5.5 hours to 6.5 hours on Day 1; n=34	26.11 (± 338.5)			
Augmented:7.5 to 8.5 hours on Day 1; n=0	99999 (± 99999)			
Normal & Mild: 25 to 30 minutes on Day 1; n=169	33.85 (± 234.46)			
Normal & Mild:3.25 to 3.5 hours on Day 1; n= 164	56.24 (± 222.32)			
Normal & Mild:5.5 to 6.5 hours on Day 1; n=160	25.03 (± 115.83)			
Normal & Mild:7.5 to 8.5 hours on Day 1; n=7	34.62 (± 54.42)			
Moderate: 25 to 30 minutes on Day 1; n= 25	54.49 (± 313.99)			
Moderate: 3.25 to 3.5 hours on Day 1; n= 24	73.72 (± 259.64)			
Moderate: 5.5 hours to 6.5 hours on Day 1; n= 20	52.45 (± 139.9)			
Moderate: 7.5 to 8.5 hours on Day 1; n=1	34 (± 99999)			
Severe: 25 to 30 min on Day 1; n=8	48.98 (± 187.86)			
Severe: 3.25 to 3.5 hours p on Day 1; n=8	50.31 (± 30.13)			
Severe: 5.5 hours to 6.5 hours on Day 1; n=2	48.54 (± 46.87)			
Severe: 7.5 to 8.5 hours on Day 1; n=5	29.42 (± 34.88)			
Augmented: 2.75 to 3 hours on Day 4; n=33	46.11 (± 234.31)			
Augmented: 3.5 to 4.5 hours on Day 4; n=38	33.56 (± 204.99)			
Augmented: 5 to 6 hours on Day 4; n=38	19.56 (± 205.84)			
Augmented: 7 to 8 hours on Day 4; n=1	14.1 (± 99999)			
Normal & Mild: 2.75 to 3 hours on Day 4; n=163	56.59 (± 404.54)			
Normal & Mild: 3.5 to 4.5 hours on Day 4; n=168	35.69 (± 422.52)			
Normal & Mild: 5 to 6 hours on Day 4; n=154	21.75 (± 271.62)			
Normal & Mild: 7 to 8 hours on Day 4; n=6	42.98 (± 62.54)			
Moderate: 2.75 to 3 hours on Day 4; n=24	73.33 (± 183.2)			
Moderate: 3.5 to 4.5 hours on Day 4; n= 24	58 (± 129.36)			
Moderate: 5 to 6 hours on Day 4; n=22	44.72 (± 59.15)			

Moderate: 7 to 8 hours on Day 4; n= 1	19.8 (± 99999)			
Severe: 2.75 to 3 hours on Day 4; n= 7	54.91 (± 45.17)			
Severe: 3.5 to 4.5 hours on Day 4; n=6	45.17 (± 34.89)			
Severe: 5 to 6 hours on Day 4; n=4	45.11 (± 57.13)			
Severe: Moderate: 7 to 8 hours on Day 4; n=4	32.69 (± 55.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Avibactam

End point title	Plasma Concentration of Avibactam[2]

End point description:

Plasma concentration for avibactam according to renal function (augmented, normal and mild, moderate and severe is presented in this outcome measure. Augmented = CrCL > 150 mL/min; Normal & Mild = CrCL > 50 to <=150 mL/min; Moderate = CrCL > 30 to ≤ 50 mL/min; Severe = CrCL > 15 to ≤ 30 mL/min. PK analysis set included all subjects who had at least 1 plasma concentration data assessment available for ATM or AVI. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n= subjects evaluable for the specified categories. 99999 signifies data could not be calculated due to insufficient number of subjects.

End point type	Secondary

End point timeframe:

Anytime between 25 to 30 minutes, 3.25 to 3.5 hours, 5.5 to 6.5 hours, 7.5 to 8.5 hours post start of infusion on Day 1; 2.75 to 3 hours, 3.5 to 4.5 hours, 5 to 6 and 7 to 8 hours post start of infusion on Day 4

Notes:

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

End point values	Aztreonam-avibactam ± Metronidazole			
Subject group type	Reporting group			
Number of subjects analysed	235			
Units: Milligram/Liter				
geometric mean (geometric coefficient of variation)				
Augmented:25 to 30 minutes on Day 1; n= 36	10.77 (± 353.86)			
Augmented:3.25 to 3.5 hours on Day 1; n= 34	12.6 (± 299.27)			
Augmented: 5.5 to 6.5 hours on Day 1; n= 34	4.75 (± 366.33)			
Augmented:7.5 to 8.5 hours on Day 1; n= 0	99999 (± 99999)			
Normal & Mild: 25 to 30 minutes on Day 1; n= 170	8.81 (± 338.73)			
Normal & Mild:3.25 to 3.5 hours on Day 1; n=164	13.76 (± 242.67)			
Normal & Mild:5.5 to 6.5 hours on Day 1; n=160	4.85 (± 209.49)			

Normal & Mild:7.5 to 8.5 hours on Day 1; n=7	7.18 (± 62.62)			
Moderate: 25 to 30 min on Day 1; n=25	13.56 (± 383.79)			
Moderate: 3.25 to 3.5 hours on Day 1; n=24	20.28 (± 262.6)			
Moderate: 5.5 hours to 6.5 hours on Day 1; n=20	13.47 (± 160.75)			
Moderate: 7.5 to 8.5 hours on Day 1; n=1	7.91 (± 99999)			
Severe: 25 to 30 minutes on Day 1; n=8	14.11 (± 202.08)			
Severe: 3.25 to 3.5 hours on Day 1; n=8	13.62 (± 39.68)			
Severe: 5.5 hours to 6.5 hours on Day 1; n=2	11.6 (± 54.34)			
Severe: 7.5 to 8.5 hours on Day 1; n=5	8 (± 57.91)			
Augmented: 2.75 to 3 hours on Day 4; n=33	9.75 (± 289.96)			
Augmented: 3.5 to 4.5 hours on Day 4; n=38	6.23 (± 263.94)			
Augmented: 5 to 6 hours on Day 4; n=38	3.19 (± 265.65)			
Augmented: 7 to 8 hours on Day 4; n=1	2.72 (± 99999)			
Normal & Mild: 2.75 to 3 hours on Day 4; n=163	11.46 (± 504.77)			
Normal & Mild: 3.5 to 4.5 hours on Day 4; n=168	6.29 (± 493.48)			
Normal & Mild: 5 to 6 hours on Day 4; n=154	3.48 (± 382.3)			
Normal & Mild: 7 to 8 hours on Day 4; n=6	6.19 (± 51.22)			
Moderate: 2.75 to 3 hours on Day 4; n=24	16.98 (± 208.63)			
Moderate: 3.5 to 4.5 hours on Day 4; n=24	12.86 (± 156.96)			
Moderate: 5 to 6 hours on Day 4; n=22	9.23 (± 72.89)			
Moderate: 7 to 8 hours on Day 4; n=1	4.35 (± 99999)			
Severe: 2.75 to 3 hours on Day 4; n=7	14.35 (± 44.72)			
Severe: 3.5 to 4.5 hours on Day 4; n=6	11.68 (± 42.15)			
Severe: 5 to 6 hours on Day 4; n=4	9.99 (± 67.87)			
Severe:7 to 8 hours on Day 4; n=4	8.97 (± 47.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration for a Dosing Interval at Steady-State (Cmax, ss) According to Clinical Response by Infection Type at TOC: Aztreonam

End point title	Maximum Plasma Concentration for a Dosing Interval at Steady-State (Cmax, ss) According to Clinical Response by Infection Type at TOC: Aztreonam

End point description:

Population PK predicted Cmax, ss for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Clinical response included cure=improvement

and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure= met any criteria: death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection. cIAI:persisting or recurrent infection within abdomen at time of initial surgery; postsurgical wound infection. Indeterminate=death (after<48 hours of study drug);subject lost to follow-up. For cIAI: inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to insufficient subjects.

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Milligram per liter (mg/L)				
geometric mean (geometric coefficient of variation)				
cIAI: Clinical cure;n=151	52.47 (± 37.49)			
cIAI: Failure;n=31	56.71 (± 62.52)			
cIAI: Indeterminate;n=9	66.21 (± 12.7)			
HAP:Clinical cure;n=17	85.24 (± 48.49)			
HAP: Failure;n=16	64.57 (± 33.97)			
HAP: Indeterminate;n=5	61.79 (± 27.2)			
VAP: Clinical Cure; n=16	54.89 (± 30.42)			
VAP: Failure; n=16	56.5 (± 31.1)			
VAP: Indeterminate; n=1	85.34 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time That Free Plasma Concentrations are Above the Minimum Inhibitory Concentration Over a Dosing Interval (%fT>MIC Aztreonam (ATM) of 8 mg/L) According to Clinical Response by Infection Type at TOC: Aztreonam

End point title	Percentage of Time That Free Plasma Concentrations are Above the Minimum Inhibitory Concentration Over a Dosing Interval (%fT>MIC Aztreonam (ATM) of 8 mg/L) According to Clinical Response by Infection Type at TOC: Aztreonam

End point description:

Population PK predicted %fT>MIC ATM of 8 mg/L for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Clinical response included cure=improvement in signs and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure=met any criteria:death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection.cIAI:persisting or recurrent infection within abdomen at time of initial surgery; postsurgical

wound infection. Indeterminate=death (after <48 hours of study drug); subject lost to follow-up. For cIAI:inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to less subjects

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Percentage of time				
geometric mean (geometric coefficient of variation)				
cIAI: Clinical cure;n=151	90.4 (± 41.9)			
cIAI: Failure;n=31	73.81 (± 134.39)			
cIAI: Indeterminate;n=9	100 (± 0)			
HAP:Clinical cure;n=17	97.87 (± 7.67)			
HAP: Failure;n=16	97.2 (± 8.4)			
HAP: Indeterminate;n=5	100.0 (± 0)			
VAP: Clinical Cure; n=16	95.29 (± 8.94)			
VAP: Failure; n=16	96.38 (± 10.2)			
VAP: Indeterminate; n=1	100 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Clinical Response by Infection Type at TOC: Aztreonam

End point title	Area under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Clinical Response by Infection Type at TOC: Aztreonam

End point description:

Population PK predicted AUC24,ss for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Clinical response included, cure =improvement in signs and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure=met any criteria:death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection. cIAI: persisting or recurrent infection within abdomen at time of initial surgery; postsurgical wound infection. Indeterminate=death (after<48 hours of study drug); subject lost to follow-up. For cIAI: inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to

End point type	Secondary

End point timeframe:

0 to 24 hours at TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Milligram*hours per liter (mg*h/L)				
geometric mean (geometric coefficient of variation)				
cIAI: Clinical cure;n=151	816.18 (± 41.83)			
cIAI: Failure;n=31	877.5 (± 85.91)			
cIAI: Indeterminate;n=9	1069.1 (± 15.82)			
HAP:Clinical cure;n=17	1420.1 (± 54.62)			
HAP: Failure;n=16	1079.4 (± 34.1)			
HAP: Indeterminate;n=5	1056.8 (± 35.68)			
VAP: Clinical Cure; n=16	858.39 (± 32.49)			
VAP: Failure; n=16	912.23 (± 38.1)			
VAP: Indeterminate; n=1	1084.6 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss) According to Microbiological Response by Infection Type at TOC: Aztreonam

End point title	Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss) According to Microbiological Response by Infection Type at TOC: Aztreonam

End point description:

Population PK predicted Cmax,ss for subjects who received ATM-AVI in studies C3601002 (NCT03329092) and C3601009 (NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication: Absence of causative pathogen from specimen at site of infection. Presumed eradication: repeat culture not indicated in a subject who had clinical response of cure. Persistence: Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n= subjects evaluable for specified categories.99999=data not calculated due to insufficient subjects.

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Milligram per liter (mg/L)				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	53.26 (± 34.03)			
cIAI: Unfavorable;n=23	53.71 (± 67.14)			
cIAI: Indeterminate;n=4	62.97 (± 9.49)			
HAP:Favorable;n=8	86.9 (± 71.56)			
HAP: Unfavorable;n=5	55.48 (± 38.33)			
HAP: Indeterminate;n=3	66.2 (± 33.87)			
VAP: Favorable; n=8	50.71 (± 37.56)			
VAP: Unfavorable; n=14	59.77 (± 31.52)			
VAP: Indeterminate; n=1	85.34 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24, ss) According to Microbiological Response by Infection Type at TOC: Azetreonam

End point title	Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24, ss) According to Microbiological Response by Infection Type at TOC: Azetreonam

End point description:

Population PK predicted AUC24, ss for subjects who received ATM-AVI in studies C3601002 (NCT03329092) and C3601009 (NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication: Absence of causative pathogen from specimen at site of infection. Presumed eradication: repeat culture not indicated in a subject who had clinical response of cure. Persistence: Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n= subjects evaluable for specified categories.99999=data not calculated due to insufficient subjects.

End point type	Secondary

End point timeframe:

0 to 24 hours at TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Milligram*hours per liter				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	830.23 (± 38.42)			
cIAI: Unfavorable;n=23	826.63 (± 95.22)			
cIAI: Indeterminate;n=4	1010.2 (± 9.17)			
HAP:Favorable;n=8	1446.1 (± 82.6)			
HAP: Unfavorable;n=5	909.59 (± 45.06)			
HAP: Indeterminate;n=3	1237.9 (± 38.16)			
VAP: Favorable; n=8	760.26 (± 40.54)			
VAP: Unfavorable; n=14	974.21 (± 37.82)			
VAP: Indeterminate; n=1	1084.6 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time That Free Plasma Concentrations are Above the Minimum Inhibitory Concentration Over a Dosing Interval (%fT>MICATM of 8 mg/L) According to Microbiological Response by Infection Type at TOC: Aztreonam

End point title	Percentage of Time That Free Plasma Concentrations are Above the Minimum Inhibitory Concentration Over a Dosing Interval (%fT>MICATM of 8 mg/L) According to Microbiological Response by Infection Type at TOC: Aztreonam

End point description:

Population PK predicted %fT>MICATM of 8 mg/L for subjects who received ATM-AVI in studies C3601002 (NCT03329092) and C3601009 (NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication: Absence of causative pathogen from specimen at site of infection. Presumed eradication: repeat culture not indicated in a subject who had clinical response of cure. Persistence: Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n= subjects evaluable for specified categories.99999=data not calculated due to less subjects.

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Percentage of time				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	92.57 (± 17.66)			
cIAI: Unfavorable;n=23	68.02 (± 171.87)			
cIAI: Indeterminate;n=4	100 (± 0)			
HAP:Favorable;n=8	95.53 (± 11.05)			
HAP: Unfavorable;n=5	93.9 (± 14.14)			
HAP: Indeterminate;n=3	100 (± 0)			
VAP: Favorable; n=8	90.8 (± 12.3)			
VAP: Unfavorable; n=14	97.42 (± 9.54)			
VAP: Indeterminate; n=1	100 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Clinical Response by Infection Type at TOC: Avibactam

End point title	Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Clinical Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted AUC24,ss for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009 (NCT03580044). Clinical response included, cure=improvement in signs and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure=met any criteria: death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection. cIAI:persisting or recurrent infection within abdomen at time of initial surgery; postsurgical wound infection. Indeterminate=death (after<48 hours of study drug); subject lost to follow-up. For cIAI: inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to

End point type	Secondary

End point timeframe:

0 to 24 hours at TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Milligram*hours per liter (mg*h/L)				
geometric mean (geometric coefficient				

of variation)				
cIAI: Clinical cure;n=151	164.92 (± 45.91)			
cIAI: Failure;n=31	187.41 (± 96.93)			
cIAI: Indeterminate;n=9	213.92 (± 20.81)			
HAP:Clinical cure;n=17	291.47 (± 61.75)			
HAP: Failure;n=16	214.99 (± 36.09)			
HAP: Indeterminate;n=5	257.37 (± 71.75)			
VAP: Clinical Cure; n=16	176.95 (± 31.43)			
VAP: Failure; n=16	178.68 (± 38.99)			
VAP: Indeterminate; n=1	218.09 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss) According to Clinical Response by Infection Type at TOC: Avibactam

End point title	Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss) According to Clinical Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted Cmax, ss for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009 (NCT03580044). Clinical response included, cure=improvement in signs and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure=met any criteria: death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection. cIAI: persisting or recurrent infection within abdomen at time of initial surgery; postsurgical wound infection. Indeterminate=death (after<48 hours of study drug); subject lost to follow-up. For cIAI:inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Milligram per liter (mg/L)				
geometric mean (geometric coefficient of variation)				
cIAI: Clinical cure;n=151	11.01 (± 42.14)			

cIAI: Failure;n=31	12.48 (± 72.59)			
cIAI: Indeterminate;n=9	14.04 (± 16.52)			
HAP:Clinical cure;n=17	18.41 (± 55.07)			
HAP: Failure;n=16	13.46 (± 33.52)			
HAP: Indeterminate;n=5	15.24 (± 49.1)			
VAP: Clinical Cure; n= 16	11.64 (± 31.01)			
VAP: Failure; n= 16	11.44 (± 32.65)			
VAP: Indeterminate; n= 1	18.93 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Time That Free Plasma Concentrations are Above the Threshold Concentration Over a Dosing Interval (%fT>CT of 2.5mg/L) According to Clinical Response by Infection Type at TOC: Avibactam

End point title	Percent of Time That Free Plasma Concentrations are Above the Threshold Concentration Over a Dosing Interval (%fT>CT of 2.5mg/L) According to Clinical Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted %fT>CT of 2.5mg/L for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Clinical response included, cure=improvement in signs and symptoms, no further antimicrobial required for index infection. For cIAI, no unplanned drainage or surgical intervention was necessary since initial procedure. Failure=met any criteria:death (after at least 48 hours of study treatment; received treatment with further antibiotics for index infection. cIAI: persisting or recurrent infection within abdomen at time of initial surgery; postsurgical wound infection. Indeterminate=death (after<48 hours of study drug); subject lost to follow-up. For cIAI: inadequate infection source control at time of initial surgical procedure. Pk and ITT analysis set. Subjects under 'N' contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories. 99999=data could not be calculated due to less subjects.

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	262			
Units: Percentage of time				
geometric mean (geometric coefficient of variation)				
cIAI: Clinical cure;n=151	85.53 (± 43.26)			
cIAI: Failure;n=31	71.92 (± 133.68)			
cIAI: Indeterminate;n=9	98.52 (± 2.81)			

HAP:Clinical cure;n=17	95.99 (± 11.57)			
HAP: Failure;n=16	95.28 (± 12.12)			
HAP: Indeterminate;n=5	92.75 (± 11.19)			
VAP: Clinical Cure; n= 16	92 (± 13.01)			
VAP: Failure; n= 16	94.08 (± 12.93)			
VAP: Indeterminate; n= 1	100 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Microbiological Response by Infection Type at TOC: Avibactam

End point title	Area Under the Plasma Concentration-time Curve Over 24 Hours at Steady-state (AUC24,ss) According to Microbiological Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted AUC24,ss for subjects who received ATM-AVI in studies C3601002 (NCT03329092) and C3601009 (NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication: Absence of causative pathogen from specimen at site of infection. Presumed eradication: repeat culture not indicated in a subject who had clinical response of cure. Persistence: Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n= subjects evaluable for specified categories.99999=data not calculated due to insufficient subjects.

End point type	Secondary

End point timeframe:

0 to 24 hours at TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Milligram*hours per liter				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	166.4 (± 40.88)			
cIAI: Unfavorable;n=23	177.65 (± 106.25)			
cIAI: Indeterminate;n=4	197.01 (± 7.31)			
HAP:Favorable;n=8	293.49 (± 95.13)			
HAP: Unfavorable;n=5	196.38 (± 61.95)			

HAP: Indeterminate;n=3	359.31 (± 71.12)			
VAP: Favorable; n=8	157.79 (± 43.71)			
VAP: Unfavorable; n=14	192.85 (± 38.42)			
VAP: Indeterminate; n=1	218.09 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss (mg/L)) According to Microbiological Response by Infection Type at TOC: Avibactam

End point title	Maximum Plasma Concentration for a Dosing Interval at Steady-state (Cmax,ss (mg/L)) According to Microbiological Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted Cmax,ss (mg/L) for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication: Absence of causative pathogen from specimen at site of infection. Presumed eradication: repeat culture not indicated in a subject who had clinical response of cure. Persistence: Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories.99999=data not calculated due to insufficient

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Milligram per liter (mg/L)				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	11.1 (± 37.2)			
cIAI: Unfavorable;n=23	11.83 (± 76.48)			
cIAI: Indeterminate;n=4	13.03 (± 8.01)			
HAP:Favorable;n=8	18.55 (± 84.68)			
HAP: Unfavorable;n=5	12.31 (± 51.34)			
HAP: Indeterminate;n=3	18.72 (± 55.03)			
VAP: Favorable; n=8	10.75 (± 42.72)			

VAP: Unfavorable; n=14	12.28 (± 32.85)			
VAP: Indeterminate; n=1	18.93 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Time That Free Plasma Concentrations are Above the Threshold Concentration Over a Dosing Interval; (%fT>CT of 2.5 mg/L) According to Microbiological Response by Infection Type at TOC: Avibactam

End point title	Percent of Time That Free Plasma Concentrations are Above the Threshold Concentration Over a Dosing Interval; (%fT>CT of 2.5 mg/L) According to Microbiological Response by Infection Type at TOC: Avibactam

End point description:

Population PK predicted %fT>CT of 2.5 mg/L for subjects who received ATM-AVI in studies C3601002(NCT03329092) and C3601009(NCT03580044). Microbiological response=favorable (eradicated or presumed eradicated) or unfavorable (persistence, presumed persistence, indeterminate). Eradication:Absence of causative pathogen from specimen at site of infection. Presumed eradication:repeat culture not indicated in a subject who had clinical response of cure. Persistence:Causative organism present in specimen obtained at site of infection. Presumed persistence: assessed clinical failure and repeat culture of specimens not performed/clinically indicated. Indeterminate: death, lost to follow-up. cIAI: Inadequate infection source control at time of initial surgical procedure. Pk and Micro-ITT analysis set. Subjects under N contributed data to table but may not have evaluable data for every category. n=subjects evaluable for specified categories.99999=data

End point type	Secondary

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-Avibactam			
Subject group type	Subject analysis set			
Number of subjects analysed	174			
Units: Percentage of time				
geometric mean (geometric coefficient of variation)				
cIAI: Favorable;n=108	87.93 (± 21.78)			
cIAI: Unfavorable;n=23	66.43 (± 170.59)			
cIAI: Indeterminate;n=4	99.24 (± 1.52)			
HAP:Favorable;n=8	92.26 (± 16.44)			
HAP: Unfavorable;n=5	90.03 (± 18.83)			
HAP: Indeterminate;n=3	100 (± 0)			
VAP: Favorable; n=8	87.47 (± 16.8)			
VAP: Unfavorable; n=14	95.52 (± 11.79)			
VAP: Indeterminate; n=1	100 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Significant Hematology Abnormalities

End point title	Number of Subjects With Potentially Clinically Significant Hematology Abnormalities

End point description:

Criteria for potential clinically significant hematology results were as follows: hemoglobin, hematocrit and erythrocyte <0.7*lower limit of normal [LLN] and >30% decrease from Baseline (DFB); >1.3*upper limit of normal (ULN) and>30% increase from Baseline (IFB). Platelet count <0.65*LLN and> 50% (DFB); > 1.5 * ULN and > 100% (IFB). leukocyte: < 0.65* LLN and > 60% (DFB); > 1.6* ULN and 100% (IFB). Neutrophils/leukocytes < 0.65 * LLN and >75% (DFB); > 1.6*ULN and > 100% (IFB). Lymphocytes/leukocytes < 0.25* LLN and > 75% (DFB);> 1.5* ULN and > 100% (IFB), Eosinophils/leukocytes, Monocytes/leukocytes, Basophils/leukocytes > 4.0* ULN and > 300% (IFB). Safety analysis set included all subjects who received any amount of study treatment. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'n= number of subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

From start of study treatment until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Subjects				
Hematocrit < 0.7*LLN and > 30%;n=258,127	6	3		
Hematocrit >1.3* ULN and >30%;n=258,127	0	0		
Hemoglobin< 0.7* LLN and > 30%;n=259,133	8	3		
Hemoglobin > 1.3* ULN and > 30%;n=259,133	0	0		
Erythrocytes < 0.7* LLN and > 30%;n=259,133	7	3		
Erythrocytes > 1.3* ULN and > 30%;n=259,133	0	0		
Leukocytes < 0.65* LLN and > 60%;n=260,133	0	0		
Leukocytes > 1.5* ULN and > 100%;n=260,133	12	5		
Neutrophils/Leukocytes<0.65*LLN and>75%;n=259,131	0	0		
Neutrophils/Leukocytes>1.6* ULN and>100%;n=259,131	0	0		

Monocytes/Leukocytes >4.0* ULN and>300%;n=258,131	0	0		
Lymphocytes/Leukocytes<0.25*LLN and>75%;n=258,132	1	1		
Lymphocytes/Leukocytes>1.5*ULN and>100%;n=258,132	0	0		
Eosinophils/Leukocytes>4.0*ULN and>300%;n=258,131	0	0		
Basophils/Leukocytes>4.0*ULN and >300%;n=258,131	0	0		
Platelets<0.65* LLN and > 50%;n=259,131	3	2		
Platelets >1.5* ULN and > 100%;n=259,131	12	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs) and Serious AEs

End point title	Number of Subjects With Adverse Events (AEs) and Serious AEs

End point description:

An adverse event (AE) was any untoward medical occurrence in a study subject administered medicinal product, the event need not necessarily have a causal relationship with product treatment or usage. A serious adverse event (SAE) was any untoward medical occurrence at any dose that: resulted in death; was life-threatening; required inpatient hospitalization or prolongation of hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); resulted in congenital abnormal/birth defect or considered an important medical event. Safety analysis set included all subjects who received any amount of study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment until end of late follow-up (Up to Day 45)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Subjects				
AEs	177	87		
SAEs	53	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Significant Clinical Chemistry Abnormalities

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

End point description:

Albumin < 0.5* LLN and> 50% decrease from baseline (DFB);> 1.5 * ULN and> 50% increase from baseline (IFB). Alkaline phosphatase < 0.5 * LLN and> 80% DFB;> 3.0 * ULN and> 100%. Alanine and Aspartate aminotransferase > 3.0 * ULN and> 100% IFB. Bicarbonate < 0.7 * LLN and > 40% DFB;> 1.3 * ULN and> 40% IFB. Blood urea nitrogen < 0.2 * LLN and > 100% DFB; > 3.0 * ULN and > 200% IFB. Calcium < 0.7 * LLN and > 30% DFB;> 1.3 * ULN and> 30% IFB. Chloride < 0.8 * LLN >and 20% DFB; > 1.2 * ULN and > 20% IFB. Creatinine > 2.0 * ULN and> 100% IFB; Glucose < 0.6 * LLN and> 40% DFB; > 3.0 * ULN and> 200% IFB. Potassium < 0.8 * LLN and > 20% DFB; > 1.2 * ULN and> 20% IFB. Sodium < 0.85 * LLN and> 10% DFB;> 1.1 * ULN and >10% IFB. Bilirubin > 1.5 * ULN and > 100% IFB.; Direct bilirubin > 2.0 * ULN and > 150% IFB. Safety analysis set. n= number of subjects evaluable for specified categories

End point type	Secondary

End point timeframe:

From start of study treatment until At TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Subjects				
ALT>3.0* ULN and>100%;n=262,133	25	14		
ALT>3.0*ULN and >100%;n=264,132	24	10		
ALP < 0.5* LLN and >80%;n=264,133	0	0		
ALP >3.0* ULN and >100%;n=264,133	5	4		
Bilirubin >1.5* ULN and > 100%;n=263,132	2	3		
Direct Bilirubin >2.0* ULN and > 150%;n=258,130	2	0		
Creatinine>2.0* ULN and > 100;n=270,136	0	3		
Sodium< 0.85* LLN and > 10%;n=263,133	0	0		
Sodium>1.1* ULN and > 10%;n=263,133	0	0		
Potassium < 0.8* LLN and > 20%;n=262,132	6	1		
Potassium >1.2* ULN and > 20%;n=262,132	5	4		
Chloride< 0.8* LLN and > 20%;n=263,133	0	0		
Chloride > 1.2* ULN and > 20%;n=263,133	1	0		
Bicarbonate< 0.7* LLN and > 40%;n=257,129	0	0		
Bicarbonate >1.3* ULN and > 40%;n=257,129	3	1		
Calcium < 0.7* LLN and > 30%;n=262,130	2	1		
Calcium > 1.3* ULN and > 30%;n=262,130	0	0		
Albumin < 0.5* LLN and > 50%;n=261,132	0	0		
Albumin >1.5* ULN and > 50%;n=261,132	0	0		

Glucose < 0.6* LLN and > 40%;n=261,132	0	1		
Glucose > 3.0* ULN and > 200%;n=261,132	2	0		
Urea Nitrogen < 0.2* LLN and > 100%;n=259,130	0	0		
Urea Nitrogen>3.0* ULN and > 200%;n=259,130	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Vital Signs

End point title	Number of Subjects With Abnormalities in Vital Signs

End point description:

Vitals signs, included blood pressure and, heart rate. Blood pressure (BP) and heart rate were measured using a semiautomatic BP recording device with the subject in a supine position after at least 10 minutes of rest. Criteria for abnormalities included: Systolic BP (millimeters of mercury [mmHg]): value more than (>) 150 and increase from baseline (IFB) more than equal (>= 30) or value less than (<) 90 and decrease from baseline (DFB)>= 30; DBP: value > 100 and increase from baseline >=20 or 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. Here, Number of Subjects Analyzed' signifies subjects evaluable for this endpoint, and n signifies= number of subjects evaluable for specified category. 99999=data could not be calculated due to insufficient subjects.

End point type	Secondary

End point timeframe:

From start of study treatment until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	136		
Units: Subjects				
SBP; Value >150 and IFB ≥ 30;n=271,136	35	16		
SBP; Value< 90 and DFB ≥ 30;n=271,136	8	3		
DBP; Value>100 and IFB ≥ 20;n=271,136	8	99999		
DBP Value< 50 and DFB≥ 20;n=271,136	10	5		
Heart Rate (BPM) Value < 40 or > 120;n=270,136	265	135		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Physical Examination Finding

End point title	Number of Subjects With Abnormal Physical Examination Finding

End point description:

A complete physical examination was performed and included an assessment of the following: general appearance including site of infection, skin, head and throat (head, eyes, ears, nose, and throat), lymph nodes, lungs, cardiovascular (CV), abdomen, musculoskeletal, and neurological systems. The safety analysis set included all subjects who received any amount of study treatment. Here, n=number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Screening, End of treatment (up to 24 hours post infusion on Day 14) and Test of Cure (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Subjects				
Abdomen: Screening;n=275,137	184	103		
Abdomen: End of Treatment;n=263,130	56	30		
Abdomen: Test of Cure;n=230,112	31	12		
Cardiovascular: Screening;n=275,137	50	22		
Cardiovascular: End of Treatment;n=264,129	27	14		
Cardiovascular: Test of Cure;n=230,113	20	10		
Ears: Screening;n=270,137	1	1		
Ears: End of Treatment;n=261,128	0	1		
Ears:Test of Cure;n=228,112	0	1		
Eyes: Screening;n=272,137	13	4		
Eyes End of Treatment;n=262,128	7	1		
Eyes: Test of Cure;n=228,112	6	1		
General appearance: Screening;n=273,137	77	35		
General appearance: End of Treatment;n=263,129	34	15		
General appearance: Test of Cure;n=228,113	16	8		
Head: Screening;n=271,136	12	4		
Head: End of Treatment;n=263,127	10	5		
Head: Test of Cure;n=229,111	6	2		
Lungs: Screening;n=275,137	70	37		
Lungs: End of Treatment;n=264,129	45	15		
Lungs: Test of Cure;n=231,113	22	8		
Lymph nodes: Screening;n=271,136	1	0		
Lymph nodes: End of Treatment;n=258,128	1	0		
Lymph nodes: Test of Cure;n=228,112	0	0		
Musculoskeletal: Screening;n=275,137	21	10		
Musculoskeletal: End of Treatment;n=262,129	17	9		
Musculoskeletal: Test of Cure;n=228,112	9	3		

Neurological: Screening;n=273,136	37	13		
Neurological: End of Treatment;n=262,130	34	9		
Neurological: Test of Cure;n=229,112	17	6		
Nose: Screening;n=271,137	4	3		
Nose: End of Treatment;n=262,128	2	0		
Nose: Test of Cure;n=228,112	1	0		
Skin: Screening;n=274,137	47	25		
Skin: End of Treatment;n=262,129	33	22		
Skin: Test of Cure;n=229,113	21	12		
Throat: Screening;n=266,136	9	0		
Throat: End of Treatment;n=258,128	10	1		
Throat: Test of Cure;n=227,111	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Findings

End point title	Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Findings

End point description:

Standard 12-lead ECGs were recorded with the subjects in the supine position after the subject had rested in this position for 10 minutes. Clinically significant findings were based on investigators assessment. The safety analysis set included all subjects who received any amount of study treatment.

End point type	Secondary

End point timeframe:

Baseline (latest non-missing value before start of treatment) and Day 3

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Subjects				
Baseline	16	5		
Day 3	11	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Clinical Cure at End of Treatment (EOT) Visit: ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure at End of Treatment

	(EOT) Visit: ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. The ITT analysis set included all randomized subjects regardless of the treatment received.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of subjects				
number (confidence interval 95%)	75.9 (70.6 to 80.6)	73.6 (65.8 to 80.3)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	11.5

Other pre-specified: Percentage of Subjects With Clinical Cure at EOT Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure at EOT Visit: Micro-ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (confidence interval 95%)	79.7 (73.3 to 85.1)	80.9 (72.0 to 87.8)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.7
upper limit	9.4

Other pre-specified: Percentage of Subjects With Clinical Cure at EOT Visit: CE Analysis Set

End point title	Percentage of Subjects With Clinical Cure at EOT Visit: CE Analysis Set

End point description:

Clinical cure = improvement in signs and symptoms after treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey’s method. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Percentage of subjects				
number (confidence interval 95%)	82.2 (76.6 to 86.8)	81.9 (73.7 to 88.4)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	9.9

Other pre-specified: Percentage of Subjects With Clinical Cure by Type of Infection at EOT Visit: ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Type of Infection at EOT Visit: ITT Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey’s method. The ITT analysis set included all randomized subjects regardless of the treatment received. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of subjects				
number (confidence interval 95%)				
cIAI;n=208,104	81.7 (76.1 to 86.5)	79.8 (71.3 to 86.6)		
HAP/VAP;n=74,36	59.5 (48.1 to 70.1)	55.6 (39.4 to 70.8)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Statistical analysis description: HAP/VAP	
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	23.4

Statistical analysis title	ATM± AVI and MER± COL
Statistical analysis description: cIAI	
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	11.9

Other pre-specified: Percentage of Subjects With Clinical Cure at EOT Visit: ME Analysis Set

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

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (confidence interval 95%)	84.6 (78.1 to 89.7)	83.5 (74.2 to 90.4)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL
Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	12

Other pre-specified: Percentage of Subjects With Clinical Cure by Type of Infection at EOT Visit: CE Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Type of Infection at EOT Visit: CE Analysis Set

End point description:

Clinical cure was defined as improvement in baseline signs and symptoms such that after study treatment, no further antimicrobial treatment for the index infection (i.e., cIAI or HAP/VAP) was

required. Additionally, for cIAI subjects, no unplanned drainage or surgical intervention was necessary since the initial procedure. Clinical cure was determined by the Independent Clinical Adjudication Committee. 95% CI was based on Jeffrey's method. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 24)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Percentage of subjects				
number (confidence interval 95%)				
cIAI;n=168,83	88.7 (83.2 to 92.8)	85.5 (76.8 to 91.8)		
HAP/VAP;n=45,22	57.8 (43.2 to 71.4)	68.2 (47.4 to 84.5)		

Statistical analyses

Statistical analysis title	ATM± AVI and MER± COL

Statistical analysis description:

HAP/VAP

Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	-10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.6
upper limit	14.9

Statistical analysis title	ATM± AVI and MER± COL

Statistical analysis description:

cIAI

Comparison groups	Aztreonam-avibactam ± Metronidazole v Meropenem± colistimethate

Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical cure rate
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	13.2

Other pre-specified: Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point description:

Clinical cure= improvement in signs and symptoms after treatment, no further antimicrobial treatment for index infection was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary in initial procedure. Percentage of subjects with clinical cure by pathogen resistance type type (ATM non-suscpetible, Meropenem non-susceptible based on European Committee on Antimicrobial Susceptibility Testing [EUCAST] criteria and Clinical and Laboratory Standards Institute [CLSI] criteria, criteria, ESBL, Carbapenemase, and Serene Carbapenemase and MBL-positive) is reported in this endpoint. Micro-ITT analysis set included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible, EUCAST;n=55,36	74.5	75.0		
ATM non-susceptible, CLSI;n=38,31	68.4	74.2		
Meropenem non-susceptible, EUCAST;n=19,11	57.9	72.7		
Meropenem non-susceptible, CLSI;n=17,12	58.8	75.0		
ESBL-positive;n=25,20	72.0	75.0		
Carbapenemase-positive;n=13,6	61.5	50.0		
Serene Carbapenemase;n=7,3	57.1	33.3		
MBL-positive;n=7,3	57.1	66.7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point description:

Clinical cure =improvement in signs and symptoms after treatment, no further antimicrobial treatment for the index infection was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary in initial procedure. Percentage of subjects with clinical cure by pathogen resistance type (ATM non-suscpetible, Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL, Carbapenemase, and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported in this endpoint. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At TOC (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible, EUCAST;n=55,36	63.6	55.6		
ATM non-susceptible, CLSI;n=38,31	60.5	61.3		
Meropenem non-susceptible;n=19,11	42.1	45.5		
Meropenem non-susceptible, CLSI;n=17,12	41.2	50.0		
ESBL-positive;n=25,20	68.0	70.0		
Carbapenemase-positive;n=13,6	30.8	33.3		
Serene Carbapenemase;n=7,3	28.6	0		
Metallo-beta-lactamase-positive;n=7,3	28.6	66.7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point description:

Clinical cure= improvement in signs and symptoms after treatment, no further antimicrobial treatment for the index infection was required. For cIAI subjects, no unplanned drainage or surgical intervention

was necessary in initial procedure. Percentage of subjects with clinical cure by pathogen resistance type (ATM non-suscpetible, Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL, Carbapenemase, and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported in this endpoint. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible, EUCAST;n=37,28	81.1	78.6		
ATM non-susceptible, CLSI;n=30,25	76.7	76.0		
Meropenem non-susceptible, EUCAST;n=13,8	69.2	62.5		
Meropenem non-susceptible, CLSI;n=13,8	69.2	62.5		
ESBL-positive;n=22,17	77.3	82.4		
Carbapenemase-positive;n=10,4	80.0	25.0		
Serene Carbapenemase;n=6,3	66.7	33.3		
Metallo-beta-lactamase-positive;n=4,1	100.0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point title	Percentage of Subjects With Clinical Cure by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point description:

Clinical cure= improvement in signs and symptoms after treatment, no further antimicrobial treatment for the index infection was required. For cIAI subjects, no unplanned drainage or surgical intervention was necessary in initial procedure. Percentage of subjects with clinical cure by pathogen resistance type (ATM non-suscpetible, Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL, Carbapenemase, and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported in this endpoint. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects reported under Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible, EUCAST Criteria;n=37,28	70.3	60.7		
ATM non-susceptible, CLSI;n=30,25	66.7	64.0		
Meropenem non-susceptible, EUCAST Criteria;n=13,8	46.2	37.5		
Meropenem non-susceptible, CLSI Criteria;n=13,8	46.2	37.5		
ESBL-positive;n=22,17	72.7	76.5		
Carbapenemase-positive;n=10,4	40.0	0		
Serene Carbapenemase;n=6,3	33.3	0		
Metallo-beta-lactamase-positive;n=4,1	50.0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Subject Microbiological Response at EOT Visit: Micro-ITT Analysis Set

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

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. Micro-ITT analysis set is a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to 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	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	93		
Units: Percentage of subjects				
number (not applicable)	84.6	83.9		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per- Subject Microbiological Response at EOT Visit : ME Analysis Set

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

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who have at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents.

End point type	Other pre-specified

End point timeframe:

At EOT visit (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)	85.9	86.1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Favorable Microbiological Response per-Pathogen at EOT Visit: Micro-ITT Analysis Set

End point title	Number of Subjects With Favorable Microbiological Response per-Pathogen at EOT Visit: Micro-ITT Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. Micro-ITT analysis set is a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. All subjects reported under 'Overall Number of subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories. Only those pathogens are reported which had more than or equal to 10 isolates for either treatment group.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Subjects				
Escherichia coli; n=114,58	95	48		
Klebsiella pneumoniae; n=27,23	19	18		
Pseudomonas aeruginosa; n=18,6	14	5		
Streptococcus anginosus group; n=17,6	13	4		
Bacteroides fragilis; n=16,9	13	7		
Bacteroides thetaiotaomicron; n=11,1	8	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Favorable Microbiological Response per-Pathogen at TOC Visit: Micro-ITT Analysis Set

End point title	Number of Subjects With Favorable Microbiological Response per-Pathogen at TOC Visit: Micro-ITT Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. Micro-ITT analysis set is a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. Here, all subjects reported under 'Overall Number of subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects evaluable for specified categories. Only those pathogens are reported which had more than or equal to 10 isolates for either treatment group.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Subjects				
Escherichia coli; n=114,58	91	44		
Klebsiella pneumoniae; n=27,23	14	15		
Pseudomonas aeruginosa; n=18,6	12	3		
Streptococcus anginosus group; n=17,6	12	4		
Bacteroides fragilis; n=16,9	14	7		
Bacteroides thetaiotaomicron; n=11,1	8	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Favorable Microbiological Response per-Pathogen at EOT Visits: ME Analysis Set

End point title	Number of Subjects With Favorable Microbiological Response per-Pathogen at EOT Visits: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence 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. ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. Here, n= number of subjects available for specified rows. Only those pathogens are reported which had more than or equal to 10 isolates for either treatment group.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Subjects				
Escherichia coli; n=101,53	90	44		
Klebsiella pneumoniae; n=23,20	17	17		
Streptococcus anginosus group; n=14,5	13	3		
Bacteroides fragilis; n=15,8	13	6		
Bacteroides thetaiotaomicron; n=11,1	8	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Favorable Microbiological Response per-Pathogen at TOC Visits: ME Analysis Set

End point title	Number of Subjects With Favorable Microbiological Response per-Pathogen at TOC Visits: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. The ME analysis set included all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. Here, n = number of subjects available for specified categories. Only those pathogens are reported which had more than or equal to 10 isolates for either treatment group.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Subjects				
Escherichia coli; n=101,53	86	40		
Klebsiella pneumoniae; n=23,20	13	14		
Streptococcus anginosus group; n=14,5	12	3		
Bacteroides fragilis; n=15,8	14	6		
Bacteroides thetaiotaomicron; n=11,1	8	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all baseline pathogens for that subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence of causative pathogen from specimen at the site of infection. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. Participants with per participant response of indeterminate were excluded from analysis. Micro-ITT analysis set was used. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects available for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=32,28	68.8	78.6		
ATM non-susceptible : EUCAST:n=42,31	76.2	80.6		
Meropenem non-susceptible : CLSI:n=14,9	57.1	66.7		
Meropenem non-susceptible : EUCAST:n=14,9	57.1	66.7		
ESBL-positive:n=23,19	78.3	84.2		
Carbapenamase-positive:n=10,4	50.0	25.0		
Serene Carbapenamase-positive:n=6,3	33.3	33.3		
Metallo-beta-lactamase-positive:n=4,1	75.0	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point description:

Favorable microbiological response=all baseline pathogens for subject had a favorable outcome (eradicated or presumed eradicated). Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase, Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. Subjects with per subject response of indeterminate were excluded from analysis. Micro-ITT analysis included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of treatment. Here, 'Number of Subjects Analyzed' contributed data to table but may not have evaluable data for every category. n=number of subjects available for specified categories.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=32,27	59.4	59.3		
ATM non-susceptible: EUCAST:n=42,30	66.7	60.0		
Meropenem non-susceptible: CLSI:n=14,8	28.6	25.0		
Meropenem non-susceptible : EUCAST:n=14,8	28.6	25.0		
ESBL-positive:n=23,19	73.9	73.7		
Carbapenamase-positive:n=10,4	20.0	0.0		
Serene Carbapenamase-positive:n=6,3	16.7	0.0		
Metallo-beta-lactamase-positive:n=4,1	25.0	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point title	Percentage of subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. The ME analysis set, all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here,'n=number of subjects available for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=30,25	70.0	80.0		
ATM non-susceptible: EUCAST:n=36,28	75.0	82.1		

Meropenem non-susceptible: CLSI:n=13,8	53.8	62.5		
Meropenem non-susceptible: EUCAST:n=13,8	53.8	62.5		
ESBL-positive:n=22,17	77.3	88.2		
Carbapenamase-positive:n=9,4	44.4	25.0		
Serene Carbapenamase-positive:n=6,3	33.3	33.3		
Metallo-beta-lactamase-positive:n=3,1	66.7	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point title	Percentage of Subjects With Favorable per-Subject Microbiological Response by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. ME analysis set=all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n=number of subjects available for specified categories.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=30,25	60.0	60.0		
ATM non-susceptible: EUCAST:n=36,28	66.7	60.7		
Meropenem non-susceptible: CLSI:n=13,8	30.8	25.0		
Meropenem non-susceptible: EUCAST:n=13,8	30.8	25.0		
ESBL-positive:n=22,17	72.7	76.5		
Carbapenamase-positive:n=9,4	22.2	0.0		
Serene Carbapenamase-positive:n=6,3	16.7	0.0		
Metallo-beta-lactamase-positive:n=3,1	33.3	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at EOT Visit: Micro-ITT Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=41,31	68.3	77.4		
ATM non-susceptible: EUCAST:n=60,37	73.3	78.4		
Meropenem non-susceptible: CLSI:n=20,12	60.0	75.0		
Meropenem non-susceptible : EUCAST:n=22,11	59.1	72.7		
ESBL-positive:n=25,20	72.0	80.0		
Carbapenemase-positive:n=13,6	61.5	50.0		
Serine-carbapenemase-positive:n=7,3	42.9	33.3		
Metallo-beta-lactamase-positive:n=7,3	71.4	66.7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point title	Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at TOC Visit: Micro-ITT Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. Micro-ITT analysis set was a subset of the ITT analysis set and included all subjects who had at least one Gram-negative baseline pathogen from an adequate specimen obtained prior to the start of study treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At TOC visit (Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	94		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI;n=41,31	58.5	58.1		
ATM non-susceptible: EUCAST;n=60,37	63.3	56.8		
Meropenem non-susceptible: CLSI;n=20,12	30.0	41.7		
Meropenem non-susceptible: EUCAST;n=22,11	31.8	36.4		
ESBL-positive;n=25,20	72.0	70.0		
Carbapenemase-positive;n=13,6	23.1	33.3		
Serine-carbapenemase-positive;n=7,3	14.3	0.0		
Metallo-beta-lactamase-positive;n=7,3	28.6	66.7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point title	Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at EOT Visit: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. The ME analysis set, all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'n=number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

At EOT (Within 24 hours after last infusion on Day 14)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI;n=33,25	75.8	80.0		
ATM non-susceptible: EUCAST;n=42,29	78.6	82.8		
Meropenem non-susceptible: CLSI;n=16,8	62.5	62.5		
Meropenem non-susceptible: EUCAST;n=16,8	62.5	62.5		
ESBL-positive;n=22,17	77.3	88.2		
Carbapenemase-positive;n=10,4	70.0	25.0		
Serine-carbapenemase-positive;n=6,3	50.0	33.3		
Metallo-beta-lactamase-positive;n=4,1	100.0	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point title	Percentage of Subjects With Favorable per-Pathogen Microbiological Response by Pathogen Resistance Type at TOC Visit: ME Analysis Set

End point description:

Subjects were determined to have a favorable microbiological response if all pathogens had a favorable outcome. Eradication: Absence of causative pathogen from specimen. Presumed eradication: repeat culture of specimens were not indicated in a subject who had a clinical response of cure. Percentage of Subjects with favorable per-subject microbiological response by pathogen resistance type (ATM and Meropenem non-susceptible based on EUCAST and CLSI criteria, ESBL-Positive, Carbapenemase and Serene Carbapenemase and Metallo-beta-lactamase-positive) is reported. The ME analysis set, all subjects commonly included in both micro-ITT and CE analysis sets and included subjects who had at least 1 etiologic pathogen from an adequate baseline culture regardless of susceptibility to study agents. All subjects under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'n=number of subjects evaluable for specified categories.

End point type	Other pre-specified
End point timeframe: At TOC visit (Day 28)	

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	79		
Units: Percentage of subjects				
number (not applicable)				
ATM non-susceptible: CLSI:n=33,25	63.6	60.0		
ATM non-susceptible: EUCAST;n=42,29	66.7	62.1		
Meropenem non-susceptible: CLSI;n=16,8	31.3	25.0		
Meropenem non-susceptible : EUCAST;n=16,8	31.3	25.0		
ESBL-positive;n=22,17	77.3	76.5		
Carbapenemase-positive;n=10,4	30.0	0.0		
Serine-carbapenemase-positive;n=6,3	16.7	0.0		
Metallo-beta-lactamase-positive;n=4,1	50.0	0.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects According to Total Score for the Composite Endpoint of Symptom-Based Objective Clinical Measures: ITT Analysis Set

End point title	Number of Subjects According to Total Score for the Composite Endpoint of Symptom-Based Objective Clinical Measures: ITT Analysis Set
End point description: Analysis was not performed as composite score was not developed prior to study completion. The ITT analysis set included all randomized subjects regardless of receipt of study drug.	
End point type	Other pre-specified
End point timeframe: Up to Day 28	

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: Subjects				

Notes:

[3] - Analysis was not performed as composite score was not developed prior to study completion.

[4] - Analysis was not performed as composite score was not developed prior to study completion.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects According to Total Score for the Composite Endpoint of Symptom-Based Objective Clinical Measures: CE Analysis Set

End point title	Number of Subjects According to Total Score for the Composite Endpoint of Symptom-Based Objective Clinical Measures: CE Analysis Set

End point description:

Analysis was not performed as composite score was not developed prior to study completion.CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have Gram-positive pathogens.

End point type	Other pre-specified

End point timeframe:

Up to Day 28

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Subjects				

Notes:

[5] - Analysis was not performed as composite score was not developed prior to study completion.

[6] - Analysis was not performed as composite score was not developed prior to study completion.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects who Died on or Before 14 Days From Randomization: ITT Analysis Set

End point title	Percentage of Subjects who Died on or Before 14 Days From Randomization: ITT Analysis Set

End point description:

Percentage of subjects who died on or before 14 days from randomization is reported in this endpoint. The ITT analysis set included all randomized subjects regardless of receipt of study drug.

End point type	Other pre-specified

End point timeframe:

From randomization up to 14 days

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Percentage of subjects				
number (not applicable)	2.8	3.6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Total Length of Hospital Stay up to TOC Visit: ITT Analysis Set

End point title	Total Length of Hospital Stay up to TOC Visit: ITT Analysis Set

End point description:

The total length of hospital stay was defined as the total number of calendar days on which the subject was in the hospital from the date of randomization up to and including the specified time point of TOC. The ITT analysis set included all randomized subjects regardless of receipt of study drug. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization up to Day 28

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	281	139		
Units: Days				
arithmetic mean (standard deviation)	13.6 (± 9.42)	12.9 (± 8.05)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Length of Intensive Care Unit (ICU) Stay: ITT Analysis Set

End point title	Length of Intensive Care Unit (ICU) Stay: ITT Analysis Set

End point description:

The total length of ICU stay was defined as the total number of calendar days on which the subject was in ICU for the period from date of randomization until the TOC visit. The ITT analysis set included all randomized subjects regardless of receipt of study drug. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	39		
Units: Days				
arithmetic mean (standard deviation)	11.6 (± 9.10)	12.5 (± 9.45)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Total Length of Hospital Stay up to TOC Visit: CE Analysis Set

End point title	Total Length of Hospital Stay up to TOC Visit: CE Analysis Set

End point description:

The total length of hospital stay was defined as the total number of calendar days on which the subject was in the hospital from the date of randomization up to and including the specified time point of TOC. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens.

End point type	Other pre-specified

End point timeframe:

From randomization up to Day 28

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Days				
arithmetic mean (standard deviation)	13.0 (± 8.55)	12.3 (± 7.29)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Duration of Study Treatment

End point title	Duration of Study Treatment

End point description:

The duration of therapy in calendar days were calculated as follows: Date of last dose of study drug - date of first dose of study drug +1. The safety analysis set included all subjects who received any amount of study treatment.

End point type	Other pre-specified

End point timeframe:

From first dose of study treatment until last dose of treatment (Up to 14 days)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	137		
Units: Days				
arithmetic mean (standard deviation)	8.5 (± 3.52)	8.9 (± 3.17)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Length of Intensive Care Unit (ICU) Stay: CE Analysis Set

End point title	Length of Intensive Care Unit (ICU) Stay: CE Analysis Set

End point description:

The total length of ICU stay was defined as the total number of calendar days on which the subject was in ICU for the period from date of randomization until the TOC visit. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	24		
Units: Days				
arithmetic mean (standard deviation)	12.1 (± 9.23)	12.4 (± 9.38)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Mechanical Ventilation: ITT Analysis Set

End point title	Number of Subjects With Mechanical Ventilation: ITT Analysis Set

End point description:

Number of subjects with mechanical ventilation were reported in this endpoint measure. The ITT analysis set included all randomized subjects regardless of receipt of study drug. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	36		
Units: Subjects	43	21		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects Admitted to the ICU: CE Analysis Set

End point title	Number of Subjects Admitted to the ICU: CE Analysis Set

End point description:

The number of subjects admitted to the ICU were reported in this endpoint measure. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	105		
Units: Subjects	54	24		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects Admitted to the ICU: ITT Analysis Set

End point title	Number of Subjects Admitted to the ICU: ITT Analysis Set

End point description:

Number of subjects admitted to the ICU up to TOC were reported in this endpoint. The ITT analysis set included all randomized subjects regardless of receipt of study drug.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	140		
Units: Subjects	80	39		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Mechanical Ventilation: CE Analysis Set

End point title	Number of Subjects With Mechanical Ventilation: CE Analysis Set

End point description:

Number of subjects with mechanical ventilation were reported in this endpoint measure. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	22		
Units: Subjects	24	13		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Duration of Mechanical Ventilation in HAP/VAP Subjects: ITT Analysis Set

End point title	Duration of Mechanical Ventilation in HAP/VAP Subjects: ITT Analysis Set

End point description:

Duration of mechanical ventilation was defined as the total number of calendar days on which the subject required mechanical ventilation from the date of randomization up to TOC. The ITT analysis set included all randomized subjects regardless of receipt of study drug. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	21		
Units: Days				
arithmetic mean (standard deviation)	14.2 (± 9.94)	16.7 (± 11.16)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Duration of Mechanical Ventilation in HAP/VAP Subjects: CE Analysis Set

End point title	Duration of Mechanical Ventilation in HAP/VAP Subjects: CE Analysis Set

End point description:

Duration of mechanical ventilation was defined as the total number of calendar days on which the subject required mechanical ventilation from the date of randomization up to TOC. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study

treatment or <48 hours of treatment before discontinuing study drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC (except protocol-allowed antibiotics); no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections due to non-eligible pathogens and did not have only Gram-positive pathogens. Here, 'Number of Subjects Analyzed' signifies subjects evaluable for this endpoint measure.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	13		
Units: Days				
arithmetic mean (standard deviation)	17.4 (± 8.99)	19.5 (± 11.16)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Unplanned Surgical Interventions in Complicated Intra-abdominal Infections (cIAI) Subjects: ITT Analysis Set

End point title	Number of Subjects With Unplanned Surgical Interventions in Complicated Intra-abdominal Infections (cIAI) Subjects: ITT Analysis Set

End point description:

Unplanned surgical interventions was defined as those occurring after the initial qualifying surgical intervention and prior to the TOC visit. Number of cIAI participants with unplanned surgical intervention according to clinical response categories of cure and failure is reported in this endpoint measure. The ITT analysis set included all randomized subjects regardless of receipt of study drug. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, 'signifies= number of subjects available for specified categories.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	100		
Units: Subjects				
Cure;n=159,77	1	1		
Failure;n=34,23	5	10		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Unplanned Surgical Interventions in cIAI Subjects: CE Analysis Set

End point title	Number of Subjects With Unplanned Surgical Interventions in cIAI Subjects: CE Analysis Set

End point description:

Unplanned surgical interventions were defined as those occurring after the initial qualifying surgical intervention and prior to the TOC visit. Number of cIAI subjects with unplanned surgical intervention according to clinical response categories of cure and failure is reported in this endpoint measure. CE analysis set: all subjects in ITT analysis set; met criteria for cIAI, or HAP/VAP; received at least 48 hours of study treatment or <48 hours of treatment before discontinuing drug due to AE; no concomitant antibiotics for any baseline pathogens between first dose and TOC; no prior antibiotics other than allowed per protocol; no important protocol deviations; no clinical outcome of indeterminate at TOC; no monomicrobial infections and did not have only Gram-positive pathogens. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table but may not have evaluable data for every category. Here, n= Subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

From randomization until TOC visit (Up to Day 28)

End point values	Aztreonam-avibactam ± Metronidazole	Meropenem± colistimethate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	83		
Units: Subjects				
Cure; n=143,66	1	1		
Failure; n=25,17	5	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment until end of late follow-up visit (Up to Day 45)

Adverse event reporting additional description:

Data is presented for Safety analysis set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Meropenem

Reporting group description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 1000 mg meropenem every 8 hours by IV infusion. A higher dose of 2000 mg was given by IV infusion over 180 minutes if carbapenem resistant pathogen was strongly suspected. Subjects were administered colistimethate sodium at investigator's discretion.

Reporting group title	ATM-AVI (+/-MTZ)

Reporting group description:

Subjects hospitalized with cIAI or NP (including HAP and VAP) were randomized to receive 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 IV infusion over 3 hours on Day 1. Subjects were administered a maintenance dose of ATM-AVI by IV infusion over 3 hours on Days 2 to 14. Subjects with cIAI also received metronidazole (MTZ) 500 milligrams (mg) IV every 8 hours.

Serious adverse events	Meropenem	ATM-AVI (+/-MTZ)	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 137 (18.25%)	53 / 275 (19.27%)	
number of deaths (all causes)	11	19	
number of deaths resulting from adverse events	11	19	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of appendix			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			

subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colorectal cancer			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Shock			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 137 (0.73%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Deep vein thrombosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Localised oedema			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sudden death			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Social circumstances			
Convalescent			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural fibrosis			

subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 137 (1.46%)	3 / 275 (1.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 137 (0.00%)	4 / 275 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transaminases increased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	1 / 137 (0.73%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal anastomosis complication			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fat embolism			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Cardiac arrest			
subjects affected / exposed	2 / 137 (1.46%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Myxomatous mitral valve degeneration			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain dislocation syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Splenic infarction			

subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal fluid collection			
subjects affected / exposed	2 / 137 (1.46%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			

subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	2 / 137 (1.46%)	4 / 275 (1.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal wall infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related bacteraemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatitis B			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 137 (0.00%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 137 (0.00%)	3 / 275 (1.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			

subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 137 (0.73%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 137 (0.73%)	4 / 275 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	2 / 137 (1.46%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Septic shock			
subjects affected / exposed	3 / 137 (2.19%)	2 / 275 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Tracheobronchitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Meropenem	ATM-AVI (+/-MTZ)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 137 (32.85%)	113 / 275 (41.09%)	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 137 (2.19%)	1 / 275 (0.36%)	
occurrences (all)	3	1	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 137 (3.65%)	15 / 275 (5.45%)	
occurrences (all)	6	15	
Alanine aminotransferase increased			

subjects affected / exposed	7 / 137 (5.11%)	18 / 275 (6.55%)	
occurrences (all)	7	18	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 137 (2.19%)	5 / 275 (1.82%)	
occurrences (all)	3	6	
Phlebitis			
subjects affected / exposed	0 / 137 (0.00%)	6 / 275 (2.18%)	
occurrences (all)	0	8	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 137 (0.73%)	6 / 275 (2.18%)	
occurrences (all)	1	6	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 137 (5.11%)	20 / 275 (7.27%)	
occurrences (all)	9	27	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	4 / 137 (2.92%)	1 / 275 (0.36%)	
occurrences (all)	8	2	
Pyrexia			
subjects affected / exposed	5 / 137 (3.65%)	14 / 275 (5.09%)	
occurrences (all)	7	16	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 137 (1.46%)	10 / 275 (3.64%)	
occurrences (all)	2	10	
Nausea			
subjects affected / exposed	3 / 137 (2.19%)	10 / 275 (3.64%)	
occurrences (all)	3	10	
Constipation			
subjects affected / exposed	2 / 137 (1.46%)	8 / 275 (2.91%)	
occurrences (all)	2	9	
Abdominal pain			

subjects affected / exposed	4 / 137 (2.92%)	6 / 275 (2.18%)	
occurrences (all)	5	7	
Abdominal distension			
subjects affected / exposed	3 / 137 (2.19%)	5 / 275 (1.82%)	
occurrences (all)	3	5	
Diarrhoea			
subjects affected / exposed	5 / 137 (3.65%)	16 / 275 (5.82%)	
occurrences (all)	5	16	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 137 (0.73%)	7 / 275 (2.55%)	
occurrences (all)	1	7	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 137 (0.73%)	6 / 275 (2.18%)	
occurrences (all)	1	6	
Hepatic function abnormal			
subjects affected / exposed	3 / 137 (2.19%)	11 / 275 (4.00%)	
occurrences (all)	3	13	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 137 (0.00%)	7 / 275 (2.55%)	
occurrences (all)	0	7	
Decubitus ulcer			
subjects affected / exposed	1 / 137 (0.73%)	6 / 275 (2.18%)	
occurrences (all)	1	7	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	4 / 137 (2.92%)	16 / 275 (5.82%)	
occurrences (all)	5	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 May 2022	Increased sample size, Updated Single Reference Safety Document and References list to reflect current and additional sources of study drugs or comparators. Updated risk/benefit language to replace "Drug induced liver injury" with "Increased liver transaminases" to be consistent with Investigator Brochure, Clarification to the study drug characteristics and on when ECG should be performed for both treatment arms.

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. However, actual number of deaths were, for Aztreonam-avibactam ± Metronidazole 20 and Meropenem± colistimethate 11.

Notes: