Clinical trial results:
A Phase III, Randomized, Multicenter, Double-Blind, Double-Dummy, Parallel-Group, Comparative Study to Determine the Efficacy, Safety, and Tolerability of Ceftazidime-Avibactam (CAZ-AVI, formerly CAZ104) Versus Doripenem Followed by Appropriate Oral Therapy in the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis, With a Gram-Negative Pathogen in Hospitalized Adults

Summary

EudraCT number	2011-005721-43
Trial protocol	GR BE BG DE CZ SK PT HU
Global end of trial date	21 July 2015

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	05 February 2016

Trial information

Trial identification

Sponsor protocol code	D4280C00002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	S-151 85, Södertälje, Sweden,
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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	04 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 August 2014
Global end of trial reached?	Yes
Global end of trial date	21 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the noninferiority of ceftazidime-avibactam (CAZ-AVI, formerly CAZ104) compared with doripenem with respect to the following FDA coprimary endpoints and EU primary endpoint in the microbiological modified intent-to-treat (mMITT) analysis set:

FDA Primary Objective (Coprimary Endpoints):

Symptomatic resolution (or return to premorbid state) of UTI-specific symptoms except flank pain (frequency/urgency/dysuria/suprapubic pain) and resolution of, or improvement in, flank pain based on the patient-reported symptom assessment response at the Day 5 visit.

Both per-patient favourable microbiological response and symptomatic resolution (or return to premorbid state) of all UTI-specific symptoms (frequency/urgency/dysuria/suprapubic pain/flank pain) based on the patient-reported symptom assessment response at the Test of Cure (TOC) visit.

EU Primary Objective:

Per patient favourable microbiological response at the TOC visit.

Protection of trial subjects:

The study will be performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with the International Conference on Harmonisation (ICH) harmonised tripartite guideline E6(R1): Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.'

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 77
Country: Number of subjects enrolled	Croatia: 53
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Romania: 154
Country: Number of subjects enrolled	Russian Federation: 184
Country: Number of subjects enrolled	Serbia: 8
Country: Number of subjects enrolled	Slovakia: 22
Country: Number of subjects enrolled	Turkey: 4

Country: Number of subjects enrolled	Ukraine: 215
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Argentina: 15
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Mexico: 29
Country: Number of subjects enrolled	Peru: 61
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Japan: 55
Worldwide total number of subjects	1033
EEA total number of subjects	409

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)	710
From 65 to 84 years	313
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

A total of 1033 patients were randomized in 133 centers in 25 countries. The first patient was randomized on 10OCT2012 and the last patient was randomized on 30JUN2014. A total of 5 patients in the CAZ-AVI arm and 8 patients in Doripenem arm were randomized but did not receive study drug.

Pre-assignment

Screening details:

None

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CAZ-AVI

Arm description:

Ceftazidime-avibactam treatment group

Arm type	Experimental
Investigational medicinal product name	Ceftazidime-avibactam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile crystalline powder, 2000 mg ceftazidime and 500 mg avibactam

Arm title	Doripenem

Arm description:

Doripenem treatment group

Arm type	Active comparator
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile powder, 500 mg

Number of subjects in period 1	CAZ-AVI	Doripenem
Started	516	517
Completed	473	476
Not completed	43	41
Consent withdrawn by subject	12	12
Other Eligibility criteria	11	9
Lost to follow-up	20	20

Baseline characteristics

Reporting groups	
Reporting group title	CAZ-AVI
Reporting group description: Ceftazidime-avibactam treatment group	
Reporting group title	Doripenem
Reporting group description: Doripenem treatment group	

Reporting group values	CAZ-AVI	Doripenem	Total
Number of subjects	516	517	1033
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)	357	353	710
From 65-84 years	153	160	313
85 years and over	6	4	10
Age Continuous | Units: Years			
arithmetic mean	51.6	52.3	
standard deviation	± 19.82	± 18.89	-
Gender, Male/Female Units: Participants			
Female	353	364	717
Male	163	153	316
Age, Customized Units: Subjects			
18-45	195	175	370
46-64	162	178	340
65-74	80	100	180
75-90	79	64	143

End points

End points reporting groups	
Reporting group title	CAZ-AVI
Reporting group description: Ceftazidime-avibactam treatment group	
Reporting group title	Doripenem
Reporting group description: Doripenem treatment group	

Primary: Patient-reported symptomatic response at day 5 (mMITT analysis set): non-inferiority hypothesis test

End point title	Patient-reported symptomatic response at day 5 (mMITT analysis set): non-inferiority hypothesis test

End point description:

Proportion of patients with symptomatic resolution (or return to premorbid state) of UTI-specific symptoms except flank pain (frequency/urgency/dysuria/suprapubic pain) with resolution of or improvement in flank pain based on the patient-reported symptom assessment response at the Day 5 visit in the mMITT analysis set. The sponsor will conclude noninferiority if the lower limit of the 95% CI of difference (corresponding to a 97.5% 1-sided lower bound) is greater than -12.5% for both FDA coprimary outcome variables (symptomatic resolution at day 5 or favorable combined response at test of cure (TOC)).

End point type	Primary

End point timeframe:

At Day 5 visit. Day 5 visit is based on 24 hour periods from the first dose date and time.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Symptomatic resolution	276	276		
Symptom persistence	103	124		
Indeterminate	14	17		
Symptomatic resolution rate	70.2	66.2		

Statistical analyses

Statistical analysis title	Non-inferiority hypothesis test

Statistical analysis description:

H0: Difference (CAZ-AVI treatment group minus Doripenem treatment group) of symptomatic resolution rates ≤ -12.5%

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Difference of symp resolution rates
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.39
upper limit	10.42

Primary: Combined patient-reported symptomatic and microbiological response at TOC (mMITT analysis set): non-inferiority hypothesis test

End point title	Combined patient-reported symptomatic and microbiological response at TOC (mMITT analysis set): non-inferiority hypothesis test

End point description:

Proportion of patients with both a favorable per patient microbiological response and symptomatic resolution (or return to premorbid state) of all UTI-specific symptoms (frequency/urgency/dysuria/suprapubic pain/flank pain) based on the patient-reported symptom assessment response at the TOC visit in the mMITT analysis set. The sponsor will conclude noninferiority if the lower limit of the 95% CI of difference (corresponding to a 97.5% 1-sided lower bound) is greater than -12.5% for both FDA coprimary outcome variables (symptomatic resolution at day 5 or favorable combined response at test of cure (TOC)).

End point type	Primary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Favorable	280	269		
Unfavorable	81	109		
Indeterminate	32	39		
Favorable response rate	71.2	64.5		

Statistical analyses

Statistical analysis title	Non-inferiority hypothesis test

Statistical analysis description:

H0: Difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable combined response rates ≤ -12.5%

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable combined resp rates
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	13.12

Primary: Per-patient microbiological response at TOC (mMITT analysis set): non-inferiority hypothesis test

End point title	Per-patient microbiological response at TOC (mMITT analysis set): non-inferiority hypothesis test

End point description:

Proportion of patients with a favorable per patient microbiological response at TOC. The primary efficacy outcome variable for ROW is the proportion of patients with a favorable per-patient microbiological response at the TOC visit in the mMITT analysis set.

End point type	Primary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Favorable	304	296		
Unfavorable	58	83		
Indeterminate	31	38		
Favorable response rate	77.4	71		

Statistical analyses

Statistical analysis title	Non-inferiority hypothesis test

Statistical analysis description:

H0: Difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates ≤ -12.5%

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	12.36

Secondary: Per-patient microbiological response at EOT (IV) (mMITT analysis set)

End point title	Per-patient microbiological response at EOT (IV) (mMITT analysis set)

End point description:

Proportion of patients with a favorable per-patient microbiological response at EOT (IV)

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Favorable	374	395		
Unfavorable	1	3		
Indeterminate	18	19		
Favorable response rate	95.2	94.7		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	3.56

Secondary: Per-patient microbiological response at LFU (mMITT analysis set)

End point title	Per-patient microbiological response at LFU (mMITT analysis set)

End point description:

Proportion of patients with a favorable per patient microbiological response at LFU

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Favorable	268	254		
Unfavorable	83	125		
Indeterminate	42	38		
Favorable response rate	68.2	60.9		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	13.81

Secondary: Per-patient microbiological response at EOT (IV) (ME at EOT (IV) analysis set)

End point title	Per-patient microbiological response at EOT (IV) (ME at EOT (IV) analysis set)

End point description:

Proportion of patients with a favorable per-patient microbiological response at EOT (IV)

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	361		
Units: Participants				
number (not applicable)				
Favorable	324	359		
Unfavorable	1	2		
Favorable response rate	99.7	99.4		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	686
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	1.72

Secondary: Per-patient microbiological response at TOC (ME at TOC analysis set)

End point title	Per-patient microbiological response at TOC (ME at TOC analysis set)
End point description:	
Proportion of patients with a favorable per patient microbiological response at TOC	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participants				
number (not applicable)				
Favorable	241	225		
Unfavorable	45	73		
Favorable response rate	84.3	75.5		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	584
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	8.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.27
upper limit	15.24

Secondary: Per-patient microbiological response at LFU (ME at LFU analysis set)

End point title	Per-patient microbiological response at LFU (ME at LFU analysis set)

End point description:

Proportion of patients with a favorable per patient microbiological response at LFU

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	262		
Units: Participants				
number (not applicable)				
Favorable	182	166		
Unfavorable	63	96		
Favorable response rate	74.3	63.4		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	507
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.86
upper limit	18.85

Secondary: Per-patient microbiological response at EOT (IV) (Extended ME at EOT (IV) analysis set)

End point title	Per-patient microbiological response at EOT (IV) (Extended ME at EOT (IV) analysis set)

End point description:

Proportion of patients with a favorable per-patient microbiological response at EOT (IV)

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	371		
Units: Participants				
number (not applicable)				
Favorable	335	369		
Favorable response rate	99.7	99.5		
Unfavorable	1	2		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	1.68

Secondary: Per-patient microbiological response at TOC (Extended ME at TOC analysis set)

End point title	Per-patient microbiological response at TOC (Extended ME at TOC analysis set)

End point description:

Proportion of patients with a favorable per patient microbiological response at TOC

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participants				
number (not applicable)				
Favorable	243	236		
Favorable response rate	83.2	75.9		
Unfavorable	49	75		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	13.74

Secondary: Per-patient microbiological response at LFU (Extended ME at LFU analysis set)

End point title	Per-patient microbiological response at LFU (Extended ME at LFU analysis set)

End point description:

Proportion of patients with a favorable per patient microbiological response at LFU

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	272		
Units: Participants				
number (not applicable)				
Favorable	184	173		
Favorable response rate	73.3	63.6		
Unfavorable	67	99		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.72
upper limit	17.55

Secondary: Investigator determined clinical response at EOT (IV) (mMITT analysis set)

End point title	Investigator determined clinical response at EOT (IV) (mMITT analysis set)
End point description:	
Proportion of patients with a clinical cure at EOT (IV). The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Clinical cure	378	407		
Clinical cure rate	96.2	97.6		
Clinical failure	5	5		
Indeterminate	10	5		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.07
upper limit	1.02

Secondary: Investigator determined clinical response at TOC (mMITT analysis set)

End point title	Investigator determined clinical response at TOC (mMITT analysis set)
End point description:	
Proportion of patients with a clinical cure at TOC. The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Clinical cure	355	377		
Clinical cure rate	90.3	90.4		
Clinical failure	11	24		
Indeterminate	27	16		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.23
upper limit	4.03

Secondary: Investigator determined clinical response at LFU (mMITT analysis set)

End point title	Investigator determined clinical response at LFU (mMITT analysis set)
End point description:	
Proportion of patients with a clinical cure at LFU. The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At LFU visit. LFU visit is 45 to 52 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Clinical cure	335	350		
Clinical cure rate	85.2	83.9		
Clinical failure	23	39		
Indeterminate	35	28		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	6.3

Secondary: Investigator determined clinical response at EOT (IV) (ME at EOT (IV) analysis set)

End point title	Investigator determined clinical response at EOT (IV) (ME at EOT (IV) analysis set)

End point description:

Proportion of patients with a clinical cure at EOT (IV). The investigator should consider the entirety of the patient’s clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient’s clinical response.

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	361		
Units: Participants				
number (not applicable)				
Clinical cure	318	358		
Clinical cure rate	97.8	99.2		
Clinical failure	4	2		
Indeterminate	3	1		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	686
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	0.55

Secondary: Investigator determined clinical response at TOC (ME at TOC analysis set)

End point title	Investigator determined clinical response at TOC (ME at TOC analysis set)

End point description:

Proportion of patients with a clinical cure at TOC. The investigator should consider the entirety of the patient’s clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient’s clinical response.

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participants				
number (not applicable)				
Clinical cure	277	285		
Clinical cure rate	96.9	95.6		
Clinical failure	4	13		
Indeterminate	5	0		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	584
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	4.56

Secondary: Investigator determined clinical response at LFU (ME at LFU analysis set)

End point title	Investigator determined clinical response at LFU (ME at LFU analysis set)

End point description:

Proportion of patients with a clinical cure at LFU. The investigator should consider the entirety of the patient’s clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient’s clinical response.

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	262		
Units: Participants				
number (not applicable)				
Clinical cure	226	236		
Clinical cure rate	92.2	90.1		
Clinical failure	15	24		
Indeterminate	4	2		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	507
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	7.24

Secondary: Investigator determined clinical response at EOT (IV) (Extended ME at EOT (IV) analysis set)

End point title	Investigator determined clinical response at EOT (IV) (Extended ME at EOT (IV) analysis set)

End point description:

Proportion of patients with a clinical cure at EOT (IV). The investigator should consider the entirety of the patient’s clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient’s clinical response.

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	371		
Units: Participants				
number (not applicable)				
Clinical cure	327	368		
Clinical cure rate	97.3	99.2		
Clinical failure	4	2		
Indeterminate	5	1		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	0.04

Secondary: Investigator determined clinical response at TOC (Extended ME at TOC analysis set)

End point title	Investigator determined clinical response at TOC (Extended ME at TOC analysis set)
End point description:	
Proportion of patients with a clinical cure at TOC. The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participants				
number (not applicable)				
Clinical cure	283	298		
Clinical cure rate	96.9	95.8		
Clinical failure	4	13		
Indeterminate	5	0		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.07
upper limit	4.32

Secondary: Investigator determined clinical response at LFU (Extended ME at LFU analysis set)

End point title	Investigator determined clinical response at LFU (Extended ME at LFU analysis set)

End point description:

Proportion of patients with a clinical cure at LFU. The investigator should consider the entirety of the patient’s clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient’s clinical response.

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	272		
Units: Participants				
number (not applicable)				
Clinical cure	232	246		
Clinical cure rate	92.4	90.4		
Clinical failure	15	24		
Indeterminate	4	2		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.94
upper limit	6.91

Secondary: Investigator determined clinical response at EOT (IV) (CE at EOT (IV) analysis set)

End point title	Investigator determined clinical response at EOT (IV) (CE at EOT (IV) analysis set)

End point description:

Proportion of patients with a clinical cure at EOT (IV). The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	391		
Units: Participants				
number (not applicable)				
Clinical cure	346	387		
Clinical cure rate	98.9	99		
Clinical failure	4	4		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	741
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	1.61

Secondary: Investigator determined clinical response at TOC (CE at TOC analysis set)

End point title	Investigator determined clinical response at TOC (CE at TOC analysis set)
End point description:	
Proportion of patients with a clinical cure at TOC. The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297	330		
Units: Participants				
number (not applicable)				
Clinical cure	289	309		
Clinical cure rate	97.3	93.6		
Clinical failure	8	21		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	627
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	7.16

Secondary: Investigator determined clinical response at LFU (CE at LFU analysis set)

End point title	Investigator determined clinical response at LFU (CE at LFU analysis set)
End point description:	
Proportion of patients with a clinical cure at LFU. The investigator should consider the entirety of the patient's clinical course and current status, including an evaluation of signs and symptoms (eg, fever, dysuria, costovertebral angle tenderness) and physical examination in order to classify the patient's clinical response.	
End point type	Secondary
End point timeframe:	
At LFU visit. LFU visit is 45 to 52 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	287		
Units: Participants				
number (not applicable)				
Clinical cure	235	254		
Clinical cure rate	92.5	88.5		
Clinical failure	19	33		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clinical cure rates
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	9.05

Secondary: Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (mMITT analysis set)

End point title	Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (mMITT analysis set)
End point description:	
Clinical cure at the TOC visit for patients infected with a ceftazidime resistant pathogen in the mMITT analysis set. Includes patients infected by at least one ceftazidime-resistant Gram-negative pathogen.	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
All patients - Clinical cure (n=75, 84)	67	75		
All patients - Clinical cure rate	89.3	89.3		
Escherichia coli patients - Clin cure (n=36, 37)	33	31		
Klebsiella pneumoniae patient-Clin cure(n=18,30)	17	28		
Pseudomonas aeruginosa patient-Clin cure(n=7,6)	5	6		
Enterobacter cloacae patients-Clin cure(n=7,6)	5	5		
Proteus mirabilis patients - Clin cure (n=2, 5)	2	5		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates in All patients with a ceftazidime-resistant Gram-negative pathogen	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clin cure rates in All patients
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	10.1

Secondary: Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (ME at TOC analysis set)

End point title	Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (ME at TOC analysis set)
End point description:	
Clinical cure at the TOC visit for patients infected with a ceftazidime resistant pathogen in the ME at TOC analysis set. Includes patients infected by at least one ceftazidime-resistant Gram-negative pathogen.	
End point type	Secondary
End point timeframe:	
At TOC visit. TOC visit is 21 to 25 days from Randomization.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participants				
number (not applicable)				
All patients - Clinical cure (n=48, 57)	47	55		
All patients - Clinical cure rate	97.9	96.5		
Escherichia coli patients-Clin cure (n=23,27)	22	25		
Klebsiella pneumoniae patient-Clin cure(n=14,22)	14	22		
Pseudomonas aeruginosa patient-Clin cure(n=1, 2)	1	2		
Enterobacter cloacae patients-Clin cure(n=5,5)	5	5		
Proteus mirabilis patients - Clin cure (n=0, 2)	0	2		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates in All patients with a ceftazidime-resistant Gram-negative pathogen

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	584
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clin cure rates in All patients
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	10.2

Secondary: Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (Extended ME at TOC analysis set)

End point title	Investigator determined clinical response at TOC for patients infected by ceftazidime-resistant Gram-negative pathogen (Extended ME at TOC analysis set)

End point description:

Clinical cure at the TOC visit for patients infected with a ceftazidime resistant pathogen in the Extended ME at TOC analysis set. Includes patients infected by at least one ceftazidime-resistant Gram-negative pathogen.

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participants				
number (not applicable)				
All patients - Clinical cure (n=51, 63)	50	61		
All patients - Clinical cure rate	98	96.8		
Escherichia coli patients - Clin cure (n=23, 27)	22	25		
Klebsiella pneumoniae patien-Clin cure(n=15, 23)	15	23		
Pseudomonas aeruginosa patient-Clin cure(n=3,6)	3	6		
Enterobacter cloacae patients-Clin cure(n=5,5)	5	5		
Proteus mirabilis patients - Clin cure (n=0, 2)	0	2		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of clinical cure rates in All patients with a ceftazidime-resistant Gram-negative pathogen

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of clin cure rates in All patients
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	9.2

Secondary: Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (mMITT analysis set)

End point title	Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (mMITT analysis set)

End point description:

Favorable per-patient microbiological response at the TOC visit for patients infected with a ceftazidime resistant pathogen in the mMITT analysis set.

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	84		
Units: Participants				
number (not applicable)				
Favorable	47	51		
Favorable response rate	62.7	60.7		
Unfavorable	19	27		
Indeterminate	9	6		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.18
upper limit	16.89

Secondary: Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (ME at TOC analysis set)

End point title	Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (ME at TOC analysis set)

End point description:

Favorable per-patient microbiological response at the TOC visit for patients infected with a ceftazidime resistant pathogen in the ME at TOC analysis set.

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	57		
Units: Participants				
number (not applicable)				
Favorable	35	37		
Favorable response rate	72.9	64.9		
Unfavorable	13	20		

Statistical analyses

Statistical analysis title	Confidence interval

Statistical analysis description:

Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.03
upper limit	25.21

Secondary: Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (Extended ME at TOC analysis set)

End point title	Per-patient microbiological response at TOC in patients infected by ceftazidime-resistant Gram-negative pathogen (Extended ME at TOC analysis set)

End point description:

Favorable per-patient microbiological response at the TOC visit for patients infected with a ceftazidime resistant pathogen in the Extended ME at TOC analysis set.

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	63		
Units: Participants				
number (not applicable)				
Favorable	37	41		
Favorable response rate	72.5	65.1		
Unfavorable	14	22		

Statistical analyses

Statistical analysis title	Confidence interval
Statistical analysis description:	
Confidence interval of the difference (CAZ-AVI treatment group minus Doripenem treatment group) of favorable response rates	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
Method	Unstratified Miettinen & Nurminen method
Parameter estimate	Diff of favorable response rates
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.91
upper limit	24.01

Secondary: Time to first defervescence while on IV study therapy (mMITT analysis set)

End point title	Time to first defervescence while on IV study therapy (mMITT analysis set)
End point description:	
Time to first defervescence while on IV study therapy in patients in the mMITT analysis set who have fever at study entry.	
End point type	Secondary
End point timeframe:	
Time to first defervescence is defined as the time (in days) from the first dose of IV study therapy to first absence of fever, which is temperature ≤ 37.8 C in a 24-hour period.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participants				
number (not applicable)				
Number of patients with fever (>38°C) at baseline	157	150		
Number afebrile at the time of the last obs	155	143		
Number censored at the time of the last obs	2	7		
Median time (days) to defervescence	2	3		

Statistical analyses

Statistical analysis title	Analysis of time to first defervescence
Statistical analysis description:	
H0: No difference in time to first defervescence between treatment groups	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.038
Method	Logrank

Secondary: Time to first defervescence while on IV study therapy (ME at TOC analysis set)

End point title	Time to first defervescence while on IV study therapy (ME at TOC analysis set)
End point description:	
Time to first defervescence while on IV study therapy in patients in the ME at TOC analysis set who have fever at study entry.	
End point type	Secondary
End point timeframe:	
Time to first defervescence is defined as the time (in days) from the first dose of IV study therapy to first absence of fever, which is temperature ≤ 37.8 C in a 24-hour period.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participants				
number (not applicable)				
Number of patients with fever (>38°C) at baseline	124	108		
Number afebrile at the time of the last obs	124	105		

Number censored at the time of the last obs	0	3		
Median time (days) to defervescence	3	3		

Statistical analyses

Statistical analysis title	Analysis of time to first defervescence
Statistical analysis description:	
H0: No difference in time to first defervescence between treatment groups	
Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	584
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.129
Method	Logrank

Secondary: Time to first defervescence while on IV study therapy (Extended ME at TOC analysis set)

End point title	Time to first defervescence while on IV study therapy (Extended ME at TOC analysis set)
End point description:	
Time to first defervescence while on IV study therapy in patients in the Extended ME at TOC analysis set who have fever at study entry.	
End point type	Secondary
End point timeframe:	
Time to first defervescence is defined as the time (in days) from the first dose of IV study therapy to first absence of fever, which is temperature ≤ 37.8 C in a 24-hour period.	

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participants				
number (not applicable)				
Number of patients with fever (>38°C) at baseline	124	111		
Number afebrile at the time of the last obs	124	108		
Number censored at the time of the last obs	0	3		
Median time (days) to defervescence	3	3		

Statistical analyses

Statistical analysis title	Analysis of time to first defervescence

Statistical analysis description:

H0: No difference in time to first defervescence between treatment groups

Comparison groups	CAZ-AVI v Doripenem
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.08
Method	Logrank

Secondary: Time to first defervescence while on IV study therapy (CE at TOC analysis set)

End point title	Time to first defervescence while on IV study therapy (CE at TOC analysis set)

End point description:

Time to first defervescence while on IV study therapy in patients in the CE at TOC analysis set who have fever at study entry.

End point type	Secondary

End point timeframe:

Time to first defervescence is defined as the time (in days) from the first dose of IV study therapy to first absence of fever, which is temperature ≤ 37.8 C in a 24-hour period.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297	330		
Units: Participants				
number (not applicable)				
Number of patients with fever(>38°C) at baseline	123	118		
Number afebrile at the time of the last obs	122	113		
Number censored at the time of the last obs	1	5		
Median time (days) to defervescence	3	3		

Statistical analyses

Statistical analysis title	Analysis of time to first defervescence

Statistical analysis description:

H0: No difference in time to first defervescence between treatment groups

Comparison groups	CAZ-AVI v Doripenem

Number of subjects included in analysis	627
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.155
Method	Logrank

Secondary: Per-pathogen microbiological response at EOT (IV) for baseline pathogen (mMITT analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for baseline pathogen (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the mMITT analysis set

End point type	Secondary

End point timeframe:

At EOT IV visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=292, 306)	280	293		
Klebsiella pneumoniae - Favorable (n=44, 56)	41	51		
Proteus mirabilis - Favorable (n=17, 13)	16	11		
Enterobacter cloacae - Favorable (n= 11,13)	9	13		
Pseudomonas aeruginosa - Favorable (n=18, 20)	17	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for baseline pathogen (mMITT analysis set)

End point title	Per-pathogen microbiological response at TOC for baseline pathogen (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the mMITT analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=292, 306)	229	220		
Klebsiella pneumoniae - Favorable (n=44, 56)	33	35		
Proteus mirabilis - Favorable (n=17, 13)	16	9		
Enterobacter cloacae - Favorable (n= 11,13)	6	9		
Pseudomonas aeruginosa - Favorable (n=18, 20)	12	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for baseline pathogen (mMITT analysis set)

End point title	Per-pathogen microbiological response at LFU for baseline pathogen (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the mMITT analysis set

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=292, 306)	198	189		
Klebsiella pneumoniae - Favorable (n=44, 56)	32	30		
Proteus mirabilis - Favorable (n=17, 13)	16	6		
Enterobacter cloacae - Favorable (n= 11,13)	6	9		
Pseudomonas aeruginosa - Favorable (n=18, 20)	9	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at EOT (IV) for baseline pathogen (Extended ME at EOT (IV) analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for baseline pathogen (Extended ME at EOT (IV) analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the Extended ME at EOT (IV) analysis set

End point type	Secondary

End point timeframe:

At EOT IV visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	371		
Units: Participant				
Escherichia coli - Favorable (n=250, 274)	250	274		
Klebsiella pneumoniae - Favorable (n=34, 49)	34	48		
Proteus mirabilis - Favorable (n=13, 11)	13	11		
Enterobacter cloacae - Favorable (n= 9, 12)	9	12		
Pseudomonas aeruginosa - Favorable (n=18, 18)	17	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for baseline pathogen (Extended ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC for baseline pathogen (Extended ME at TOC analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the Extended ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participant				
Escherichia coli - Favorable (n=214, 226)	180	176		
Klebsiella pneumoniae - Favorable (n=32, 42)	26	29		
Proteus mirabilis - Favorable (n=14, 7)	14	4		
Enterobacter cloacae - Favorable (n= 7, 11)	5	8		
Pseudomonas aeruginosa - Favorable (n=13, 18)	8	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for baseline pathogen (Extended ME at LFU analysis set)

End point title	Per-pathogen microbiological response at LFU for baseline pathogen (Extended ME at LFU analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the Extended ME at LFU analysis set

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	272		
Units: Participant				
Escherichia coli - Favorable (n=179, 198)	129	131		
Klebsiella pneumoniae - Favorable (n=31, 36)	24	19		
Proteus mirabilis - Favorable (n=11,5)	11	1		
Enterobacter cloacae - Favorable (n= 7, 11)	5	8		
Pseudomonas aeruginosa - Favorable (n=12, 16)	7	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at EOT (IV) for baseline pathogen (ME at EOT (IV) analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for baseline pathogen (ME at EOT (IV) analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the ME at EOT (IV) analysis set

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	361		
Units: Participant				
Escherichia coli - Favorable (n=249, 270)	249	270		
Klebsiella pneumoniae - Favorable (n=33, 48)	33	47		
Proteus mirabilis - Favorable (n=13,11)	13	11		
Enterobacter cloacae - Favorable (n= 9, 12)	9	12		
Pseudomonas aeruginosa - Favorable (n=10, 15)	9	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for baseline pathogen (ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC for baseline pathogen (ME at TOC analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participant				
Escherichia coli - Favorable (n=214, 221)	180	171		
Klebsiella pneumoniae - Favorable (n=31, 41)	25	28		
Proteus mirabilis - Favorable (n=14, 7)	14	4		
Enterobacter cloacae - Favorable (n= 7, 11)	5	8		
Pseudomonas aeruginosa - Favorable (n=9, 13)	7	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for baseline pathogen (ME at LFU analysis set)

End point title	Per-pathogen microbiological response at LFU for baseline pathogen (ME at LFU analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the ME at LFU analysis set

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	262		
Units: Participant				
Escherichia coli - Favorable (n=179, 194)	129	127		
Klebsiella pneumoniae - Favorable (n=30, 35)	23	18		
Proteus mirabilis - Favorable (n=11,5)	11	1		
Enterobacter cloacae - Favorable (n= 7, 11)	5	8		
Pseudomonas aeruginosa - Favorable (n=8, 13)	6	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at EOT (IV) for blood only (mMITT analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for blood only (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the mMITT analysis set for blood only

End point type	Secondary

End point timeframe:

At EOT IV visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=32, 28)	31	28		
Klebsiella pneumoniae - Favorable (n=4, 2)	2	2		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=1, 2)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for blood only (mMITT analysis set)

End point title	Per-pathogen microbiological response at TOC for blood only (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the mMITT analysis set for blood only

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=32, 28)	31	28		
Klebsiella pneumoniae - Favorable (n=4, 2)	3	2		

Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=1, 2)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for blood only (mMITT analysis set)

End point title	Per-pathogen microbiological response at LFU for blood only (mMITT analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the mMITT analysis set for blood only

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
Escherichia coli - Favorable (n=32, 28)	29	27		
Klebsiella pneumoniae - Favorable (n=4, 2)	3	2		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=1, 2)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at EOT (IV) for blood only (Extended ME at EOT (IV) analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for blood only (Extended ME at EOT (IV) analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the Extended ME at EOT (IV) analysis set for blood only

End point type	Secondary

End point timeframe:

At EOT IV visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	371		
Units: Participant				
Escherichia coli - Favorable (n=26, 24)	26	24		
Klebsiella pneumoniae - Favorable (n=2, 1)	1	1		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=1, 2)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for blood only (Extended ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC for blood only (Extended ME at TOC analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the Extended ME at TOC analysis set for blood only

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participant				
Escherichia coli - Favorable (n=22, 20)	22	20		
Klebsiella pneumoniae - Favorable (n=2, 2)	2	2		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=0, 1)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for blood only (Extended ME at LFU analysis set)

End point title	Per-pathogen microbiological response at LFU for blood only (Extended ME at LFU analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the Extended ME at LFU analysis set for blood only

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	272		
Units: Participant				
Escherichia coli - Favorable (n=19, 18)	19	17		
Klebsiella pneumoniae - Favorable (n=2, 1)	2	1		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=0, 1)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at EOT (IV) for blood only (ME at EOT (IV) analysis set)

End point title	Per-pathogen microbiological response at EOT (IV) for blood only (ME at EOT (IV) analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the EOT (IV) visit in the ME at EOT (IV) analysis set for blood only

End point type	Secondary

End point timeframe:

At EOT (IV) visit. EOT (IV) visit is Within 24 hours after completion of the last infusion of IV study therapy and on/before the first dose for oral study therapy

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	325	361		
Units: Participant				
Escherichia coli - Favorable (n=26, 24)	26	24		
Klebsiella pneumoniae - Favorable (n=2, 1)	1	1		

Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=1, 2)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC for blood only (ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC for blood only (ME at TOC analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the TOC visit in the ME at TOC analysis set for blood only

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participant				
Escherichia coli - Favorable (n=22, 20)	22	20		
Klebsiella pneumoniae - Favorable (n=2, 2)	2	2		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=0, 1)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at LFU for blood only (ME at LFU analysis set)

End point title	Per-pathogen microbiological response at LFU for blood only (ME at LFU analysis set)

End point description:

Number of favorable per-pathogen microbiological responses at the LFU visit in the ME at LFU analysis set for blood only

End point type	Secondary

End point timeframe:

At LFU visit. LFU visit is 45 to 52 days from Randomization.

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	262		
Units: Participant				
Escherichia coli - Favorable (n=19, 18)	19	17		
Klebsiella pneumoniae - Favorable (n=2, 1)	2	1		
Proteus mirabilis - Favorable (n=1, 0)	1	0		
Pseudomonas aeruginosa - Favorable (n=0, 1)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (mMITT analysis set)

End point title	Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (mMITT analysis set)

End point description:

Per pathogen microbiological response at TOC by CAZ-AVI MIC for baseline pathogen in the mMITT analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=5, 6)	3	5		
E. coli (MIC: 0.015) - Favorable (n=8, 7)	8	6		
E. coli (MIC: 0.03) - Favorable (n=28, 35)	24	23		
E. coli (MIC: 0.06) - Favorable (n=123, 139)	103	111		
E. coli (MIC: 0.12) - Favorable (n=90, 81)	67	54		
E. coli (MIC: 0.25) - Favorable (n=28, 25)	18	13		
E. coli (MIC: 0.5) - Favorable (n=5, 6)	4	2		
E. coli (MIC: 1) - Favorable (n=3, 0)	1	0		
E. coli (MIC: 2) - Favorable (n=1, 0)	1	0		

E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 32) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >32) - Favorable (n=0, 0)	0	0		
Kleb.pneumoniae (MIC: <=0.008)-Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015) - Favorable(n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 0.03) - Favorable (n=1, 2)	1	2		
Kleb. pneumoniae (MIC: 0.06) - Favorable (n=9, 8)	7	8		
Kleb.pneumoniae (MIC: 0.12) - Favorable(n=11, 10)	9	7		
Kleb. pneumoniae (MIC: 0.25) - Favorable(n=4, 10)	1	3		
Kleb. pneumoniae (MIC: 0.5) - Favorable(n=8, 16)	6	11		
Kleb. pneumoniae (MIC: 1) - Favorable (n=8, 5)	6	3		
Kleb. pneumoniae (MIC: 2) - Favorable (n= 2, 4)	2	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 32) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: >32) - Favorable (n=0, 1)	0	1		
Proteus mirabilis (MIC:<=0.008)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)-Favorable(n=1,1)	1	0		
Proteus mirabilis (MIC: 0.03)-Favorable(n=10, 5)	10	3		
Proteus mirabilis (MIC: 0.06)- Favorable (n=6,6)	5	5		
Proteus mirabilis (MIC: 0.12)- Favorable (n=0,0)	0	0		
Proteus mirabilis (MIC: 0.25)-Favorable(n=0, 0)	0	0		
Proteus mirabilis (MIC: 0.5)- Favorable (n=0,1)	0	1		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 32)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >32)- Favorable (n=0, 0)	0	0		

Entero. cloacae (MIC: <=0.008)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 0.03)- Favorable (n= 1,0)	1	0		
Entero. cloacae (MIC: 0.06)- Favorable (n= 0, 1)	0	1		
Entero. cloacae (MIC: 0.12)- Favorable (n= 3,2)	2	2		
Entero. cloacae (MIC: 0.25)- Favorable (n= 1,4)	0	1		
Entero. cloacae (MIC: 0.5)- Favorable (n= 1,1)	0	1		
Entero. cloacae (MIC: 1)- Favorable (n= 2,5)	1	4		
Entero. cloacae (MIC: 2)- Favorable (n= 1,0)	1	0		
Entero. cloacae (MIC: 4)- Favorable (n= 2,0)	1	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 32)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >32)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.12) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.25) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.5) - Favorable (n=0,2)	0	2		
P.aeruginosa (MIC: 1) - Favorable (n=1,4)	1	2		
P.aeruginosa (MIC: 2) - Favorable (n=5,5)	5	5		
P.aeruginosa (MIC: 4) - Favorable (n=7,6)	3	4		
P.aeruginosa (MIC: 8) - Favorable (n=2,2)	1	1		
P.aeruginosa (MIC: 16) - Favorable (n=1,1)	0	1		
P.aeruginosa (MIC: 32) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: >32) - Favorable (n=2,0)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (Extended ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (Extended ME at TOC analysis set)

End point description:

Per pathogen microbiological response at TOC by CAZ-AVI MIC for baseline pathogen in the Extended ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=4,4)	2	4		
E. coli (MIC: 0.015) - Favorable (n=5, 6)	5	5		
E. coli (MIC: 0.03) - Favorable (n=18, 21)	17	17		
E. coli (MIC: 0.06) - Favorable (n=95, 111)	83	94		
E. coli (MIC: 0.12) - Favorable (n=68, 54)	56	40		
E. coli (MIC: 0.25) - Favorable (n=19, 18)	13	8		
E. coli (MIC: 0.5) - Favorable (n=2, 5)	2	2		
E. coli (MIC: 1) - Favorable (n=2, 0)	1	0		
E. coli (MIC: 2) - Favorable (n=1, 0)	1	0		
E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 32) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >32) - Favorable (n=0, 0)	0	0		
Kleb.pneumoniae (MIC: <=0.008)- Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015) - Favorable(n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 0.03) - Favorable(n=1, 2)	1	2		
Kleb. pneumoniae (MIC: 0.06) - Favorable(n=5, 7)	4	7		
Kleb.pneumoniae (MIC: 0.12) - Favorable(n=8, 9)	7	6		
Kleb. pneumoniae (MIC: 0.25) - Favorable(n=3, 7)	1	2		
Kleb. pneumoniae (MIC: 0.5) - Favorable(n=6, 11)	4	8		
Kleb. pneumoniae (MIC: 1) - Favorable(n=6, 4)	6	3		

Kleb. pneumoniae (MIC: 2) - Favorable (n= 2, 1)	2	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 32) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: >32) - Favorable (n=0, 1)	0	1		
Proteus mirabilis (MIC:<=0.008)- Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)- Favorable(n=1,0)	1	0		
Proteus mirabilis (MIC: 0.03)- Favorable(n=9, 2)	9	0		
Proteus mirabilis (MIC: 0.06)- Favorable(n=4,5)	4	4		
Proteus mirabilis (MIC: 0.12)- Favorable (n=0,0)	0	0		
Proteus mirabilis (MIC: 0.25)- Favorable(n=0, 0)	0	0		
Proteus mirabilis (MIC: 0.5)- Favorable (n=0,0)	0	0		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 32)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >32)- Favorable (n=0, 0)	0	0		
Entero. cloacae (MIC: <=0.008)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.03)- Favorable (n= 1,0)	1	0		
Entero. cloacae (MIC: 0.06)- Favorable (n= 0, 1)	0	1		
Entero. cloacae (MIC: 0.12)- Favorable (n= 1,2)	1	2		
Entero. cloacae (MIC: 0.25)- Favorable (n= 0,3)	0	0		
Entero. cloacae (MIC: 0.5)- Favorable (n= 1,1)	0	1		
Entero. cloacae (MIC: 1)- Favorable (n= 1,4)	1	4		
Entero. cloacae (MIC: 2)- Favorable (n= 1,0)	1	0		
Entero. cloacae (MIC: 4)- Favorable (n= 2,0)	1	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		

Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 32)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >32)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.12) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.25) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.5) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 1) - Favorable (n=1,4)	1	2		
P.aeruginosa (MIC: 2) - Favorable (n=4,5)	4	5		
P.aeruginosa (MIC: 4) - Favorable (n=5,6)	1	4		
P.aeruginosa (MIC: 8) - Favorable (n=2,2)	1	1		
P.aeruginosa (MIC: 16) - Favorable (n=0,1)	0	1		
P.aeruginosa (MIC: 32) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: >32) - Favorable (n=1,0)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC by CAZ AVI MIC for baseline pathogen (ME at TOC analysis set)

End point description:

Per pathogen microbiological response at TOC by CAZ-AVI MIC for baseline pathogen in the ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=4,4)	2	4		
E. coli (MIC: 0.015) - Favorable (n=5, 6)	5	5		
E. coli (MIC: 0.03) - Favorable (n=18, 21)	17	17		
E. coli (MIC: 0.06) - Favorable (n=95, 111)	83	94		
E. coli (MIC: 0.12) - Favorable (n=68, 54)	56	40		
E. coli (MIC: 0.25) - Favorable (n=19, 18)	13	8		
E. coli (MIC: 0.5) - Favorable (n=2, 5)	2	2		
E. coli (MIC: 1) - Favorable (n=2, 0)	1	0		
E. coli (MIC: 2) - Favorable (n=1, 0)	1	0		
E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 32) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >32) - Favorable (n=0, 0)	0	0		
Kleb.pneumoniae (MIC: <=0.008)-Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015) - Favorable(n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 0.03) - Favorable(n=1, 2)	1	2		
Kleb. pneumoniae (MIC: 0.06) - Favorable(n=5, 7)	4	7		
Kleb.pneumoniae (MIC: 0.12) - Favorable(n=8, 9)	7	6		
Kleb. pneumoniae (MIC: 0.25) - Favorable(n=3, 7)	1	2		
Kleb. pneumoniae (MIC: 0.5) - Favorable(n=6, 11)	4	8		
Kleb. pneumoniae (MIC: 1) - Favorable (n=5, 4)	5	3		
Kleb. pneumoniae (MIC: 2) - Favorable (n= 2, 1)	2	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 32) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: >32) - Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC:<=0.008)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)-Favorable(n=1,0)	1	0		
Proteus mirabilis (MIC: 0.03)-Favorable(n=9, 2)	9	0		

Proteus mirabilis (MIC: 0.06)- Favorable (n=4,5)	4	4		
Proteus mirabilis (MIC: 0.12)- Favorable (n=0,0)	0	0		
Proteus mirabilis (MIC: 0.25)- Favorable(n=0, 0)	0	0		
Proteus mirabilis (MIC: 0.5)- Favorable (n=0,0)	0	0		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 32)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >32)- Favorable (n=0, 0)	0	0		
Entero. cloacae (MIC: <=0.008)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.03)- Favorable(n= 1,0)	1	0		
Entero. cloacae (MIC: 0.06)- Favorable (n= 0, 1)	0	1		
Entero. cloacae (MIC: 0.12)- Favorable (n= 1,2)	1	2		
Entero. cloacae (MIC: 0.25)- Favorable (n= 0,3)	0	0		
Entero. cloacae (MIC: 0.5)- Favorable (n= 1,1)	0	1		
Entero. cloacae (MIC: 1)- Favorable (n= 1,4)	1	4		
Entero. cloacae (MIC: 2)- Favorable (n= 1,0)	1	0		
Entero. cloacae (MIC: 4)- Favorable (n= 2,0)	1	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 32)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >32)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.12) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.25) - Favorable (n=0,0)	0	0		

P.aeruginosa (MIC: 0.5) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 1) - Favorable (n=1,4)	1	2		
P.aeruginosa (MIC: 2) - Favorable (n=4,4)	4	4		
P.aeruginosa (MIC: 4) - Favorable (n=3,4)	1	3		
P.aeruginosa (MIC: 8) - Favorable (n=1,1)	1	0		
P.aeruginosa (MIC: 16) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 32) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: >32) - Favorable (n=0,0)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (mMITT analysis set)

End point title	Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (mMITT analysis set)

End point description:

Per pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen in the mMITT analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393	417		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=1, 3)	1	3		
E. coli (MIC: 0.015) - Favorable (n=160, 160)	127	119		
E. coli (MIC: 0.03) - Favorable (n=112, 123)	89	86		
E. coli (MIC: 0.06) - Favorable (n=14, 10)	10	4		
E. coli (MIC: 0.12) - Favorable (n=3, 3)	1	2		
E. coli (MIC: 0.25) - Favorable (n=1, 0)	1	0		
E. coli (MIC: 0.5) - Favorable (n=0,0)	0	0		
E. coli (MIC: 1) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 2) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		

E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >16) - Favorable (n=0, 0)	0	0		
Kleb.pneumoniae (MIC: <=0.008)-Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015)-Favorable (n=1, 3)	1	2		
Kleb. pneumoniae (MIC: 0.03)-Favorable(n=22, 27)	16	21		
Kleb. pneumoniae (MIC: 0.06)-Favorable(n=11, 16)	10	7		
Kleb.pneumoniae (MIC: 0.12) -Favorable(n=4,4)	2	2		
Kleb. pneumoniae (MIC: 0.25) -Favorable (n=2,3)	1	2		
Kleb. pneumoniae (MIC: 0.5) -Favorable (n=2, 1)	1	0		
Kleb. pneumoniae (MIC: 1) - Favorable (n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 2) - Favorable (n= 0, 0)	0	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 1)	0	1		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 1)	0	0		
Kleb. pneumoniae (MIC: >16) -Favorable (n=1, 0)	1	0		
Proteus mirabilis (MIC:<=0.008)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.03)-Favorable(n=1, 0)	1	0		
Proteus mirabilis (MIC: 0.06)- Favorable (n=2,2)	2	1		
Proteus mirabilis (MIC: 0.12)- Favorable (n=6,5)	5	4		
Proteus mirabilis (MIC: 0.25)-Favorable(n=6, 4)	6	2		
Proteus mirabilis (MIC: 0.5)- Favorable (n=2,2)	2	2		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >16)- Favorable (n=0, 0)	0	0		
Entero. cloacae (MIC: <=0.008)-Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable (n= 3,1)	2	1		
Entero. cloacae (MIC: 0.03)- Favorable (n= 1,5)	1	2		
Entero. cloacae (MIC: 0.06)- Favorable (n= 3, 1)	1	1		

Entero. cloacae (MIC: 0.12)- Favorable (n= 0, 4)	0	4		
Entero. cloacae (MIC: 0.25)- Favorable (n= 0,1)	0	0		
Entero. cloacae (MIC: 0.5)- Favorable (n= 4,0)	2	0		
Entero. cloacae (MIC: 1)- Favorable (n= 0,1)	0	1		
Entero. cloacae (MIC: 2)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 4)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >16)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=2,3)	2	3		
P.aeruginosa (MIC: 0.12) - Favorable (n=2,2)	1	2		
P.aeruginosa (MIC: 0.25) - Favorable (n=2,5)	2	2		
P.aeruginosa (MIC: 0.5) - Favorable (n=2,1)	2	1		
P.aeruginosa (MIC: 1) - Favorable (n=1,4)	0	3		
P.aeruginosa (MIC: 2) - Favorable (n=1,0)	1	0		
P.aeruginosa (MIC: 4) - Favorable (n=2,2)	1	1		
P.aeruginosa (MIC: 8) - Favorable (n=2,1)	1	1		
P.aeruginosa (MIC: 16) - Favorable (n=2,1)	0	1		
P.aeruginosa (MIC: >16) - Favorable (n=2,1)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (Extended ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (Extended ME at TOC analysis set)

End point description:

Per pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen in the Extended ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	311		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=1,1)	1	1		
E. coli (MIC: 0.015) - Favorable (n=122, 119)	106	95		
E. coli (MIC: 0.03) - Favorable (n=79, 89)	64	70		
E. coli (MIC: 0.06) - Favorable (n=10, 8)	7	3		
E. coli (MIC: 0.12) - Favorable (n=1, 2)	1	1		
E. coli (MIC: 0.25) - Favorable (n=1, 0)	1	0		
E. coli (MIC: 0.5) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 1) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 2) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >16) - Favorable (n=0, 0)	0	0		
Kleb.pneumoniae (MIC: <=0.008)- Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015) - Favorable(n=1, 2)	1	1		
Kleb. pneumoniae (MIC:0.03) - Favorable(n=15, 23)	12	18		
Kleb. pneumoniae (MIC: 0.06) - Favorable(n=8, 12)	7	6		
Kleb.pneumoniae (MIC: 0.12) - Favorable(n=3, 2)	2	2		
Kleb. pneumoniae (MIC: 0.25) - Favorable (n=2, 2)	1	1		
Kleb. pneumoniae (MIC: 0.5) - Favorable (n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 1) - Favorable (n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 2) - Favorable (n= 0,0)	0	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 1)	0	1		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: >16) - Favorable (n=1, 0)	1	0		
Proteus mirabilis (MIC:<=0.008)- Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)- Favorable (n=0,0)	0	0		

Proteus mirabilis (MIC: 0.03)- Favorable (n=1,0)	1	0		
Proteus mirabilis (MIC: 0.06)- Favorable (n=2,2)	2	1		
Proteus mirabilis (MIC: 0.12)- Favorable (n=4,2)	4	2		
Proteus mirabilis (MIC: 0.25)- Favorable(n=6, 3)	6	1		
Proteus mirabilis (MIC: 0.5)- Favorable (n=1,0)	1	0		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >16)- Favorable (n=0, 0)	0	0		
Entero. cloacae (MIC: <=0.008)- Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable (n= 1,1)	1	1		
Entero. cloacae (MIC: 0.03)- Favorable (n= 1,4)	1	1		
Entero. cloacae (MIC: 0.06)- Favorable (n= 2, 1)	1	1		
Entero. cloacae (MIC: 0.12)- Favorable (n= 0,4)	0	4		
Entero. cloacae (MIC: 0.25)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 0.5)- Favorable (n= 3,0)	2	0		
Entero. cloacae (MIC: 1)- Favorable (n= 0,1)	0	1		
Entero. cloacae (MIC: 2)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 4)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >16)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=2,3)	2	3		
P.aeruginosa (MIC: 0.12) - Favorable (n=1,2)	0	2		
P.aeruginosa (MIC: 0.25) - Favorable (n=2,4)	2	1		
P.aeruginosa (MIC: 0.5) - Favorable (n=2,1)	2	1		

P.aeruginosa (MIC: 1) - Favorable (n=1,3)	0	2		
P.aeruginosa (MIC: 2) - Favorable (n=1,0)	1	0		
P.aeruginosa (MIC: 4) - Favorable (n=0,2)	0	1		
P.aeruginosa (MIC: 8) - Favorable (n=1,1)	0	1		
P.aeruginosa (MIC: 16) - Favorable (n=2,1)	0	1		
P.aeruginosa (MIC: >16) - Favorable (n=1,1)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (ME at TOC analysis set)

End point title	Per-pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen (ME at TOC analysis set)

End point description:

Per pathogen microbiological response at TOC by Doripenem MIC for baseline pathogen in the ME at TOC analysis set

End point type	Secondary

End point timeframe:

At TOC visit. TOC visit is 21 to 25 days from Randomization

End point values	CAZ-AVI	Doripenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	298		
Units: Participant				
E. coli (MIC: <=0.008) - Favorable (n=1,1)	1	1		
E. coli (MIC: 0.015) - Favorable (n=122, 119)	106	95		
E. coli (MIC: 0.03) - Favorable (n=79, 89)	64	70		
E. coli (MIC: 0.06) - Favorable (n=10, 8)	7	3		
E. coli (MIC: 0.12) - Favorable (n=1,2)	1	1		
E. coli (MIC: 0.25) - Favorable (n=1,0)	1	0		
E. coli (MIC: 0.5) - Favorable (n=0,0)	0	0		
E. coli (MIC: 1) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 2) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 4) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 8) - Favorable (n=0, 0)	0	0		
E. coli (MIC: 16) - Favorable (n=0, 0)	0	0		
E. coli (MIC: >16) - Favorable (n=0, 0)	0	0		

Kleb.pneumoniae (MIC: <=0.008)-Favorable(n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 0.015) - Favorable(n=1, 2)	1	1		
Kleb. pneumoniae (MIC:0.03) - Favorable(n=15, 23)	12	18		
Kleb. pneumoniae (MIC: 0.06) - Favorable(n=8, 12)	7	6		
Kleb.pneumoniae (MIC: 0.12) - Favorable(n=3,2)	2	2		
Kleb. pneumoniae (MIC: 0.25) - Favorable(n=2, 2)	1	1		
Kleb. pneumoniae (MIC: 0.5) - Favorable (n=1,0)	1	0		
Kleb. pneumoniae (MIC: 1) - Favorable (n=1, 0)	1	0		
Kleb. pneumoniae (MIC: 2) - Favorable (n= 0,0)	0	0		
Kleb. pneumoniae (MIC: 4) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 8) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: 16) - Favorable (n=0, 0)	0	0		
Kleb. pneumoniae (MIC: >16) - Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC:<=0.008)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.015)-Favorable(n=0,0)	0	0		
Proteus mirabilis (MIC: 0.03)-Favorable(n=1, 0)	1	0		
Proteus mirabilis (MIC: 0.06)- Favorable (n=2,2)	2	1		
Proteus mirabilis (MIC: 0.12)- Favorable (n=4,2)	4	2		
Proteus mirabilis (MIC: 0.25)-Favorable(n=6, 3)	6	1		
Proteus mirabilis (MIC: 0.5)- Favorable (n=1,0)	1	0		
Proteus mirabilis (MIC: 1)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 2)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 4)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 8)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: 16)- Favorable (n=0, 0)	0	0		
Proteus mirabilis (MIC: >16)- Favorable (n=0, 0)	0	0		
Entero. cloacae (MIC: <=0.008)-Favorable(n= 0,0)	0	0		
Entero. cloacae (MIC: 0.015)- Favorable (n= 1,1)	1	1		
Entero. cloacae (MIC: 0.03)- Favorable (n= 1,4)	1	1		
Entero. cloacae (MIC: 0.06)- Favorable (n= 2, 1)	1	1		
Entero. cloacae (MIC: 0.12)- Favorable (n= 0,4)	0	4		

Entero. cloacae (MIC: 0.25)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 0.5)- Favorable (n= 3,0)	2	0		
Entero. cloacae (MIC: 1)- Favorable (n= 0,1)	0	1		
Entero. cloacae (MIC: 2)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 4)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 8)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: 16)- Favorable (n= 0,0)	0	0		
Entero. cloacae (MIC: >16)- Favorable (n= 0,0)	0	0		
P.aeruginosa (MIC: <=0.008) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.015) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.03) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 0.06) - Favorable (n=2,3)	2	3		
P.aeruginosa (MIC: 0.12) - Favorable (n=1,2)	0	2		
P.aeruginosa (MIC: 0.25) - Favorable (n=2,4)	2	1		
P.aeruginosa (MIC: 0.5) - Favorable (n=2,1)	2	1		
P.aeruginosa (MIC: 1) - Favorable (n=1,3)	0	2		
P.aeruginosa (MIC: 2) - Favorable (n=1,0)	1	0		
P.aeruginosa (MIC: 4) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 8) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: 16) - Favorable (n=0,0)	0	0		
P.aeruginosa (MIC: >16) - Favorable (n=0,0)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime within 15 minutes before/after dose (PK analysis set)

End point title	Plasma concentrations for ceftazidime within 15 minutes before/after dose (PK analysis set)[1]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

within 15 minutes before/after dose

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: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	480			
Units: Participants				
geometric mean (full range (min-max))	65481.2 (1260 to 3190000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime between 30 to 90 minutes after dose(PK analysis set)

End point title	Plasma concentrations for ceftazidime between 30 to 90 minutes after dose(PK analysis set)[2]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

Between 30 to 90 minutes after dose

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: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	483			
Units: Participants				
geometric mean (full range (min-max))	47575.1 (749 to 414000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime between 300 to 360 minutes after dose (PK analysis set)

End point title	Plasma concentrations for ceftazidime between 300 to 360 minutes after dose (PK analysis set)[3]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

Between 300 to 360 minutes after dose

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	481			
Units: Participants				
geometric mean (full range (min-max))	16959.6 (156 to 1640000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam between 30 to 90 minutes after dose(PK analysis set)

End point title	Plasma concentrations for avibactam between 30 to 90 minutes after dose(PK analysis set)[4]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

Between 30 to 90 minutes after dose

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	490			
Units: Participants				
geometric mean (full range (min-max))	6587.2 (113 to 105000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam within 15 minutes before/after dose (PK analysis set)

End point title	Plasma concentrations for avibactam within 15 minutes before/after dose (PK analysis set)[5]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

within 15 minutes before/after dose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	489			
Units: Participants				
geometric mean (full range (min-max))	9307.3 (125 to 1780000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam between 300 to 360 minutes after dose (PK analysis set)

End point title	Plasma concentrations for avibactam between 300 to 360 minutes after dose (PK analysis set)[6]

End point description:

Blood samples were taken on Day 3 for ceftazidime (CAZ) and avibactam (AVI) plasma concentration.

End point type	Secondary

End point timeframe:

Between 300 to 360 minutes after dose

Notes:

[6] - 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: The marketed treatment 'Doripenem' has been selected as the comparator in this protocol. However, the PK profile has already been established for the marketed treatment 'Doripenem'. Therefore, the PK analysis is only performed on the investigational product 'CAZ-AVI' in this protocol.

End point values	CAZ-AVI			
Subject group type	Reporting group			
Number of subjects analysed	488			
Units: Participants				
geometric mean (full range (min-max))	1883.2 (26 to 336000)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Includes the AEs with an onset date and time on or after the date and time of first dose and up to and including the late follow-up (LFU) visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Doripenem

Reporting group description:

Doripenem treatment group

Reporting group title	CAZ-AVI

Reporting group description:

Ceftazidime-avibactam treatment group

Serious adverse events	Doripenem	CAZ-AVI	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 509 (2.36%)	21 / 511 (4.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			

subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 509 (0.00%)	2 / 511 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 509 (0.20%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery aneurysm			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypoglycaemic seizure			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tension headache			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus ureteric			

subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 509 (0.00%)	3 / 511 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
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	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatitis C			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 509 (0.00%)	1 / 511 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 509 (0.20%)	0 / 511 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Doripenem	CAZ-AVI	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 509 (11.20%)	67 / 511 (13.11%)	
Nervous system disorders			
Headache			
subjects affected / exposed	40 / 509 (7.86%)	38 / 511 (7.44%)	
occurrences (all)	41	41	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	7 / 509 (1.38%)	11 / 511 (2.15%)	
occurrences (all)	8	11	
Diarrhoea			
subjects affected / exposed	6 / 509 (1.18%)	13 / 511 (2.54%)	
occurrences (all)	6	14	
Nausea			
subjects affected / exposed	10 / 509 (1.96%)	15 / 511 (2.94%)	
occurrences (all)	10	16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2013	Combined the 2 protocols (D4280C00002 and D4280C00004) into a single study database
09 August 2013	All data analyses based on data from the combined studies (D4280C00002 and D4280C00004)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported