Clinical trial results:
A Multicenter, Double-Blind, Randomized, Phase 3 Study to Compare the Efficacy and Safety of Intravenous CXA-201 with that of Meropenem in Complicated Intraabdominal Infections

Summary

EudraCT number	2011-002119-27
Trial protocol	ES BE LV SK LT EE RO
Global end of trial date	10 September 2013

Results information

Result version number	v2 (current)
This version publication date	20 April 2019
First version publication date	28 September 2018
Version creation reason	• Correction of full data set updating the End of Trial date for consistency

Trial information

Trial identification

Sponsor protocol code	CXA-cIAI-10-08 and CXA-cIAI-10-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01445678
WHO universal trial number (UTN)	-
Other trial identifiers	2011-002120-41: EudraCT

Notes:

Sponsors

Sponsor organisation name	Cubist Pharmaceuticals, Inc.
Sponsor organisation address	65 Hayden Drive, Lexington, MA, United States,
Public contact	Medical Director, Cubist Pharmaceuticals, Inc., 001 781-860-8660,
Scientific contact	Medical Director, Cubist Pharmaceuticals, Inc., 001 781-860-8660,

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	18 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2013
Global end of trial reached?	Yes
Global end of trial date	10 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a Phase 3, multicenter, prospective, randomized, double-blind, double dummy study of CXA-201 intravenous (IV) infusions to demonstrate the noninferiority of ceftolozane/tazobactam (CXA-201) plus metronidazole versus meropenem in adult subjects with complicated intraabdominal infections (cIAI).

Two identical Phase 3 protocol were initiated: CXA-cIAI-10-09 (2011-002120-41) and CXA-cIAI-10-08 (2011-002119-27). Based on this guidance and following scientific advice from the CHMP (Procedure No.: EMEA/H/SA/2181/2/2012/II; taking into account existing CHMP guidance) and agreement from the US FDA, Cubist revised its clinical development program for ceftolozane/tazobactam (CXA-201) leading to a single-study approval pathway for each indication.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation (ICH) Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2011
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	United States: 55
Country: Number of subjects enrolled	Argentina: 75
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Croatia: 13
Country: Number of subjects enrolled	Estonia: 75
Country: Number of subjects enrolled	Georgia: 31
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 65
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Latvia: 74
Country: Number of subjects enrolled	Lithuania: 70

Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Moldova, Republic of: 31
Country: Number of subjects enrolled	Peru: 13
Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Romania: 109
Country: Number of subjects enrolled	Russian Federation: 51
Country: Number of subjects enrolled	Serbia: 29
Country: Number of subjects enrolled	Slovakia: 47
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 32
Country: Number of subjects enrolled	Spain: 23
Country: Number of subjects enrolled	Ukraine: 73
Worldwide total number of subjects	994
EEA total number of subjects	550

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)	770
From 65 to 84 years	215
85 years and over	9

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects enrolled in this study were at least 18 years of age with a complicated intra-abdominal infection. Subjects were eligible to participate in the study if they met all of the inclusion criteria and none of the exclusion criteria at the Screening visit.

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	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	CXA-201 and Metronidazole as treatment for cIAI

Arm description:

CXA-201 and metronidazole: CXA-201 IV infusion (ceftolozane 1000 milligrams [mg] + tazobactam 500 mg q8h) and metronidazole IV infusion (500 mg q8h) for 4 to 14 days.

Arm type	Experimental
Investigational medicinal product name	Ceftolozane/ Tazobactam
Investigational medicinal product code	
Other name	CXA-201
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

CXA-201 intravenous (IV) infusion (ceftolozane 1000 milligrams [mg] and tazobactam 500 mg q8h) for 4 to 14 days

Investigational medicinal product name	Metronidazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Metronidazole IV infusion (500 mg q 8h) for 4 to 14 days

Arm title	Meropenem as treatment for cIAI

Arm description:

Meropenem: Meropenem IV infusion (1000 mg q8h) for 4-14 days

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

Dosage and administration details:

Meropenem: Meropenem IV infusion (1000mg q8h) for 4-14 days Of the 979 treated subjects in the integrated analysis set, 497 received meropenem.

Number of subjects in period 1	CXA-201 and Metronidazole as treatment for cIAI	Meropenem as treatment for cIAI
Started	488	506
Received at least 1 dose of study drug	482	497
Completed	452	476
Not completed	36	30
Physician decision	1	-
Consent withdrawn by subject	11	7
Adverse event, non-fatal	12	8
Lost to follow-up	8	5
Reason not specified	2	2
Lack of informed consent	-	2
Protocol deviation	2	4
Lack of efficacy	-	2

Baseline characteristics

Reporting groups	
Reporting group title	CXA-201 and Metronidazole as treatment for cIAI
Reporting group description:	
CXA-201 and metronidazole: CXA-201 IV infusion (ceftolozane 1000 milligrams [mg] + tazobactam 500 mg q8h) and metronidazole IV infusion (500 mg q8h) for 4 to 14 days.	
Reporting group title	Meropenem as treatment for cIAI
Reporting group description:	
Meropenem: Meropenem IV infusion (1000 mg q8h) for 4-14 days	

Reporting group values	CXA-201 and Metronidazole as treatment for cIAI	Meropenem as treatment for cIAI	Total
Number of subjects	488	506	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	50.6	50.5	
standard deviation	± 17.94	± 16.85	-
Gender, Male/Female Units: participants			
Male			0
Female			0

Subject analysis sets	
Subject analysis set title	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Microbiological intention-to-treat (MITT): all randomised subjects, regardless of whether or not the subjects went on to receive study drug, who had intra-abdominal infection (IAI) as evidenced by identification of at least 1 baseline intra-abdominal pathogen, regardless of susceptibility to study drug.	
Subject analysis set title	Meropenem--MITT population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Microbiological intention-to-treat (MITT): all randomised subjects, regardless of whether or not the subjects went on to receive study drug, who had intra-abdominal infection (IAI) as evidenced by identification of at least 1 baseline intra-abdominal pathogen, regardless of susceptibility to study drug.	
Subject analysis set title	Ceftolozane/Tazobactam (CXA-201) +Metronidazole--CE population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The clinically evaluable (CE) population was a subset of the intention-to-treat (ITT) population of subjects who received an adequate amount of study drug, met the protocol-specific disease definition of cIAI, adhered to study procedures, and had a test-of-cure (TOC) visit within the specified visit window. Subjects in this population had no confounding factors that interfered with the assessment of outcome and met the key inclusion/exclusion criteria and additional protocol-defined criteria.	
Subject analysis set title	Meropenem--CE population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The CE population was a subset of the intention-to-treat (ITT) population of subjects who received an adequate amount of study drug, met the protocol-specific disease definition of cIAI, adhered to study procedures, and had a test-of-cure (TOC) visit within the specified visit window. Subjects in this population had no confounding factors that interfered with the assessment of outcome and met the key inclusion/exclusion criteria and additional protocol-defined criteria.

Subject analysis set title	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomised subjects regardless of whether or not the subjects went on to receive study drug. Subjects in the ITT population were categorised based on the treatment that the subjects were randomised to, irrespective of what they actually received.

Subject analysis set title	Meropenem--ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomised subjects regardless of whether or not the subjects went on to receive study drug. Subjects in the ITT population were categorised based on the treatment that the subjects were randomised to, irrespective of what they actually received.

Subject analysis set title	Ceftolozane/ Tazobactam(CA-201)+Met-expanded ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The expanded microbiologically evaluable (ME) population consisted of all subjects in the MITT population who met all CE population criteria.

Subject analysis set title	Meropenem--expanded ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The expanded ME population consisted of all subjects in the MITT population who met all CE population criteria.

Subject analysis set title	Ceftolozane/ Tazobactam(CXA-201)+ Metronidazole--ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The ME population was the subset of CE subjects who had at least 1 baseline infecting pathogen identified that was susceptible to study drug. For subjects receiving nonstudy antibiotics with only Gram-positive activity, the per-pathogen outcome for Gram-positive organisms was indeterminate.

Subject analysis set title	Meropenem--ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The ME population was the subset of CE subjects who had at least 1 baseline infecting pathogen identified that was susceptible to study drug. For subjects receiving nonstudy antibiotics with only Gram-positive activity, the per-pathogen outcome for Gram-positive organisms was indeterminate.

Reporting group values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population	Meropenem--MITT population	Ceftolozane/Tazobactam (CXA-201) +Metronidazole--CE population
Number of subjects	389	417	375
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	50.8	50.4	
standard deviation	± 18.25	± 16.87	±

Gender, Male/Female Units: participants			
Male	218	248	
Female	171	169	

Reporting group values	Meropenem--CE population	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population	Meropenem--ITT population
Number of subjects	399	476	494
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: participants			
Male			
Female			

Reporting group values	Ceftolozane/Tazobactam(CA-201)+Met-expanded ME population	Meropenem--expanded ME population	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ME population
Number of subjects	307	345	275
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: participants			
Male			
Female			

Reporting group values	Meropenem--ME population		
Number of subjects	321		
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	±		
Gender, Male/Female Units: participants			
Male			
Female			

End points

End points reporting groups

Reporting group title	CXA-201 and Metronidazole as treatment for cIAI

Reporting group description:

CXA-201 and metronidazole: CXA-201 IV infusion (ceftolozane 1000 milligrams [mg] + tazobactam 500 mg q8h) and metronidazole IV infusion (500 mg q8h) for 4 to 14 days.

Reporting group title	Meropenem as treatment for cIAI

Reporting group description:

Meropenem: Meropenem IV infusion (1000 mg q8h) for 4-14 days

Subject analysis set title	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Microbiological intention-to-treat (MITT): all randomised subjects, regardless of whether or not the subjects went on to receive study drug, who had intra-abdominal infection (IAI) as evidenced by identification of at least 1 baseline intra-abdominal pathogen, regardless of susceptibility to study drug.

Subject analysis set title	Meropenem--MITT population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Microbiological intention-to-treat (MITT): all randomised subjects, regardless of whether or not the subjects went on to receive study drug, who had intra-abdominal infection (IAI) as evidenced by identification of at least 1 baseline intra-abdominal pathogen, regardless of susceptibility to study drug.

Subject analysis set title	Ceftolozane/Tazobactam (CXA-201) +Metronidazole--CE population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The clinically evaluable (CE) population was a subset of the intention-to-treat (ITT) population of subjects who received an adequate amount of study drug, met the protocol-specific disease definition of cIAI, adhered to study procedures, and had a test-of-cure (TOC) visit within the specified visit window. Subjects in this population had no confounding factors that interfered with the assessment of outcome and met the key inclusion/exclusion criteria and additional protocol-defined criteria.

Subject analysis set title	Meropenem--CE population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The CE population was a subset of the intention-to-treat (ITT) population of subjects who received an adequate amount of study drug, met the protocol-specific disease definition of cIAI, adhered to study procedures, and had a test-of-cure (TOC) visit within the specified visit window. Subjects in this population had no confounding factors that interfered with the assessment of outcome and met the key inclusion/exclusion criteria and additional protocol-defined criteria.

Subject analysis set title	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomised subjects regardless of whether or not the subjects went on to receive study drug. Subjects in the ITT population were categorised based on the treatment that the subjects were randomised to, irrespective of what they actually received.

Subject analysis set title	Meropenem--ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomised subjects regardless of whether or not the subjects went on to receive study drug. Subjects in the ITT population were categorised based on the treatment that the subjects were randomised to, irrespective of what they actually received.

Subject analysis set title	Ceftolozane/ Tazobactam(CA-201)+Met-expanded ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The expanded microbiologically evaluable (ME) population consisted of all subjects in the MITT population who met all CE population criteria.

Subject analysis set title	Meropenem--expanded ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The expanded ME population consisted of all subjects in the MITT population who met all CE population criteria.

Subject analysis set title	Ceftolozane/ Tazobactam(CXA-201)+ Metronidazole--ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The ME population was the subset of CE subjects who had at least 1 baseline infecting pathogen identified that was susceptible to study drug. For subjects receiving nonstudy antibiotics with only Gram-positive activity, the per-pathogen outcome for Gram-positive organisms was indeterminate.

Subject analysis set title	Meropenem--ME population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The ME population was the subset of CE subjects who had at least 1 baseline infecting pathogen identified that was susceptible to study drug. For subjects receiving nonstudy antibiotics with only Gram-positive activity, the per-pathogen outcome for Gram-positive organisms was indeterminate.

Primary: The percentage of subjects with clinical outcome of cure at the test of cure (TOC) visit in the clinically evaluable (CE) population

End point title	The percentage of subjects with clinical outcome of cure at the test of cure (TOC) visit in the clinically evaluable (CE) population

End point description:

Clinical cure is complete resolution or significant improvement in signs and symptoms of the index infection, such that no additional antibacterial therapy or surgical or drainage procedure was required for the index infection.

End point type	Primary

End point timeframe:

TOC; 26-30 days after start of study drug administration

End point values	Ceftolozane/Tazobactam (CXA-201) +Metronidazole --CE population	Meropenem--CE population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	375[1]	399[2]		
Units: percentage of subjects				
number (not applicable)				
Cure	94.1	94		
Failure	5.9	6		

Notes:

[1] - CE population

[2] - CE population

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Meropenem--CE population v Ceftolozane/Tazobactam (CXA-

	201) +Metronidazole--CE population
Number of subjects included in analysis	774
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-4.16
upper limit	4.3

Notes:

[3] - The hypotheses were tested at the 1-sided 0.005 significance level, through a 2-sided 99% confidence interval (CI) approach. The 2-sided 99% CI on the difference of proportions for ceftolozane/tazobactam plus metronidazole minus comparator (meropenem) was constructed using stratified Newcombe CI with Minimum Risk weights. Noninferiority was concluded if the lower bound of the 2-sided 99% CI was greater than minus 12.5%, in the CE population.

Secondary: The percentage of subjects with clinical outcome of cure at the TOC visit in the intention-to-treat (ITT) Population

End point title	The percentage of subjects with clinical outcome of cure at the TOC visit in the intention-to-treat (ITT) Population

End point description:

Clinical cure is complete resolution or significant improvement in signs and symptoms of the index infection, such that no additional antibacterial therapy or surgical or drainage procedure was required for the index infection.

End point type	Secondary

End point timeframe:

TOC; 26-30 days after start of study drug administration

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population	Meropenem--ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	476[4]	494[5]		
Units: percentage of subjects				
number (not applicable)				
Cure	83.8	85.8		
Failure	16.2	14.2		

Notes:

[4] - ITT population

[5] - ITT population

Statistical analyses

Statistical analysis title	Statistial Analysis

Statistical analysis description:

The hypotheses were tested at the 1-sided 0.005 significance level, through a 2-sided 99% confidence interval (CI) approach. The 2-sided 99% CI on the difference of proportions for ceftolozane/tazobactam plus metronidazole minus comparator (meropenem) was constructed using stratified Newcombe CI with Minimum Risk weights as described. Noninferiority was concluded if the lower bound of the 2-sided 99%

CI was greater than minus 12.5%, in the the ITT population

Comparison groups	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population v Meropenem--ITT population
Number of subjects included in analysis	970
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Percentage difference
Point estimate	-2.2
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-7.95
upper limit	3.44

Secondary: The percentage of subjects with clinical outcome of cure at the test of cure (TOC) visit in the microbiologically evaluable (ME), MITT, and expanded ME population

End point title	The percentage of subjects with clinical outcome of cure at the test of cure (TOC) visit in the microbiologically evaluable (ME), MITT, and expanded ME population

End point description:

Clinical cure is complete resolution or significant improvement in signs and symptoms of the index infection, such that no additional antibacterial therapy or surgical or drainage procedure was required for the index infection.

End point type	Secondary

End point timeframe:

TOC; 26-30 days after start of study drug administration

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population	Meropenem--MITT population	Ceftolozane/Tazobactam(CA-201)+Met-expanded ME population	Meropenem--expanded ME population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	389[6]	417[7]	307[8]	345[9]
Units: percentage of subjects				
number (not applicable)				
Cure	83	87.3	93.8	93.6
Failure	17	12.7	6.2	6.4

Notes:

[6] - MITT

[7] - MITT

[8] - Expanded ME

[9] - Expanded ME

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ME population	Meropenem--ME population		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	275[10]	321[11]		
Units: percentage of subjects				
number (not applicable)				
Cure	94.2	94.7		
Failure	5.8	5.3		

Notes:

[10] - ME population

[11] - ME population

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects with microbiological success at the TOC visit in the MITT, ME, and expanded ME populations

End point title	The percentage of subjects with microbiological success at the TOC visit in the MITT, ME, and expanded ME populations

End point description:

An overall microbiological response was determined for each subject based on individual microbiological responses for each baseline pathogen at the TOC visit. In order for the subject to have a favourable overall microbiological response (ie, success), each baseline pathogen must have had a favourable microbiological outcome. If the outcome for any pathogen was unfavourable, the subject was considered an overall microbiological failure.

End point type	Secondary

End point timeframe:

TOC visit; 26-30 days after start of study drug administration

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population	Meropenem--MITT population	Ceftolozane/Tazobactam(CA-201)+Met-expanded ME population	Meropenem--expanded ME population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	389[12]	417[13]	307[14]	345[15]
Units: percentage of subjects				
number (not applicable)				
Microbiological success	85.3	88.7	95.4	94.5
Microbiological failure	6.4	6.7	4.6	5.5

Notes:

[12] - MITT population

[13] - MITT population

[14] - Expanded ME population

[15] - Expanded ME population

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ME population	Meropenem--ME population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	275[16]	321[17]		

Units: percentage of subjects				
number (not applicable)				
Microbiological success	96	95.6		
Microbiological failure	4	4.4		

Notes:

[16] - ME population

[17] - ME population

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects with a gram-negative aerobes microbiological response at the TOC visit in the ME population

End point title	The percentage of subjects with a gram-negative aerobes microbiological response at the TOC visit in the ME population

End point description:

A microbiological response for gram-negative aerobes isolated at baseline at both the EOT and TOC visits. Microbiological response categories were eradication, presumed eradication, persistence, persistence acquiring resistance, presumed persistence, and indeterminate. Favourable microbiological responses included "eradication" or "presumed eradication." Unfavourable responses were considered "persistence," "persistence acquiring resistance," and "presumed persistence."

End point type	Secondary

End point timeframe:

End of treatment (EOT) through TOC; 26-30 days after start of study drug administration

End point values	Ceftolozane/ Tazobactam(CXA-201)+ Metronidazole--ME population	Meropenem--ME population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	243[18]	282[19]		
Units: percentage of subjects				
number (not applicable)	96.3	95.4		

Notes:

[18] - ME population

[19] - ME population

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects with sustained clinical cure at LFU Visit in the CE, ITT, and ME populations

End point title	The percentage of subjects with sustained clinical cure at LFU Visit in the CE, ITT, and ME populations

End point description:

Sustained clinical cure at LFU is defined as no signs and symptoms recur or worsen since the TOC visit.

End point type	Secondary

End point timeframe:

Last follow up (LFU) visit; 38 to 45 days after first study drug administration

End point values	Ceftolozane/Tazobactam (CXA-201) +Metronidazole --CE population	Meropenem--CE population	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ITT population	Meropenem--ITT population
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	350[20]	374[21]	476[22]	494[23]
Units: percentage of subjects				
number (not applicable)	100	99.5	83	85

Notes:

[20] - CE population with evaluable LFU data

[21] - CE population with evaluable LFU data

[22] - ITT population

[23] - ITT population

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--ME population	Meropenem--ME population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	258[24]	304[25]		
Units: percentage of subjects				
number (not applicable)	100	99.3		

Notes:

[24] - ME population with evaluable LFU data

[25] - ME population with evaluable LFU data

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with superinfections or new infections in the MITT population

End point title	Percentage of subjects with superinfections or new infections in the MITT population

End point description:

Superinfection outcome was defined as isolation of a pathogen, other than the original baseline pathogen(s), from an intra-abdominal specimen taken from a subject with signs or symptoms of infection while on study drug. A new infection was defined as isolation of a pathogen, other than the original baseline pathogen(s), from an intra-abdominal specimen in a subject with signs or symptoms of infection after treatment with study drug.

End point type	Secondary

End point timeframe:

Baseline through TOC visit

End point values	Ceftolozane/Tazobactam(CXA-201)+Metronidazole--MITT population	Meropenem--MITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	389[26]	417[27]		
Units: Percentage				
number (not applicable)				
Superinfection	2.6	3.1		
New infection	3.1	2.2		

Notes:

[26] - MITT population

[27] - MITT population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded for all subjects from the start of study drug administration through the last follow up visit, which occurred 38 to 45 days after the first dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Ceftolozane/Tazobactam + Metronidazole
Reporting group description: -	
Reporting group title	Meropenem

Reporting group description: -

Serious adverse events	Ceftolozane/Tazobactam + Metronidazole	Meropenem	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 482 (8.09%)	36 / 497 (7.24%)	
number of deaths (all causes)	11	8	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic venous thrombosis			

subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shock haemorrhagic			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	2 / 482 (0.41%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	3 / 482 (0.62%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Reproductive system and breast disorders			
Atrophic vulvovaginitis			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleurisy			

subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory distress			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 482 (0.21%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (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			

Abdominal wound dehiscence			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoconiosis			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaemia postoperative			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture rupture			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	2 / 482 (0.41%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Cardiopulmonary failure			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiogenic shock			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	2 / 482 (0.41%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			

subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal perforation			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 482 (0.21%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 482 (0.00%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary fistula			

subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforation bile duct			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (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			
Renal failure acute			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (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			
Muscular weakness			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (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	2 / 482 (0.41%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			

subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal abscess			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 482 (0.21%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 482 (0.00%)	3 / 497 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gallbladder abscess			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious peritonitis			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection pseudomonal			

subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 482 (0.21%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peridiverticular abscess			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (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	0 / 482 (0.00%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 482 (0.62%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pneumonia staphylococcal			

subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (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 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdiaphragmatic abscess			
subjects affected / exposed	0 / 482 (0.00%)	2 / 497 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 482 (0.00%)	1 / 497 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 482 (0.21%)	0 / 497 (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: 5 %

Non-serious adverse events	Ceftolozane/Tazobactam + Metronidazole	Meropenem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 482 (16.18%)	61 / 497 (12.27%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	25 / 482 (5.19%)	20 / 497 (4.02%)	
occurrences (all)	27	21	

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	37 / 482 (7.68%)	28 / 497 (5.63%)	
occurrences (all)	40	31	
Diarrhoea			
subjects affected / exposed	30 / 482 (6.22%)	25 / 497 (5.03%)	
occurrences (all)	31	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Cubist revised its clinical development program for ceftolozane/tazobactam leading to a single-study approval pathway for each indication, based guidance and following scientific advice from the CHMP and agreement from the US FDA.

Notes: