Clinical trial results:
A Multicenter, Randomized, Observer-Blinded, Active-Controlled Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Ceftaroline Versus Ceftriaxone in Pediatric Subjects With Community-acquired Bacterial Pneumonia Requiring Hospitalization

Summary

EudraCT number	2012-002203-18
Trial protocol	Outside EU/EEA HU GR ES PL BG
Global end of trial date	14 April 2014

Results information

Result version number	v1 (current)
This version publication date	09 August 2018
First version publication date	09 August 2018

Trial information

Trial identification

Sponsor protocol code	P903-31

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cerexa, Inc (a subsidiary of Allergan, plc)
Sponsor organisation address	185 Hudson Street, Plaza 5, New Jersey, United States, NJ 07302-3908
Public contact	Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, CTRegistration@allergan.com
Scientific contact	Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, CTRegistration@allergan.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000769-PIP01-09
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	17 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the safety and tolerability of ceftaroline versus ceftriaxone in pediatric subjects ages 2 months to < 18 years with CABP requiring hospitalization.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. Written informed consent from parent or legally acceptable representative and verbal informed assent from subject (if age appropriate and according to local requirements) were obtained before initiating study-related assessments or procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Hungary: 65
Country: Number of subjects enrolled	Ukraine: 20
Country: Number of subjects enrolled	United States: 12
Country: Number of subjects enrolled	Georgia: 9
Worldwide total number of subjects	161
EEA total number of subjects	120

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)	30
Children (2-11 years)	121
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 161 paediatric subjects between the ages of 2 months to < 18 years with Community-acquired Bacterial Pneumonia (CABP) were enrolled in the study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

At each study centre, at least 1 blinded investigator ("Blinded Observer") did not know the subject's treatment assignment and conducted clinical assessments (including efficacy and safety).

Arms

Are arms mutually exclusive?	Yes
Arm title	Ceftaroline fosamil

Arm description:

122 subjects were randomised (ITT) to receive a minimum of 7 IV doses of ceftaroline fosamil (a minimum of 3 days of IV therapy). A switch to open-label oral study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol-specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12 hours. The total duration of study drug therapy was 5 to 14 days, inclusive.

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

Dosage and administration details:

IV ceftaroline fosamil was infused over 60 (± 10) minutes every 8 hours (q8h [± 1 hour]) as follows:
- Children ≥ 6 months: ceftaroline fosamil 12 mg/kg for subjects weighing ≤ 33 kg or 400 mg for subjects weighing > 33 kg
- Children < 6 months: ceftaroline fosamil 8 mg

Arm title	Comparator

Arm description:

39 subjects were randomised (ITT) to receive ceftriaxone for a minimum of 3 days of IV therapy. A switch to oral open-label study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12h. The total duration of study drug therapy was 5 to 14 days, inclusive.

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

Dosage and administration details:

IV ceftriaxone at a total daily dose of 75 mg/kg/day up to a maximum of 4 g/day, was given in equally divided doses, each infused over 30 (± 10) minutes every 12 hours (q12h [± 2 hours]).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Blinding of subject IV dosing regimens was not necessary because treatment was administered by unblinded study centre staff not involved in assessments of clinical response

Number of subjects in period 1	Ceftaroline fosamil	Comparator
Started	122	39
Completed	116	38
Not completed	6	1
Consent withdrawn by subject	2	-
Other reasons	3	-
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	161	161	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	30	30	
Children (2-11 years)	121	121	
Adolescents (12-17 years)	10	10	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	76	76	
Male	85	85	

Subject analysis sets	
Subject analysis set title	Ceftaroline - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set consists of all patients who received any amount of IV study drug.

Subject analysis set title	Comparator - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set consists of all patients who received any amount of IV study drug.

Subject analysis set title	Ceftaroline - MITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP.

Subject analysis set title	Comparator - MITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP.

Subject analysis set title	Ceftaroline - mMITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated

from an adequate microbiological specimen at baseline.

Subject analysis set title	Comparator - mMITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline.

Subject analysis set title	Ceftaroline - Clinically Evaluable Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

Subject analysis set title	Comparator - Clinically Evaluable Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

Reporting group values	Ceftaroline - Safety Set	Comparator - Safety Set	Ceftaroline - MITT Set
Number of subjects	121	39	107
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)	23	7	23
Children (2-11 years)	90	30	77
Adolescents (12-17 years)	8	2	7
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female			
Male			

Reporting group values	Comparator - MITT Set	Ceftaroline - mMITT Set	Comparator - mMITT Set
Number of subjects	36	24	9
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)	6	4	2
Children (2-11 years)	28	19	7
Adolescents (12-17 years)	2	1	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0

Gender categorical Units: Subjects			
Female Male			

Reporting group values	Ceftaroline - Clinically Evaluable Set	Comparator - Clinically Evaluable Set	
Number of subjects	98	36	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	23	6	
Children (2-11 years)	69	28	
Adolescents (12-17 years)	6	2	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Ceftaroline fosamil

Reporting group description:

122 subjects were randomised (ITT) to receive a minimum of 7 IV doses of ceftaroline fosamil (a minimum of 3 days of IV therapy). A switch to open-label oral study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol-specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12 hours. The total duration of study drug therapy was 5 to 14 days, inclusive.

Reporting group title	Comparator

Reporting group description:

39 subjects were randomised (ITT) to receive ceftriaxone for a minimum of 3 days of IV therapy. A switch to oral open-label study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12h. The total duration of study drug therapy was 5 to 14 days, inclusive.

Subject analysis set title	Ceftaroline - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set consists of all patients who received any amount of IV study drug.

Subject analysis set title	Comparator - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set consists of all patients who received any amount of IV study drug.

Subject analysis set title	Ceftaroline - MITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP.

Subject analysis set title	Comparator - MITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP.

Subject analysis set title	Ceftaroline - mMITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline.

Subject analysis set title	Comparator - mMITT Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline.

Subject analysis set title	Ceftaroline - Clinically Evaluable Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

Subject analysis set title	Comparator - Clinically Evaluable Set
Subject analysis set type	Per protocol

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

Primary: Extent of exposure - Safety Set

End point title	Extent of exposure - Safety Set[1]

End point description:

Extent of exposure is defined as calendar days of exposure to study drug during the IV and oral treatment periods.

End point type	Primary

End point timeframe:

Extent of exposure has been evaluated from date of the first dose of study drug to date of the last dose of study drug + 1 day.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary objective of this study is to evaluate the safety and tolerability of ceftaroline in children and it is not powered for inferential statistical analysis.

End point values	Ceftaroline - Safety Set	Comparator - Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	39		
Units: Number of patients				
< 3 days	2	0		
3 - 5 days	7	1		
6 - 8 days	36	8		
9 - 15 days	74	30		
> 15 days	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Adverse Events - Safety Set

End point title	Adverse Events - Safety Set[2]

End point description:

The safety assessment includes monitoring of adverse events (AEs), serious adverse events, deaths, and discontinuations due to AEs, including cephalosporin class effects and additional AEs.

End point type	Primary

End point timeframe:

Adverse events have been reported from signing the ICF through the late-follow up visit (21 to 35 days after the last dose of any study drug [IV or oral]) or until 30 days after last dose of study drug, whichever occurred later.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary objective of this study is to evaluate the safety and tolerability of ceftaroline in children and it is not powered for inferential statistical analysis.

End point values	Ceftaroline - Safety Set	Comparator - Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	39		
Units: Number of patients				
Subjects with any TEAE	55	18		

Subjects with any study drug-related TEAEs	12	3		
Subjects with any SAEs	6	1		
Subjects with any study drug-related SAEs	0	0		
Discontinuations due to any study drug due to AE	3	0		
Discontinuations of IV study drug due to AE	2	0		
Deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Study Day 4 - MITT Set

End point title	Clinical Response at Study Day 4 - MITT Set

End point description:

Clinical response at Study Day 4 is defined as improvement in at least 2 out of 7 symptoms (cough, dyspnoea, chest pain, sputum
production, chills, feeling of warmth/feverish and exercise intolerance or lethargy) and have worsening in none.

End point type	Secondary

End point timeframe:

Clinical response at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	36		
Units: Number of patients				
Responder	74	24		
Non-responder	24	11		
Incomplete data	9	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Stability at Study Day 4 - MITT Set

End point title	Clinical Stability at Study Day 4 - MITT Set

End point description:

Clinical stability at Study Day 4 is defined as meeting all of the following criteria: Afebrile (temperature ≤ 38.0°C); age-appropriate normal pulse and respiratory rates; oxygen saturation ≥ 92% on room air; worsening of none of the following symptoms relative to baseline: cough, dyspnoea, chest pain, sputum production, chills or rigors, feeling feverish, and exercise intolerance or lethargy.

End point type	Secondary

End point timeframe:

Clinical stability at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	36		
Units: Number of patients				
Stability	37	13		
No stability	60	23		
Incomplete data	10	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Study Day 4 - mMITT Set

End point title	Clinical Response at Study Day 4 - mMITT Set

End point description:

Clinical response at Study Day 4 is defined as improvement in at least 2 out of 7 symptoms (cough, dyspnoea, chest pain, sputum
production, chills, feeling of warmth/feverish and exercise intolerance or lethargy) and have worsening in none.

End point type	Secondary

End point timeframe:

Clinical Response at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	9		
Units: Number of patients				
Responder	14	7		
Non-responder	7	1		
Incomplete data	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Stability at Study Day 4 - mMITT Set

End point title	Clinical Stability at Study Day 4 - mMITT Set

End point description:

Clinical stability at Study Day 4 is defined as meeting all of the following criteria: Afebrile (temperature ≤ 38.0°C); age-appropriate normal pulse and respiratory rates; oxygen saturation ≥ 92% on room air; worsening of none of the following symptoms relative to baseline: cough, dyspnoea, chest pain, sputum production, chills or rigors, feeling feverish, and exercise intolerance or lethargy.

End point type	Secondary

End point timeframe:

Clinical Stability at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	9		
Units: Number of patients				
Stability	5	1		
No stability	15	8		
Incomplete data	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Outcome at TOC - MITT Set

End point title	Clinical Outcome at TOC - MITT Set

End point description:

Clinical Outcome at TOC is defined as assessment of clinical cure, clinical failure and indeterminate for the MITT population at Test-Of-Cure.

End point type	Secondary

End point timeframe:

Clinical Outcome at Test-of-Cure (TOC) has been evaluated 8 to 15 days after administration of the last dose of any study drug [IV or PO].

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	36		
Units: Number of patients				
Clinical cure	94	32		
Clinical failure	8	4		
Indeterminate	5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Outcome at TOC - Clinically Evaluable Set

End point title	Clinical Outcome at TOC - Clinically Evaluable Set

End point description:

Clinical Outcome at TOC is defined as assessment of clinical cure, clinical failure and indeterminate for the CE population at Test-Of-Cure.

End point type	Secondary

End point timeframe:

Clinical Outcome at Test-of-Cure (TOC) has been evaluated 8 to 15 days after administration of the last dose of any study drug [IV or PO].

End point values	Ceftaroline - Clinically Evaluable Set	Comparator - Clinically Evaluable Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	98	36		
Units: Number of patients				
Clinical cure	90	32		
Clinical failure	8	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of first dose of study drug through the late follow-up visit or 30 days after the last dose of IV or oral study drug, whichever occurred later.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Ceftaroline - Safety Population
Reporting group description: -	
Reporting group title	Comparator - Safety Population

Reporting group description: -

Serious adverse events	Ceftaroline - Safety Population	Comparator - Safety Population	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 121 (4.96%)	1 / 39 (2.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary thrombosis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			

subjects affected / exposed	1 / 121 (0.83%)	0 / 39 (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 / 121 (0.83%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 121 (0.83%)	0 / 39 (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	1 / 121 (0.83%)	0 / 39 (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	Ceftaroline - Safety Population	Comparator - Safety Population	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 121 (16.53%)	12 / 39 (30.77%)	
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	2 / 121 (1.65%)	3 / 39 (7.69%)	
occurrences (all)	2	3	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 121 (2.48%)	2 / 39 (5.13%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 121 (8.26%)	2 / 39 (5.13%)	
occurrences (all)	10	2	
Vomiting			

subjects affected / exposed occurrences (all)	4 / 121 (3.31%) 4	2 / 39 (5.13%) 2	
Infections and infestations Otitis media subjects affected / exposed occurrences (all)	 1 / 121 (0.83%) 1	 3 / 39 (7.69%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2012	The following changes were implemented with Amendment 1: Clarification of the efficacy outcome measures of clinical response, clinical stability, and clinical and microbiological outcomes in the Modified Intent-to-Treat (MITT) and the Microbiological Modified Intent-to-Treat (mMITT) populations; updates to the dosing language; updates to the clinical laboratory tests; addition of a symptom questionnaire to be performed by the Blinded Observer and other clarifications.
26 October 2012	The following changes were implemented with Amendment 2: Change of Study Phase designation; updates to dosing regimen; change in criteria for switching to outpatient parenteral antimicrobial therapy (OPAT) and other clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported