Clinical trial results:
A Multicenter, Multinational, Randomized, Double-blind Study to Evaluate the Efficacy and Safety of Ceftaroline fosamil Versus Ceftriaxone Plus Vancomycin in Adult Subjects with Community-acquired Bacterial Pneumonia at Risk for Infection Due to Methicillin-resistant Staphylococcus aureus

Summary

EudraCT number	2012-002182-35
Trial protocol	ES HU PL
Global end of trial date	03 December 2013

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	P903-25

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, Jersey City, New Jersey, United States, NJ 07302-3908
Public contact	Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, IR-CTRegistration@allergan.com
Scientific contact	Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, IR-CTRegistration@allergan.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• Evaluate the efficacy of ceftaroline and azithromycin versus ceftriaxone and azithromycin plus vancomycin in adult subjects with Community-acquired Bacterial Pneumonia (CABP) at risk for infection due to methicillin-resistant Staphylococcus aureus (MRSA)
• Evaluate the safety of ceftaroline and azithromycin versus ceftriaxone and azithromycin plus vancomycin in adult subjects with CABP at risk for infection due to MRSA
• Evaluate the pharmacokinetics of ceftaroline in adult subjects with CABP at risk for infection due to MRSA

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 subject or legally acceptable representative was obtained before initiating study-related assessments or procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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	Georgia: 18
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Ukraine: 12
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	49
EEA total number of subjects	9

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)	29
From 65 to 84 years	18
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 49 subjects (male and female) ≥ 18 years of age with Community-acquired Bacterial Pneumonia (CABP) that warranted 3 days of initial hospitalization, a minimum of 3 days of IV antibacterial therapy, and a minimum of 5 days but no more than 14 days total of study therapy (IV and oral combined) 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	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Ceftaroline fosamil

Arm description:

32 subjects aged ≥ 18 years were randomized to receive IV ceftaroline fosamil infusion every 8 hours (q8h). IV saline placebo q12h was infused to maintain blinding of vancomycin dosing. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

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 every 8 hours (q8h) as follows:
- First daily dose: two 300-mg doses infused consecutively, each over 30 (± 5) minutes
- Second and third daily doses: 600 mg infused over 60 (± 10) minutes

Investigational medicinal product name	Azithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Azithromycin (open-label adjunctive macrolide) was given q24h as a single 500-mg dose on Study Day 1, followed by 250 mg daily up to Study Day 5 (3 days minimum); azithromycin dosed oral then IV (over 60 [± 10] min), or IV then oral.

Arm title	Comparator

Arm description:

17 subjects aged ≥ 18 years were randomized to receive comparator (ceftriaxone plus vancomycin) in the Intent-to-Treat (ITT) Population. IV saline placebo was infused approximately q8h to match the second and third ceftaroline fosamil infusions. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

Arm type	Active comparator

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

Dosage and administration details:

IV vancomycin was infused every 12 hours (q12h) at an initial dose of 15 mg/kg; subsequent dosing should be infused at 10 mg/min to maintain serum trough concentrations of 15 – 20 mg/L. Vancomycin was only to be discontinued if a non-MRSA respiratory pathogen was identified.

Investigational medicinal product name	Cetriaxone
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 ceftriaxone 2 g was infused over 30 (± 5) minutes q24h immediately followed by IV saline placebo infused over 30 (± 5) minutes.

Investigational medicinal product name	Azithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Azithromycin (open-label adjunctive macrolide) was given q24h as a single 500-mg dose on Study Day 1, followed by 250 mg daily up to Study Day 5 (3 days minimum); azithromycin dosed oral then IV (over 60 [± 10] min), or IV then oral.

Number of subjects in period 1	Ceftaroline fosamil	Comparator
Started	32	17
Completed	27	15
Not completed	5	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	1
Lack of efficacy	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Ceftaroline fosamil
Reporting group description:	
32 subjects aged ≥ 18 years were randomized to receive IV ceftaroline fosamil infusion every 8 hours (q8h). IV saline placebo q12h was infused to maintain blinding of vancomycin dosing. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.	
Reporting group title	Comparator
Reporting group description:	
17 subjects aged ≥ 18 years were randomized to receive comparator (ceftriaxone plus vancomycin) in the Intent-to-Treat (ITT) Population. IV saline placebo was infused approximately q8h to match the second and third ceftaroline fosamil infusions. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.	

Reporting group values	Ceftaroline fosamil	Comparator	Total
Number of subjects	32	17	49
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)	23	6	29
From 65-84 years	9	9	18
85 years and over	0	2	2
Gender categorical Units: Subjects			
Female	20	13	33
Male	12	4	16

End points

End points reporting groups

Reporting group title	Ceftaroline fosamil

Reporting group description:

32 subjects aged ≥ 18 years were randomized to receive IV ceftaroline fosamil infusion every 8 hours (q8h). IV saline placebo q12h was infused to maintain blinding of vancomycin dosing. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

Reporting group title	Comparator

Reporting group description:

17 subjects aged ≥ 18 years were randomized to receive comparator (ceftriaxone plus vancomycin) in the Intent-to-Treat (ITT) Population. IV saline placebo was infused approximately q8h to match the second and third ceftaroline fosamil infusions. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

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

Subject analysis set description:

The Modified-Intent-to-Treat (MITT) Population consists of all randomised subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP with risk factors for MRSA (excluding those that have a sole atypical pathogen).

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

Subject analysis set description:

The Modified-Intent-to-Treat (MITT) Population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP with risk factors for MRSA (excluding those that have a sole atypical pathogen).

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

Subject analysis set description:

The microbiological Modified Intent-to-Treat (mMITT Population) consists of all subjects for whom at least 1 typical bacterial pathogen has been identified 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 microbiological Modified Intent-to-Treat (mMITT) Population consists of all subjects for whom at least 1 typical bacterial pathogen has been identified from an adequate microbiological specimen at baseline.

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

Subject analysis set description:

The Safety Population consists of all randomized subjects who received any amount of IV study drug, and will be analysed according to the treatment actually received.

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

Subject analysis set description:

The Safety Population consists of all randomized subjects who received any amount of IV study drug, and will be analysed according to the treatment actually received.

Primary: Symptom Improvement at Study Day 4 - MITT Set

End point title	Symptom Improvement at Study Day 4 - MITT Set[1]

End point description:

A response for symptom improvement at Study Day 4 is defined as improvement in at least 2 and no worsening of any of the following symptoms: cough, dyspnoea, sputum production, and chest pain.

End point type	Primary

End point timeframe:

Symptom Improvement at Study Day 4 was evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	17		
Units: Number of patients				
Responder	24	14		
Non-responder	5	2		
Incomplete data	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Stability at Study Day 4 - MITT Set

End point title	Clinical Stability at Study Day 4 - MITT Set[2]

End point description:

A response for clinical stability at Study Day 4 is defined as meeting all of the following criteria: (1) Temperature ≤ 37.8°C), (2) Heart rate ≤ 100 beats/min, (3) Respiratory rate ≤ 24 breaths/min, (4) Systolic blood pressure ≥ 90 mm Hg, and (5) Oxygen saturation ≥ 90%.

End point type	Primary

End point timeframe:

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

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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	17		
Units: Number of patients				
Responder	15	9		
Non-responder	14	7		
Incomplete data	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Success at Study day 4 - MITT Set

End point title	Clinical Success at Study day 4 - MITT Set[3]

End point description:

A response for clinical success is defined as a subject with a response for both symptom improvement and clinical stability.

End point type	Primary

End point timeframe:

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

Notes:

[3] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	17		
Units: Number of patients				
Responder	14	8		
Non-responder	16	8		
Incomplete data	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Symptom Improvement at Study Day 4 - mMITT Set

End point title	Symptom Improvement at Study Day 4 - mMITT Set[4]

End point description:

A response for symptom improvement at Study Day 4 is defined as improvement in at least 2 and no worsening of any of the following symptoms: cough, dyspnoea, sputum production, and chest pain.

End point type	Primary

End point timeframe:

Symptom Improvement at Study Day 4 was evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

Notes:

[4] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	14		
Units: Number of patients				
Responder	22	11		
Non-responder	2	2		
Incomplete data	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Stability at Study Day 4 - mMITT Set

End point title	Clinical Stability at Study Day 4 - mMITT Set[5]

End point description:

A response for clinical stability at Study Day 4 is defined as meeting all of the following criteria: (1) Temperature ≤ 37.8°C), (2) Heart rate ≤ 100 beats/min, (3) Respiratory rate ≤ 24 breaths/min, (4) Systolic blood pressure ≥ 90 mm Hg, and (5) Oxygen saturation ≥ 90%.

End point type	Primary

End point timeframe:

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

Notes:

[5] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	14		
Units: Number of patients				
Responder	13	6		
Non-responder	9	7		
Incomplete data	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Success at Study Day 4 - mMITT Set

End point title	Clinical Success at Study Day 4 - mMITT Set[6]

End point description:

A response for clinical success is defined as a subject with a response for both symptom improvement and clinical stability.

End point type	Primary

End point timeframe:

Clinical Success at Study Day 4 was evaluated from Study Day 1 (the first day of IV study drug

administration) to Study Day 4.

Notes:

[6] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	14		
Units: Number of patients				
Responder	12	5		
Non-responder	11	8		
Incomplete data	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Outcome at TOC - MITT Set

End point title	Clinical Outcome at TOC - MITT Set[7]

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	Primary

End point timeframe:

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

Notes:

[7] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - MITT Set	Comparator - MITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	17		
Units: Number of patients				
Clinical cure	27	15		
Clinical failure	3	2		
Indeterminate	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Outcome at TOC - mMITT Set

End point title	Clinical Outcome at TOC - mMITT Set[8]

End point description:

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

End point type	Primary

End point timeframe:

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

Notes:

[8] - 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: This study is not powered for inferential statistical analysis.

End point values	Ceftaroline - mMITT Set	Comparator - mMITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	14		
Units: Number of patients				
Clinical cure	23	12		
Clinical failure	0	2		
Indeterminate	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the ICF to 21 to 35 days after last dose of any study drug [IV or PO]).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Ceftaroline fosamil

Reporting group description:

32 subjects aged ≥ 18 years of age were randomized to receive IV ceftaroline fosamil infusion every 8 hours (q8h). IV saline placebo q12h was infused to maintain blinding of vancomycin dosing. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

Reporting group title	Comparator

Reporting group description:

17 subjects ≥ 18 years of age were randomized to comparator (ceftriaxone plus vancomycin) in the Intent-to-Treat (ITT) Population. IV saline placebo was infused approximately q8h to match the second and third ceftaroline fosamil infusions. For coverage of atypical pathogens, all subjects were to receive a minimum of 3 and up to 5 days of open-label azithromycin (oral, IV, or combination), administered as a single 500-mg dose on Study Day 1, followed by a 250 mg once daily dose up through Study Day 5.

Serious adverse events	Ceftaroline fosamil	Comparator	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 32 (9.38%)	2 / 17 (11.76%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Computerised tomogram abnormal			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
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 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	1 / 32 (3.13%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 32 (3.13%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 32 (3.13%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 17 (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 fosamil	Comparator	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 32 (53.13%)	9 / 17 (52.94%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Computerised tomogram thorax abnormal			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Neutrophil count increased			

subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 32 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 32 (9.38%)	1 / 17 (5.88%)	
occurrences (all)	3	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	0 / 32 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Oedema peripheral			

subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 32 (6.25%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	0 / 32 (0.00%)	3 / 17 (17.65%)	
occurrences (all)	0	3	

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? Yes

Date	Interruption	Restart date
29 October 2013	Study early termination	-

Notes:

Limitations and caveats

None reported