Clinical trial results:
A Phase III, Multicentre, Randomised, Double-Blind, Comparative Study to Evaluate the Efficacy and Safety of Ceftaroline Fosamil (600 mg every 8 hours) Versus Vancomycin Plus Aztreonam in the Treatment of Patients With Complicated Bacterial Skin and Soft Tissue Infections With Evidence of Systemic Inflammatory Response or Underlying Comorbidities

Summary

EudraCT number	2011-004013-16
Trial protocol	GR BE CZ BG DE AT PL ES GB SK IT
Global end of trial date	30 April 2015

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	19 July 2015

Trial information

Trial identification

Sponsor protocol code	D3720C00001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85 Södertälje, Södertälje, Sweden,
Public contact	Jesus Gonzalez, AstraZeneca, UK +44 (0)7557 541 031 , Jesus.Gonzalez@astrazeneca.com
Scientific contact	Matthew Dryden, Royal Hampshire County Hospital, Department of Microbiology, UK +44 (0)1962 824451, Matthew.Dryden@hhft.nhs.uk

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	05 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2014
Global end of trial reached?	Yes
Global end of trial date	30 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess whether ceftaroline fosamil was non inferior to vancomycin plus aztreonam in the clinical cure rate at the TOC visit in both the MITT and CE analysis sets of adult patients with cSSTI.

Protection of trial subjects:

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

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	17 May 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	Argentina: 10
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	Bulgaria: 83
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	China: 151
Country: Number of subjects enrolled	Croatia: 46
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Peru: 35

Country: Number of subjects enrolled	Philippines: 5
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Russian Federation: 115
Country: Number of subjects enrolled	South Africa: 22
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 18
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	Turkey: 14
Country: Number of subjects enrolled	Ukraine: 29
Country: Number of subjects enrolled	United States: 120
Worldwide total number of subjects	772
EEA total number of subjects	188

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)	578
From 65 to 84 years	178
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

Overall, 802 patients were enrolled from 111 centres in 6 regions in this study. The first patient was enrolled on 17 May 2012 and the last patient last visit was on 26 June 2014.

Pre-assignment

Screening details:

None

Period 1

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

Blinding implementation details:

Individual treatment codes, indicating the treatment randomisation for each randomised patient, will be available to the investigators from the IVRS/IWRS. Routines for this will be described in the IVRS/IWRS user manual that will be provided to each centre.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ceftaroline fosamil at 600 mg every 8 hours (q8h)

Arm description: -

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

Dosage and administration details:

Sterile crystalline powder in a single-dose, clear glass 20-mL vial,

Arm title	Vancomycin Plus Aztreonam

Arm description: -

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

Dosage and administration details:

Lyophilized powder, intravenous, dose strength (based on patient’s

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

Dosage and administration details:

Sterile powder containing approximately 1 gram of aztreonam per

Number of subjects in period 1[1]	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam
Started	506	255
Completed	459	223
Not completed	47	32
Adverse event, serious fatal	3	2
Consent withdrawn by subject	16	6
Lack of therapeutic response	5	6
Adverse event, non-fatal	3	6
Other	3	1
Lost to follow-up	15	8
Protocol deviation	2	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Overall 802 patients were recruited, 772 patients were randomized, but only 761 patients had data for the study.

Baseline characteristics

Reporting groups	
Reporting group title	Ceftaroline fosamil at 600 mg every 8 hours (q8h)
Reporting group description: -	
Reporting group title	Vancomycin Plus Aztreonam
Reporting group description: -	

Reporting group values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam	Total
Number of subjects	506	255	761
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)	387	183	570
From 65-84 years	111	64	175
85 years and over	8	8	16
Age Continuous | Units: Years			
arithmetic mean	52.6	53.6	
standard deviation	± 16.51	± 16.25	-
Gender, Male/Female Units: Participants			
Female	196	107	303
Male	310	148	458

End points

End points reporting groups

Reporting group title	Ceftaroline fosamil at 600 mg every 8 hours (q8h)
Reporting group description: -	
Reporting group title	Vancomycin Plus Aztreonam
Reporting group description: -	

Primary: Clinical response at Test of Cure in MITT

End point title	Clinical response at Test of Cure in MITT
End point description:	
The observed difference in the clinical cure rates at TOC (ceftaroline group minus vancomycin plus aztreonam group) in MITT	
End point type	Primary
End point timeframe:	
7 to 20 days after the last dose of study drug	

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	506	255		
Units: Participants				
Clinical cure	396	202		
Clinical failure	58	34		
Indeterminate	52	19		

Statistical analyses

Statistical analysis title	Difference in clinical cure rates at TOC in MITT
Statistical analysis description:	
Difference in clinical cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.	
Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	761
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	5.41

Primary: Clinical response at Test-of cure in CE

End point title	Clinical response at Test-of cure in CE

End point description:

The observed difference in the clinical cure rates at TOC (ceftaroline group minus vancomycin plus aztreonam group) in CE

End point type	Primary

End point timeframe:

7 to 20 days after the last dose of study drug

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	211		
Units: Participants				
Clinical cure	342	211		
Clinical failure	53	31		

Statistical analyses

Statistical analysis title	Difference in clinical cure rates at TOC in CE

Statistical analysis description:

Difference in clinical cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.

Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.32
upper limit	7.48

Secondary: Per patient microbiological response at TOC in mMITT

End point title	Per patient microbiological response at TOC in mMITT

End point description:

Difference in microbiological favorable response rate at TOC in mMITT

End point type	Secondary

End point timeframe:

7 to 20 days after the last dose of study drug

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	248	136		
Units: Participants				
Favorable	203	109		
Unfavorable	17	17		
Indeterminate	28	10		

Statistical analyses

Statistical analysis title	Difference in favorable rates at TOC in mMITT

Statistical analysis description:

Difference in favorable rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.

Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.21
upper limit	10.39

Secondary: Per-patient micro response at TOC for ME

End point title	Per-patient micro response at TOC for ME

End point description:

Difference in microbiological favorable response rate at TOC in ME

End point type	Secondary

End point timeframe:

7 to 20 days after the last dose of study drug

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	112		
Units: Participants				
Favorable	167	98		
Unfavorable	14	14		

Statistical analyses

Statistical analysis title	Difference in favorable rates at TOC in ME

Statistical analysis description:

Difference in favorable rates (Ceftaroline minus Vancomycin/Aztreonam).CI was calculated by unstratified Miettinen and Nurminen CI.

Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	293
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	4.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	12.86

Secondary: Clinical response at EOT in MITT

End point title	Clinical response at EOT in MITT

End point description:

The observed difference in the clinical cure rates at EOT (ceftaroline group minus vancomycin plus aztreonam group) in MITT

End point type	Secondary

End point timeframe:

On day of last dose of study drug (or + 1 day)

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	506	255		
Units: Participants				
Clinical cure	429	213		
Clinical fialure	44	29		
Indeterminate	31	11		
Missing	2	2		

Statistical analyses

Statistical analysis title	Difference in cure rates at EOT in MITT
Statistical analysis description:	
Difference in cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.	
Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	761
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.05
upper limit	7.06

Secondary: Clinical response at EOT in CE

End point title	Clinical response at EOT in CE
End point description:	
The observed difference in the clinical cure rates at EOT (ceftaroline group minus vancomycin plus aztreonam group) in CE	
End point type	Secondary
End point timeframe:	
On day of last dose of study drug (or +1 day)	

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	211		
Units: Participants				
Clinical cure	356	184		
Clinical failure	39	27		

Statistical analyses

Statistical analysis title	Difference in cure rates at EOT in CE
Statistical analysis description:	
Difference in cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.	
Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	2.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	8.73

Secondary: clinical relapse rates at LFU in CE (patients with clinical cure at TOC)

End point title	clinical relapse rates at LFU in CE (patients with clinical cure at TOC)
End point description:	
The observed difference in the clinical relapse rates at LFU (ceftaroline group minus vancomycin plus aztreonam group) in CE	
End point type	Secondary
End point timeframe:	
21 to 42 days after the last dose of study drug	

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342	180		
Units: Participants				
Relapse	3	3		

No relapse	335	174		
Indeterminate	3	3		
Missing	1	0		

Statistical analyses

Statistical analysis title	Difference in relapse rates at LFU in CE
Statistical analysis description:	
Difference in relapse rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.	
Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.98
upper limit	1.18

Secondary: Early response at 48 to 72 hours of treatment in MITT

End point title	Early response at 48 to 72 hours of treatment in MITT
End point description:	
The observed difference in the early success rates at 48 to 72 hours of treatment (ceftaroline group minus vancomycin plus aztreonam group) in MITT	
End point type	Secondary
End point timeframe:	
48 to 72 hours after first dose of study drug	

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	506	255		
Units: Participants				
Success	445	229		
Failure	28	11		
Indeterminate	33	15		

Statistical analyses

Statistical analysis title	Difference in success rates at 48-72 hours in MITT

Statistical analysis description:

Difference in success rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.

Comparison groups	Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam
Number of subjects included in analysis	761
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.34
upper limit	3.15

Secondary: Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME

End point title	Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME

End point description:

Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME analysis set

End point type	Secondary

End point timeframe:

7 to 20 days after the last dose of study drug

End point values	Ceftaroline fosamil at 600 mg every 8 hours (q8h)	Vancomycin Plus Aztreonam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	112		
Units: Participants				
MSSA - Patients reported	94	57		
MSSA - Favorable	91	49		
MSSA - Unfavorable	3	8		
MRSA - Patients reported	25	15		
MRSA - Favorable	22	12		
MRSA - Unfavorable	3	3		
Streptococcus pyogenes - Patients reported	15	7		
Streptococcus pyogenes - Favorable	14	7		
Streptococcus pyogenes - Unfavorable	1	0		
Streptococcus agalactiae - Patients reported	6	9		
Streptococcus agalactiae - Favorable	6	9		

Streptococcus agalactiae - Unfavorable	0	0		
Streptococcus dysgalactiae - Patients reported	9	0		
Streptococcus dysgalactiae - Favorable	9	0		
Streptococcus dysgalactiae - Unfavorable	0	0		
Enterococcus faecalis - Patients reported	6	5		
Enterococcus faecalis - Favorable	5	4		
Enterococcus faecalis - Unfavorable	1	1		
Escherichia coli - Patients reported	12	10		
Escherichia coli - Favorable	12	9		
Escherichia coli - Unfavorable	0	1		
Klebsiella pneumoniae - Patients reported	7	4		
Klebsiella pneumoniae - Favorable	6	3		
Klebsiella pneumoniae - Unfavorable	1	1		
Klebsiella oxytoca - Patients reported	4	1		
Klebsiella oxytoca - Favorable	4	1		
Klebsiella oxytoca - Unfavorable	0	0		
Proteus mirabilis - Patients reported	7	2		
Proteus mirabilis - Favorable	6	2		
Proteus mirabilis - Unfavorable	1	0		
Morganella morganii - Paitents reported	4	2		
Morganella morganii - Favorable	4	2		
Morganella morganii - Unfavorable	0	0		
Enterobacter cloacae - Patients reported	4	5		
Enterobacter cloacae - Favorable	4	5		
Enterobacter cloacae - Unfavorable	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from time of administration of the first dose of study therapy up to and including the TOC visit. Serious AEs were collected from time of signature of informed consent up to and including the LFU visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Vancomycin/Aztreonam

Reporting group description:

Vancomycin Plus Aztreonam

Reporting group title	Ceftaroline fosamil 600 mg 120 min IV

Reporting group description: -

Serious adverse events	Vancomycin/Aztreonam	Ceftaroline fosamil 600 mg 120 min IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 255 (5.88%)	31 / 506 (6.13%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 255 (0.39%)	2 / 506 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			

subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemosiderosis			

subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Metal poisoning			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 255 (0.00%)	3 / 506 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 255 (0.39%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ventricular tachycardia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 255 (0.39%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephropathy toxic			

subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	2 / 255 (0.78%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 255 (0.00%)	2 / 506 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	1 / 255 (0.39%)	0 / 506 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 255 (0.00%)	1 / 506 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Vancomycin/Aztreonam	Ceftaroline fosamil 600 mg 120 min IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 255 (18.04%)	82 / 506 (16.21%)	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	7 / 255 (2.75%)	3 / 506 (0.59%)	
occurrences (all)	7	3	

Vascular disorders Hypertension subjects affected / exposed occurrences (all)	8 / 255 (3.14%) 8	7 / 506 (1.38%) 8	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	12 / 255 (4.71%) 13	17 / 506 (3.36%) 17	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	9 / 255 (3.53%) 9	10 / 506 (1.98%) 10	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	5 / 255 (1.96%) 5 8 / 255 (3.14%) 8 11 / 255 (4.31%) 11 5 / 255 (1.96%) 5	12 / 506 (2.37%) 12 9 / 506 (1.78%) 9 20 / 506 (3.95%) 20 13 / 506 (2.57%) 15	
Skin and subcutaneous tissue disorders Pruritus generalised subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	6 / 255 (2.35%) 6 6 / 255 (2.35%) 6	4 / 506 (0.79%) 4 10 / 506 (1.98%) 11	
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	8 / 255 (3.14%) 9	14 / 506 (2.77%) 14	

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

None reported