Clinical trial results:
A Phase 3, Randomized, Double-Blind, Double-Dummy, Multicenter, Prospective Study to Assess the Efficacy and Safety of Eravacycline Compared with Ertapenem in Complicated Intra-abdominal Infections

Summary

EudraCT number	2013-001913-34
Trial protocol	LV CZ EE LT DE BG
Global end of trial date	26 August 2014

Results information

Result version number	v1 (current)
This version publication date	23 August 2017
First version publication date	23 August 2017

Trial information

Trial identification

Sponsor protocol code	TP-434-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01844856
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Tetraphase Pharmaceuticals, Inc.
Sponsor organisation address	480 Arsenal Street, Suite 110, Watertown, United States, 02472
Public contact	Chief Medical Officer, Tetraphase Pharmaceuticals, Inc., 1 617-715-3600,
Scientific contact	Chief Medical Officer, Tetraphase Pharmaceuticals, Inc., 1 617-715-3600,

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	26 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 August 2014
Global end of trial reached?	Yes
Global end of trial date	26 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a Phase 3, randomized, double-blind, double-dummy, multicenter, prospective study to assess the efficacy, safety, and pharmacokinetics of eravacycline compared with ertapenem in the treatment of adult complicated intra-abdominal infections (cIAI).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) E6 Good Clinical Practice (GCP) (consolidated guidelines pertaining to informed consent). At the first visit, prior to initiation of any study-related procedures, participants gave their written consent to participate in the study after having been informed about the nature and purpose of the study, participation/termination conditions, and risks and benefits; however, microbiologic specimens collected during routine operative care prior to participant consent may have been used for study purposes with the participant's knowledge and consent. Additionally, a Data Safety Monitoring Board was established to periodically review safety data (unblinded) from all participants and advise the Sponsor regarding the continuing safety of current participants and those yet to be recruited.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 August 2013
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	Russian Federation: 52
Country: Number of subjects enrolled	Romania: 84
Country: Number of subjects enrolled	United States: 38
Country: Number of subjects enrolled	Ukraine: 76
Country: Number of subjects enrolled	Czech Republic: 31
Country: Number of subjects enrolled	Latvia: 48
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Bulgaria: 89
Country: Number of subjects enrolled	Lithuania: 52
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Estonia: 66
Worldwide total number of subjects	541
EEA total number of subjects	374

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)	377
From 65 to 84 years	158
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants enrolled in this study were at least 18 years of age with a cIAI. Participants 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	Eravacycline, 1.0 mg/kg q12h

Arm description:

Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram of body weight (mg/kg) every 12 hours (q12h) for a minimum of 4 days and a maximum of 14 days.

Arm type	Experimental
Investigational medicinal product name	Eravacycline
Investigational medicinal product code	TP-434
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0 mg/kg q12h for 4-14 days

Arm title	Ertapenem, 1.0 g q24h

Arm description:

Ertapenem was administered IV at a dose of 1.0 gram (g) every 24 hours (q24h) for a minimum of 4 days and a maximum of 14 days.

Arm type	Active comparator
Investigational medicinal product name	Ertapenem
Investigational medicinal product code	
Other name	Invanz
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0 g q24h for 4-14 days

Number of subjects in period 1	Eravacycline, 1.0 mg/kg q12h	Ertapenem, 1.0 g q24h
Started	270	271
Received any amount of study drug	270	268
Completed	246	255
Not completed	24	16
Consent withdrawn by subject	3	2
Enterococcus Resistant	-	1
Adverse event, non-fatal	3	6
Randomized but was a Screen Failure	-	1
Lost to follow-up	15	3
Inadvertently Not Scheduled	1	-
Noncompliance	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Eravacycline, 1.0 mg/kg q12h
Reporting group description:	
Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram of body weight (mg/kg) every 12 hours (q12h) for a minimum of 4 days and a maximum of 14 days.	
Reporting group title	Ertapenem, 1.0 g q24h
Reporting group description:	
Ertapenem was administered IV at a dose of 1.0 gram (g) every 24 hours (q24h) for a minimum of 4 days and a maximum of 14 days.	

Reporting group values	Eravacycline, 1.0 mg/kg q12h	Ertapenem, 1.0 g q24h	Total
Number of subjects	270	271	541
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)	182	195	377
From 65-84 years	85	73	158
85 years and over	3	3	6
Age Continuous Units: years			
arithmetic mean	54.8	54.8	
standard deviation	± 16.92	± 16.09	-
Gender, Male/Female Units: participants			
Female	114	108	222
Male	156	163	319
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	9	17
Not Hispanic or Latino	261	262	523
Unknown or Not Reported	1	0	1
Race/Ethnicity, Customized Units: Subjects			
White	263	260	523
Black or African American	1	3	4
Asian	1	3	4
Other Race	4	5	9
Unknown or Not Reported	1	0	1
Region of Enrollment Units: Subjects			
Russian Federation	28	24	52

Romania	42	42	84
United States	18	20	38
Ukraine	38	38	76
Czech Republic	14	17	31
Latvia	25	23	48
South Africa	0	1	1
Bulgaria	45	44	89
Lithuania	26	26	52
Germany	2	2	4
Estonia	32	34	66

End points

End points reporting groups

Reporting group title	Eravacycline, 1.0 mg/kg q12h

Reporting group description:

Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram of body weight (mg/kg) every 12 hours (q12h) for a minimum of 4 days and a maximum of 14 days.

Reporting group title	Ertapenem, 1.0 g q24h

Reporting group description:

Ertapenem was administered IV at a dose of 1.0 gram (g) every 24 hours (q24h) for a minimum of 4 days and a maximum of 14 days.

Subject analysis set title	Eravacycline, 1.0 mg/kg q12h - micro-ITT Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who had baseline bacterial pathogens that cause cIAI and against at least one of which the investigational drug has in vitro antibacterial activity (microbiological Intent-to-Treat [micro-ITT] Population).

Subject analysis set title	Ertapenem, 1.0 g q24h - micro-ITT Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who had baseline bacterial pathogens that cause cIAI and against at least one of which the investigational drug has in vitro antibacterial activity (micro-ITT Population).

Subject analysis set title	Eravacycline, 1.0 mg/kg q12h - MITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized participants who received any amount of study drug (Modified Intent-to-Treat [MITT] Population).

Subject analysis set title	Ertapenem, 1.0 g q24h - MITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized participants who received any amount of study drug (MITT Population).

Subject analysis set title	Eravacycline, 1.0 mg/kg q12h - CE Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who had no major protocol deviations (Clinically Evaluable [CE] Population).

Subject analysis set title	Ertapenem, 1.0 g q24h - CE Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who had no major protocol deviations (CE Population).

Primary: Clinical Response Of Eravacycline And Ertapenem Treatment Arms At The Test-Of-Cure (TOC) Visit In The MITT Population

End point title	Clinical Response Of Eravacycline And Ertapenem Treatment Arms At The Test-Of-Cure (TOC) Visit In The MITT Population

End point description:

This was the co-primary outcome measure for the European Medicines Agency (EMA). Clinical response was classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection), failure (death related to cIAI, unplanned surgical procedures or percutaneous drainage procedures, persisting or recurrent infection within the abdomen, postsurgical wound infection, or administration of effective concomitant antibacterial therapy), or indeterminate (outcome was neither cure nor failure, or assessment was not available). Participants who were failures at the End-of-Treatment (EOT) visit (within 24 hours of last dose) were considered failures at the TOC visit. The number of participants with a clinical response classification of cure, failure, or indeterminate is

presented.

End point type	Primary

End point timeframe:

TOC visit: 25-31 days after the first dose of study drug

End point values	Eravacycline, 1.0 mg/kg q12h - MITT Population	Ertapenem, 1.0 g q24h - MITT Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	270[1]	268[2]		
Units: participants				
number (not applicable)				
Cure	235	238		
Failure	19	15		
Indeterminate	16	15		

Notes:

[1] - All randomized participants who received any amount of study drug.

[2] - All randomized participants who received any amount of study drug.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

A 2-sided 99% confidence interval (CI) for the observed difference in primary outcome rates (eravacycline treatment group minus ertapenem treatment group) was calculated. If the lower limit of the 99% CI for the difference in clinical cure rates exceeded −12.5%, then the null hypothesis was rejected, and the non-inferiority of eravacycline to ertapenem was declared.

Comparison groups	Eravacycline, 1.0 mg/kg q12h - MITT Population v Ertapenem, 1.0 g q24h - MITT Population
Number of subjects included in analysis	538
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (net)
Point estimate	-1.8
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-9.2
upper limit	5.6

Primary: Clinical Response Of Eravacycline And Ertapenem Treatment Arms In The CE Population At The TOC Visit

End point title	Clinical Response Of Eravacycline And Ertapenem Treatment Arms In The CE Population At The TOC Visit

End point description:

This was the co-primary outcome measure for the EMA. Clinical response was classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection), failure (death related to cIAI, unplanned surgical procedures or percutaneous drainage procedures, persisting or recurrent infection within the abdomen, postsurgical wound infection, or administration of effective

concomitant antibacterial therapy), or indeterminate (outcome was neither cure nor failure, or assessment was not available). Participants who were failures at the EOT visit (within 24 hours of last dose) were considered failures at the TOC visit. The number of participants with a clinical response classification of cure, failure, or indeterminate is presented.

End point type	Primary

End point timeframe:

TOC visit: 25-31 days after first dose

End point values	Eravacycline, 1.0 mg/kg q12h - CE Population	Ertapenem, 1.0 g q24h - CE Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	239[3]	238[4]		
Units: participants				
number (not applicable)				
Cure	222	225		
Failure	17	13		
Indeterminate	0	0		

Notes:

[3] - All randomized participants who had no major protocol deviations.

[4] - All randomized participants who had no major protocol deviations.

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

A 2-sided 99% CI for the observed difference in primary outcome rates (eravacycline treatment group minus ertapenem treatment group) was calculated. If the lower limit of the 99% CI for the difference in clinical cure rates exceeded −12.5%, then the null hypothesis was rejected, and the non-inferiority of eravacycline to ertapenem was declared.

Comparison groups	Eravacycline, 1.0 mg/kg q12h - CE Population v Ertapenem, 1.0 g q24h - CE Population
Number of subjects included in analysis	477
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	-1.7
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-7.9
upper limit	4.4

Secondary: Clinical Response Of Eravacycline And Ertapenem Treatment Arms In The Micro-ITT Population At The TOC Visit

End point title	Clinical Response Of Eravacycline And Ertapenem Treatment Arms In The Micro-ITT Population At The TOC Visit

End point description:

This was an outcome measure for the Food and Drug Administration (FDA). Clinical response was

classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection), failure (death related to cIAI, unplanned surgical procedures or percutaneous drainage procedures, persisting or recurrent infection within the abdomen, postsurgical wound infection, or administration of effective concomitant antibacterial therapy), or indeterminate (outcome was neither cure nor failure, or assessment was not available). Participants who were failures at the EOT visit (within 24 hours of last dose) were considered failures at the TOC visit. The number of participants with a clinical response classification of cure, failure, or indeterminate is presented.

End point type	Secondary

End point timeframe:

TOC visit: 25-31 days after first dose

End point values	Eravacycline, 1.0 mg/kg q12h - micro-ITT Population	Ertapenem, 1.0 g q24h - micro-ITT Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220[5]	226[6]		
Units: participants				
number (not applicable)				
Cure	191	198		
Failure	19	11		
Indeterminate	10	17		

Notes:

[5] - Randomized participants who had baseline bacterial pathogens and in vitro antibacterial activity.

[6] - Randomized participants who had baseline bacterial pathogens and in vitro antibacterial activity.

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 participants from the start of study drug administration through the follow-up visit, which occurred 38 to 50 days after the first dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Eravacycline, 1.0 mg/kg q12h

Reporting group description:

Eravacycline was administered IV at a dose of 1.0 mg/kg q12h for a minimum of 4 days and a maximum of 14 days.

Reporting group title	Ertapenem, 1.0 g q24h

Reporting group description:

Ertapenem was administered IV at a dose of 1.0 g q24h for a minimum of 4 days and a maximum of 14 days.

Serious adverse events	Eravacycline, 1.0 mg/kg q12h	Ertapenem, 1.0 g q24h	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 270 (6.30%)	16 / 268 (5.97%)	
number of deaths (all causes)	3	6	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	2 / 270 (0.74%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (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 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiopulmonary failure			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Biliary drainage			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (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			
Cerebrovascular accident			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
multi-organ failure			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 270 (0.37%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic fistula			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal fistula			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (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 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis necrotising			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal fistula			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (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			
Acute respiratory failure			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 270 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Empyema			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	1 / 270 (0.37%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 270 (0.37%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 268 (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	2 / 270 (0.74%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Eravacycline, 1.0 mg/kg q12h	Ertapenem, 1.0 g q24h	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 270 (15.93%)	28 / 268 (10.45%)	
Vascular disorders			
Phlebitis			
subjects affected / exposed	8 / 270 (2.96%)	1 / 268 (0.37%)	
occurrences (all)	18	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 270 (2.59%)	9 / 268 (3.36%)	
occurrences (all)	8	11	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 270 (2.22%)	8 / 268 (2.99%)	
occurrences (all)	6	8	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 270 (8.15%)	2 / 268 (0.75%)	
occurrences (all)	24	2	
Vomiting			

subjects affected / exposed occurrences (all)	11 / 270 (4.07%) 11	9 / 268 (3.36%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2013	Amendment number 1 was implemented before any participants were enrolled and documented the following: the increase in the study sample size, inclusion of the micro-ITT population, change in assessment timing, change in microbiological specimen collection, clarification of inclusion and exclusion criteria, refinement of clinical response assessment, and other global administrative changes and clarifications.
31 October 2013	Amendment number 2 was implemented after 197 participants were enrolled and documented the following: the change in primary analysis populations and non-inferiority margin for the EMA, revision of the inclusion and exclusion criteria, change in the dose of eravacycline was limited to 1.0 mg/kg, up to a maximum of 150 mg q12h, changes in the restricted concomitant medications, clarification on study drug and placebo preparation, change in the maximum dosage in 24 hours, and other global administrative changes and clarifications. Changes to the protocol were considered to have no negative impact on the safety of participants already enrolled into the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported