Clinical trial results:
A Phase 3 Randomized Double-blind Study Comparing TR-701 FA and Linezolid in Ventilated Gram-positive Nosocomial Pneumonia

Summary

EudraCT number	2013-004154-22
Trial protocol	LV HU AT DE BE ES GR SK CZ EE GB HR PT IT
Global end of trial date	22 June 2018

Results information

Result version number	v1
This version publication date	26 June 2019
First version publication date	26 June 2019

Trial information

Trial identification

Sponsor protocol code	1986-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02019420
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-1986-002, Cubist Protocol Number: TR701-132

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States,
Public contact	Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	22 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2018
Global end of trial reached?	Yes
Global end of trial date	22 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a 1:1 ratio, randomized, double-blind, double-dummy, multicenter, global Phase 3 study of tedizolid phosphate (TR-701 FA) 200 mg intravenous (IV) once daily for 7 days versus linezolid (Zyvox®, Zyvoxid®, etc.) 600 mg IV every 12 hours for 10 days for the treatment of ventilated participants with presumed gram-positive hospital-acquired bacterial pneumonia (HABP) or ventilator-associated bacterial pneumonia (VABP), collectively referred to as ventilated nosocomial pneumonia (VNP). Participants with concurrent gram-positive bacteremia are to receive 14 days of active therapy in either treatment arm.

The primary objective is to determine the noninferiority (NI) in clinical response at Test of Cure (TOC) following treatment with IV tedizolid phosphate compared with IV linezolid in the Intent to Treat (ITT) Analysis Set (NI is declared when the lower bound of the 95% CI > -12.5).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2014
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	Australia: 2
Country: Number of subjects enrolled	Belarus: 11
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Brazil: 53
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	China: 18
Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	Estonia: 7
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Georgia: 123
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Guatemala: 27
Country: Number of subjects enrolled	Israel: 26

Country: Number of subjects enrolled	Japan: 53
Country: Number of subjects enrolled	Kazakhstan: 6
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Latvia: 7
Country: Number of subjects enrolled	Mexico: 43
Country: Number of subjects enrolled	Peru: 4
Country: Number of subjects enrolled	Philippines: 37
Country: Number of subjects enrolled	Russian Federation: 111
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	South Africa: 10
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Thailand: 5
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	Ukraine: 48
Country: Number of subjects enrolled	United States: 34
Country: Number of subjects enrolled	Lebanon: 1
Country: Number of subjects enrolled	Sri Lanka: 1
Worldwide total number of subjects	726
EEA total number of subjects	72

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)	435
From 65 to 84 years	251
85 years and over	40

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Ventilated participants with presumed gram-positive hospital-acquired bacterial pneumonia (HABP) or ventilator-associated bacterial pneumonia (VABP) were enrolled at study sites located in 34 countries.

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	Tedizolid

Arm description:

Ventilated HABP/VABP participants received tedizolid phosphate 200 mg IV once daily for 7 days, or for 14 days for concurrent bacteremia.

Arm type	Experimental
Investigational medicinal product name	Tedizolid phosphate
Investigational medicinal product code	
Other name	SIVEXTRO® TR-701 FA MK-1986
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tedizolid phosphate IV 200 mg once daily

Arm title	Linezolid

Arm description:

Ventilated HABP/VABP participants received linezolid 600 mg IV every 12 hours for 10 days, or for 14 days for concurrent bacteremia.

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

Dosage and administration details:

Linezolid IV 600 mg once daily

Number of subjects in period 1	Tedizolid	Linezolid
Started	366	360
Treated	361	357
Completed	258	254
Not completed	108	106
Adverse event, serious fatal	104	99
Consent withdrawn by subject	1	3
At request of sponsor or investigator	-	1
Did not receive study drug	2	2
Transferred to other care facility	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Tedizolid
Reporting group description:	
Ventilated HABP/VABP participants received tedizolid phosphate 200 mg IV once daily for 7 days, or for 14 days for concurrent bacteremia.	
Reporting group title	Linezolid
Reporting group description:	
Ventilated HABP/VABP participants received linezolid 600 mg IV every 12 hours for 10 days, or for 14 days for concurrent bacteremia.	

Reporting group values	Tedizolid	Linezolid	Total
Number of subjects	366	360	726
Age categorical Units: Subjects			
Adults (18-64 years)	221	214	435
65 years and over	145	146	291
Age Continuous Units: Years			
arithmetic mean	58.1	58.7	
standard deviation	± 18.41	± 17.44	-
Sex: Female, Male Units: Subjects			
Female	117	106	223
Male	249	254	503
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	65	61	126
Not Hispanic or Latino	290	289	579
Unknown or Not Reported	11	10	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	68	70	138
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	11	14
White	269	258	527
More than one race	2	1	3
Unknown or Not Reported	23	19	42

Subject analysis sets	
Subject analysis set title	Tedizolid Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.	
Subject analysis set title	Linezolid Safety Set

Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.

Reporting group values	Tedizolid Safety Set	Linezolid Safety Set	
Number of subjects	357	361	
Age categorical Units: Subjects			
Adults (18-64 years)	216	215	
65 years and over	141	146	
Age Continuous Units: Years			
arithmetic mean	57.9	58.7	
standard deviation	± 18.43	± 17.49	
Sex: Female, Male Units: Subjects			
Female	114	105	
Male	243	256	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	63	63	
Not Hispanic or Latino	283	288	
Unknown or Not Reported	11	10	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	66	70	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	10	
White	263	259	
More than one race	2	1	
Unknown or Not Reported	22	20	

End points

End points reporting groups

Reporting group title	Tedizolid
Reporting group description:	
Ventilated HABP/VABP participants received tedizolid phosphate 200 mg IV once daily for 7 days, or for 14 days for concurrent bacteremia.	
Reporting group title	Linezolid
Reporting group description:	
Ventilated HABP/VABP participants received linezolid 600 mg IV every 12 hours for 10 days, or for 14 days for concurrent bacteremia.	
Subject analysis set title	Tedizolid Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.	
Subject analysis set title	Linezolid Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.	

Primary: Clinical Response at Test of Cure (TOC) Visit in the Intent-to-Treat (ITT) Population

End point title	Clinical Response at Test of Cure (TOC) Visit in the Intent-to-Treat (ITT) Population
End point description:	
The clinical response in the ITT population at the TOC visit (derived from the Investigator's assessment at the EOT and TOC visits) was determined by the investigator to be either: clinical success, clinical failure, or indeterminate. Clinical success was declared when most or all clinical signs were completely resolved, with no new signs of infection, no additional antibiotic therapy was required, and the participant was alive. Indeterminate was declared when the investigator could not determine success or failure. Clinical failure was declared with progression, relapse, or recurrence of new symptoms of infection, or a persistence or insufficient improvement in signs and symptoms of VNP. The ITT set includes all randomized participants.	
End point type	Primary
End point timeframe:	
7-14 days after end of therapy - TOC	

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	360		
Units: Participants				
Clinical Success	206	230		
Clinical Failure	144	110		
Indeterminate	16	20		

Statistical analyses

Statistical analysis title	Difference in success (tedizolid - linezolid)
Statistical analysis description:	
Difference and 95% CI were calculated with the Miettinen and Nurminen method without stratification.	
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	726
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.7
upper limit	-0.5

Secondary: Number of Participants with All-Cause Mortality in the Intent-to-Treat (ITT) Population

End point title	Number of Participants with All-Cause Mortality in the Intent-to-Treat (ITT) Population
End point description:	
The numbers of participants with all-cause mortality within 28 days after randomization was determined in the ITT population. Any participants who were lost to follow-up and not known to be alive or deceased by Day 28 were imputed as deceased. The ITT set is all randomized participants.	
End point type	Secondary
End point timeframe:	
Up to 28 days	

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	360		
Units: Participants	103	95		

Statistical analyses

Statistical analysis title	Difference in mortality (linezolid - tedizolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	726
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in all-cause mortality
Point estimate	-1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	4.7

Secondary: Number of Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point title	Number of Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point description:

The numbers of participants with all-cause mortality within 28 days after randomization was determined in the mITT population. Any participants who were lost to follow-up and not known to be alive or deceased by Day 28 were imputed as deceased. The mITT set is all randomized, treated participants who have gram-positive pathogen(s) confirmed by respiratory tract/pleural fluid culture results obtained within 36 hours (or 72 hours if methicillin-resistant S. aureus [MRSA]) before first study drug dose, and bacterial pathogen against which the investigational drug has antibacterial activity.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	202		
Units: Participants	46	49		

Statistical analyses

Statistical analysis title	Difference in mortality (linezolid - tedizolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in all-cause mortality
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.3
upper limit	7.1

Secondary: Clinical Response at Test of Cure (TOC) Visit in the Clinically-Evaluable (CE) Population

End point title	Clinical Response at Test of Cure (TOC) Visit in the Clinically-Evaluable (CE) Population

End point description:

The clinical response in the CE population at the TOC visit (derived from the Investigator's assessment at the EOT and TOC visits) was determined by the investigator to be either: clinical success, clinical failure, or indeterminate. Clinical success was declared when most or all clinical signs were completely resolved, with no new signs of infection, no additional antibiotic therapy was required, and the participant was alive. Indeterminate was declared when the investigator could not determine success or failure. Clinical failure was declared with progression, relapse, or recurrence of new symptoms of infection, or a persistence or insufficient improvement in signs and symptoms of VNP. The CE set is all randomized and treated participants who had assessment data available and did not have confounding events.

End point type	Secondary

End point timeframe:

7-14 days after end of therapy - TOC

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267	243		
Units: Participants				
Clinical Success	143	146		
Clinical Failure	124	97		
Indeterminate	0	0		

Statistical analyses

Statistical analysis title	Difference in success (tedizolid - linezolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	510
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.1
upper limit	2.1

Secondary: Number of Methicillin-Susceptible Staphylococcus Aureus (MSSA)-Infected Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point title	Number of Methicillin-Susceptible Staphylococcus Aureus (MSSA)-Infected Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point description:

The number of MSSA-infected participants with all-cause mortality within 28 days after randomization

was determined in the mITT population. Participants who had confirmed MSSA culture results from respiratory tract or pleural fluid specimens obtained within 36 hours of study Day 1 were included. Any participants who were lost to follow-up and not known to be alive or deceased by Day 28 were imputed as deceased. The MSSA-infected mITT set is all randomized, treated participants who have MSSA confirmed by respiratory tract/pleural fluid culture results obtained within 36 hours before first study drug dose, and documented bacterial pathogen against which the investigational drug has antibacterial activity.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	128		
Units: Participants	31	32		

Statistical analyses

Statistical analysis title	Difference in mortality (linezolid - tedizolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in all-cause mortality
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	9.5

Secondary: Number of Methicillin-Resistant Staphylococcus Aureus (MRSA)-Infected Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point title	Number of Methicillin-Resistant Staphylococcus Aureus (MRSA)-Infected Participants with All-Cause Mortality in the Microbiological Intent-to-Treat (mITT) Population

End point description:

The number of MRSA-infected participants with all-cause mortality within 28 days after randomization was determined in the mITT population. Participants who had confirmed MRSA culture results from respiratory tract or pleural fluid specimens obtained within 72 hours of study Day 1 were included. Any participants who were lost to follow-up and not known to be alive or deceased by Day 28 were imputed as deceased. The MRSA-infected mITT set is all randomized, treated participants who have MRSA confirmed by respiratory tract/pleural fluid culture results obtained within 72 hours before first study drug dose, and documented bacterial pathogen against which the investigational drug has antibacterial activity.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	69		
Units: Participants	14	20		

Statistical analyses

Statistical analysis title	Difference in mortality (linezolid - tedizolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in all-cause mortality
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	18.9

Secondary: Number of Participants with a Favorable Response at End-of-Therapy (EOT) Visit in the Microbiological Intent-to-Treat (mITT) Population

End point title	Number of Participants with a Favorable Response at End-of-Therapy (EOT) Visit in the Microbiological Intent-to-Treat (mITT) Population

End point description:

The number of patients in the mITT population with a favorable response at EOT was determined. Favorable response included eradication (absence of the baseline pathogen) and presumed eradication (no source specimen to culture in a participant assessed as a clinical cure by the investigator). The mITT set is all randomized, treated participants who have gram-positive pathogen(s) confirmed by respiratory tract/pleural fluid culture results obtained within 36 hours (or 72 hours if MRSA) before first study drug dose, and documented bacterial pathogen against which the investigational drug has antibacterial activity.

End point type	Secondary

End point timeframe:

1-3 days after completing study therapy (Days 8-10 or Days 15-17)

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	202		
Units: Participants	123	166		

Statistical analyses

Statistical analysis title	Difference in response (tedizolid - linezolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.7
upper limit	-4.5

Secondary: Number of Participants with a Favorable Response at End-of-Therapy (EOT) Visit in the Microbiologically-Evaluable 1 (ME-1) Population

End point title	Number of Participants with a Favorable Response at End-of-Therapy (EOT) Visit in the Microbiologically-Evaluable 1 (ME-1) Population

End point description:

The number of patients in the ME-1 population with a favorable response at EOT was determined. Favorable response included eradication (absence of the baseline pathogen) and presumed eradication (no source specimen to culture in a participant assessed as a clinical cure by the investigator). The ME-1 set is all mITT participants who did not receive an antibiotic (other than study drug) with activity against the baseline pathogen up to 28 days after randomization.

End point type	Secondary

End point timeframe:

1-3 days after completing study therapy (Days 8-10 or Days 15-17)

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	202		
Units: Participants	123	166		

Statistical analyses

Statistical analysis title	Difference in response (tedizolid - linezolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.7
upper limit	-4.5

Secondary: Number of Participants with a Favorable Response at Test-of-Cure (TOC) Visit in the Microbiological Intent-to-Treat (mITT) Population

End point title	Number of Participants with a Favorable Response at Test-of-Cure (TOC) Visit in the Microbiological Intent-to-Treat (mITT) Population

End point description:

The number of patients in the mITT population with a favorable response at TOC was determined. Favorable response included eradication (absence of the baseline pathogen) and presumed eradication (no source specimen to culture in a participant assessed as a clinical cure by the investigator). The mITT set is all randomized, treated participants who have gram-positive pathogen(s) confirmed by respiratory tract/pleural fluid culture results obtained within 36 hours (or 72 hours if MRSA) before first study drug dose, and documented bacterial pathogen against which the investigational drug has antibacterial activity.

End point type	Secondary

End point timeframe:

7-14 days after end of therapy - TOC

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	202		
Units: Participants	117	158		

Statistical analyses

Statistical analysis title	Difference in response (tedizolid - linezolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-12.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.5
upper limit	-3.5

Secondary: Number of Participants with a Favorable Response at Test-of-Cure (TOC) Visit in the Microbiologically-Evaluable 2 (ME-2) Population

End point title	Number of Participants with a Favorable Response at Test-of-Cure (TOC) Visit in the Microbiologically-Evaluable 2 (ME-2) Population

End point description:

The number of patients in the ME-2 population with a favorable response at TOC was determined. Favorable response included eradication (absence of the baseline pathogen) and presumed eradication (no source specimen to culture in a participant assessed as a clinical cure by the investigator). The ME-2 set is all mITT participants who did not receive an antibiotic (other than study drug) with activity against the baseline pathogen up to the TOC visit and is also in the clinically-evaluable (CE) set.

End point type	Secondary

End point timeframe:

7-14 days after end of therapy - TOC

End point values	Tedizolid	Linezolid		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	109		
Units: Participants	65	74		

Statistical analyses

Statistical analysis title	Difference in response (tedizolid - linezolid)
Comparison groups	Tedizolid v Linezolid
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in clinical success
Point estimate	-13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.2
upper limit	-1.2

Secondary: Number of Participants with ≥1 Adverse Events (AEs)

End point title	Number of Participants with ≥1 Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Safety analysis is based on actual treatment received instead of randomization. The safety set is all randomized participants who received any amount of study drug. A total of 4 participants were randomized to tedizolid but received linezolid.

End point type	Secondary

End point timeframe:

Up to 32 days

End point values	Tedizolid Safety Set	Linezolid Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	357	361		
Units: Participants	327	325		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Discontinuing Study Therapy Due to an Adverse Event (AE)

End point title	Number of Participants Discontinuing Study Therapy Due to an Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Safety analysis is based on actual treatment received instead of randomization. The safety set is all randomized participants who received any amount of study drug. A total of 4 participants were randomized to tedizolid but received linezolid.

End point type	Secondary

End point timeframe:

Up to 14 days

End point values	Tedizolid Safety Set	Linezolid Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	357	361		
Units: Participants	4	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 32 days

Adverse event reporting additional description:

All participants who received any amount of study drug are included. The safety assessment is based on actual treatment received, and thus the linezolid arm includes 4 participants randomized to tedizolid who received the wrong treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Tedizolid

Reporting group description:

The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.

Reporting group title	Linezolid

Reporting group description:

The Safety analysis set is based on actual treatment received. Four participants randomized to tedizolid received linezolid.

Serious adverse events	Tedizolid	Linezolid	
Total subjects affected by serious adverse events			
subjects affected / exposed	129 / 357 (36.13%)	149 / 361 (41.27%)	
number of deaths (all causes)	101	103	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cerebellopontine angle tumour			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemodynamic instability			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hypotension			
subjects affected / exposed	2 / 357 (0.56%)	3 / 361 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Neurogenic shock			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	2 / 357 (0.56%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple organ dysfunction syndrome			

subjects affected / exposed	8 / 357 (2.24%)	12 / 361 (3.32%)	
occurrences causally related to treatment / all	0 / 8	0 / 12	
deaths causally related to treatment / all	0 / 8	0 / 12	
Sudden cardiac death			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 357 (0.56%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Acute respiratory failure			
subjects affected / exposed	2 / 357 (0.56%)	6 / 361 (1.66%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 3	
Apnoea			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary			

disease			
subjects affected / exposed	2 / 357 (0.56%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Haemothorax			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 357 (0.56%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Laryngospasm			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pharyngeal haematoma			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 357 (0.28%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural thickening			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			

subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	2 / 357 (0.56%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
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	2 / 357 (0.56%)	5 / 361 (1.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pulmonary oedema			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
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	2 / 357 (0.56%)	3 / 361 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	
Respiratory tract haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain herniation			
subjects affected / exposed	4 / 357 (1.12%)	3 / 361 (0.83%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 2	
Endotracheal intubation complication			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Splenic rupture			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tracheostomy malfunction			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Pyloric stenosis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
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	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac arrest			
subjects affected / exposed	21 / 357 (5.88%)	16 / 361 (4.43%)	
occurrences causally related to treatment / all	0 / 24	0 / 16	
deaths causally related to treatment / all	0 / 18	0 / 14	

Cardiac failure			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac failure acute			
subjects affected / exposed	3 / 357 (0.84%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	0 / 357 (0.00%)	3 / 361 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Cardiac failure congestive			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	7 / 357 (1.96%)	6 / 361 (1.66%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 5	0 / 1	
Cardiogenic shock			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	2 / 357 (0.56%)	3 / 361 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Pulseless electrical activity			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular fibrillation			

subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Benign enlargement of the subarachnoid spaces			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain hypoxia			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain injury			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain oedema			
subjects affected / exposed	13 / 357 (3.64%)	7 / 361 (1.94%)	
occurrences causally related to treatment / all	0 / 13	0 / 7	
deaths causally related to treatment / all	0 / 12	0 / 7	
Cerebral infarction			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 357 (0.28%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cerebral vasoconstriction			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholinergic syndrome			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			

subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Loss of consciousness			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis crisis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ruptured cerebral aneurysm			
subjects affected / exposed	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stroke in evolution			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Transient ischaemic attack			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 357 (0.00%)	5 / 361 (1.39%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glossoptosis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic necrosis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			

subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (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			
Penile ulceration			
subjects affected / exposed	0 / 357 (0.00%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 357 (1.40%)	7 / 361 (1.94%)	
occurrences causally related to treatment / all	0 / 5	2 / 7	
deaths causally related to treatment / all	0 / 0	1 / 2	
Chronic kidney disease			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acinetobacter bacteraemia			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 357 (0.56%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacterial infection			
subjects affected / exposed	2 / 357 (0.56%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain abscess			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CNS ventriculitis			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotoxaemia			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endotoxic shock			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterobacter pneumonia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
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 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 357 (0.28%)	4 / 361 (1.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (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	4 / 357 (1.12%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 357 (1.12%)	6 / 361 (1.66%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 3	
Pneumonia acinetobacter			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	2 / 357 (0.56%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Postoperative wound infection			
subjects affected / exposed	3 / 357 (0.84%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	1 / 357 (0.28%)	2 / 361 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sepsis			
subjects affected / exposed	6 / 357 (1.68%)	5 / 361 (1.39%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 4	
Septic shock			
subjects affected / exposed	16 / 357 (4.48%)	18 / 361 (4.99%)	
occurrences causally related to treatment / all	0 / 16	0 / 18	
deaths causally related to treatment / all	0 / 10	0 / 12	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 357 (0.28%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic shock syndrome			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 357 (0.56%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Electrolyte imbalance			

subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 357 (0.00%)	1 / 361 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Propofol infusion syndrome			
subjects affected / exposed	1 / 357 (0.28%)	0 / 361 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Tedizolid	Linezolid	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	176 / 357 (49.30%)	175 / 361 (48.48%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 357 (5.32%)	14 / 361 (3.88%)	
occurrences (all)	20	14	
Hypotension			
subjects affected / exposed	27 / 357 (7.56%)	25 / 361 (6.93%)	
occurrences (all)	28	26	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	56 / 357 (15.69%)	51 / 361 (14.13%)	
occurrences (all)	66	52	
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	31 / 357 (8.68%)	28 / 361 (7.76%)	
occurrences (all)	33	31	
Diarrhoea			
subjects affected / exposed	34 / 357 (9.52%)	49 / 361 (13.57%)	
occurrences (all)	36	52	
Vomiting			
subjects affected / exposed	19 / 357 (5.32%)	15 / 361 (4.16%)	
occurrences (all)	19	16	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	22 / 357 (6.16%)	26 / 361 (7.20%)	
occurrences (all)	26	31	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	26 / 357 (7.28%)	20 / 361 (5.54%)	
occurrences (all)	26	20	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	38 / 357 (10.64%)	34 / 361 (9.42%)	
occurrences (all)	49	38	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2013	AM01: The primary purpose of the amendment was to clarify inclusion criteria and that participants with bacteremia would receive 14 days of treatment.
15 January 2014	AM02: The primary purpose of the amendment was to add the EudraCT number and clarify method of analysis of secondary objectives.
11 November 2014	AM03: The primary purpose of the amendment was to update contact information and to clarify the statistics reporting group would be part of the data monitoring committee charter.
24 January 2017	AM04: The primary purpose of the amendment was to move the CE population analysis to secondary status.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/16600048

http://www.ncbi.nlm.nih.gov/pubmed/15699079

http://www.ncbi.nlm.nih.gov/pubmed/14625336

http://www.ncbi.nlm.nih.gov/pubmed/3390511

http://www.ncbi.nlm.nih.gov/pubmed/16652315

http://www.ncbi.nlm.nih.gov/pubmed/19759040

http://www.ncbi.nlm.nih.gov/pubmed/18989656

http://www.ncbi.nlm.nih.gov/pubmed/21911576

http://www.ncbi.nlm.nih.gov/pubmed/21555763

http://www.ncbi.nlm.nih.gov/pubmed/21217178

http://www.ncbi.nlm.nih.gov/pubmed/21163725

http://www.ncbi.nlm.nih.gov/pubmed/22354302

http://www.ncbi.nlm.nih.gov/pubmed/22247123