



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