Clinical trial results:
A Phase 3 Randomized, Double-Blind, Multicenter Study Comparing the Efficacy and Safety of Intravenous to Oral 6-Day TR-701 Free Acid and Intravenous to Oral 10-Day Linezolid for the Treatment of Acute Bacterial Skin and Skin Structure Infections

Summary

EudraCT number	2011-002860-26
Trial protocol	DE ES
Global end of trial date	10 January 2013

Results information

Result version number	v3 (current)
This version publication date	09 February 2019
First version publication date	02 August 2015
Version creation reason	• Correction of full data set Correcting the Article 46 field to NO, per Regulatory Affairs confirmation

Trial information

Trial identification

Sponsor protocol code	1986-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01421511
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Trius Therapeutics, Inc.
Sponsor organisation address	6310 Nancy Ridge Drive, Suite 101, San Diego, United States, 92121
Public contact	Medical Director, Trius Therapeutics, Inc., +1 858 452 0370 249,
Scientific contact	Medical Director, Trius Therapeutics, Inc., +1 858 452 0370 241,

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	28 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2013
Global end of trial reached?	Yes
Global end of trial date	10 January 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine the non-inferiority (NI) in the rate of the Investigator's assessment of clinical success of intravenous (IV) to oral 6-day TR-701 free acid (FA) treatment compared with that of IV to oral 10-day linezolid treatment at the Post-therapy Evaluation (PTE) Visit (7 to 14 days after the End of Therapy [EOT] Visit) in the Intent-to-Treat (ITT) and Clinically Evaluable at PTE (CE-PTE) Analysis Sets.

Protection of trial subjects:

The Data and Safety Monitoring Board (DSMB) reviewed safety data at 2 time points (when approximately 33% and 67% of the patients were randomized and completed the Late Follow-up Visit). At both meetings, the DSMB concluded that the study could continue without modification. Subjects were free to withdraw from the study at any time and could be discontinued from the study at the request of the Investigator or sponsor. This study was conducted in accordance with current United States (US) Food and Drug Administration (FDA) clinical trial regulations and guidelines, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, the European Union Directive 2001/20/EC for clinical trials conducted in the European Union, and the institutional review board (IRB)/independent ethics committee (IEC)/ Research Ethics Board (REB), and local legal requirements.

Background therapy:

For subjects with wound infections only, aztreonam and/or metronidazole could be added, if needed.

Evidence for comparator:

Zyvox® (linezolid) is the only oral agent approved for methicillin-resistant Staphylococcus aureus (MRSA) activity. Linezolid has approximately 100% bioavailability, good efficacy, and an acceptable safety profile.

Actual start date of recruitment	19 September 2011
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	Poland: 10
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United States: 314
Country: Number of subjects enrolled	Argentina: 26
Country: Number of subjects enrolled	Russian Federation: 208
Country: Number of subjects enrolled	South Africa: 94
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	New Zealand: 4

Worldwide total number of subjects	666
EEA total number of subjects	15

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)	2
Adults (18-64 years)	588
From 65 to 84 years	70
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible subjects signed an informed consent form and were to meet all of the inclusion and none of the exclusion criteria prior to be randomized in this study. Randomization was done via an interactive web system in a 1:1 ratio.

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, Subject

Blinding implementation details:

The sponsor, Investigator, study staff participating in direct patient care or clinical evaluations, and subjects were blinded to treatment assignment until all subjects had completed the study and the database was locked. A double-dummy approach was chosen with placebo unique to each active treatment (placebo for TR-701 FA and placebo for linezolid for both IV and oral formulations) to maintain the treatment blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	TR-701 FA 200 mg

Arm description:

Subjects were to be randomized to receive TR-701 FA 200 milligrams (mg) once daily for 6 days, followed by 4 days of placebo treatment. Subjects received 3 infusions or 3 tablets of study treatment (1 active dose and 2 double dummy placebo doses) daily.

Arm type	Experimental
Investigational medicinal product name	TR-701 FA
Investigational medicinal product code	
Other name	Tedizolid Phosphate, tedizolid
Pharmaceutical forms	Powder for infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Subjects were dosed for 10 days. Subjects could have received IV therapy for the entire treatment duration. After Dose 1 and Dose 2 (after study day 1), subjects could be switched from IV to oral study drug at the investigator's discretion provided clinical criteria were met. All infusions were to be 60±10 minutes. Oral administration was twice daily.

Arm title	Linezolid 600 mg

Arm description:

Subjects were to be randomized to receive IV to oral linezolid 600 mg every 12 hours for 10 days. Subjects received 3 infusions or 3 tablets of study treatment (2 active doses and 1 double dummy placebo dose) daily.

Arm type	Active comparator
Investigational medicinal product name	Linezolid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Subjects were dosed for 10 days. Subjects could have received IV therapy for the entire treatment duration. After Dose 1 and Dose 2 (after study day 1), subjects could be switched from IV to oral study

drug at the investigator's discretion provided clinical criteria were met. All infusions were to be 60±10 minutes. Oral administration was twice daily.

Number of subjects in period 1	TR-701 FA 200 mg	Linezolid 600 mg
Started	332	334
Received at least 1 dose of study drug	331	327
Completed	313	306
Not completed	19	28
Consent withdrawn by subject	6	5
Physician decision	-	1
Not specified	1	1
Randomized but not drug received	1	7
Lost to follow-up	11	14

Baseline characteristics

Reporting groups	
Reporting group title	TR-701 FA 200 mg
Reporting group description:	
Subjects were to be randomized to receive TR-701 FA 200 milligrams (mg) once daily for 6 days, followed by 4 days of placebo treatment. Subjects received 3 infusions or 3 tablets of study treatment (1 active dose and 2 double dummy placebo doses) daily.	
Reporting group title	Linezolid 600 mg
Reporting group description:	
Subjects were to be randomized to receive IV to oral linezolid 600 mg every 12 hours for 10 days. Subjects received 3 infusions or 3 tablets of study treatment (2 active doses and 1 double dummy placebo dose) daily.	

Reporting group values	TR-701 FA 200 mg	Linezolid 600 mg	Total
Number of subjects	332	334	666
Age categorical			
Subjects enrolled per age group			
Units: Subjects			
Adolescents (12-17 years)	1	1	2
Adults (18-64 years)	288	300	588
From 65-84 years	40	30	70
85 years and over	3	3	6
Age continuous			
Age of randomized subjects.			
Units: years			
arithmetic mean	45.6	45.6	
standard deviation	± 15.79	± 15.57	-
Gender categorical			
The gender of all randomized subjects.			
Units: Subjects			
Female	107	120	227
Male	225	214	439
Ethnicity			
The ethnicity (Hispanic or Latino or Not Hispanic or Latino) reported for randomized subjects.			
Units: Subjects			
Hispanic or Latino	67	63	130
Not Hispanic or Latino	265	271	536

End points

End points reporting groups

Reporting group title	TR-701 FA 200 mg

Reporting group description:

Subjects were to be randomized to receive TR-701 FA 200 milligrams (mg) once daily for 6 days, followed by 4 days of placebo treatment. Subjects received 3 infusions or 3 tablets of study treatment (1 active dose and 2 double dummy placebo doses) daily.

Reporting group title	Linezolid 600 mg

Reporting group description:

Subjects were to be randomized to receive IV to oral linezolid 600 mg every 12 hours for 10 days. Subjects received 3 infusions or 3 tablets of study treatment (2 active doses and 1 double dummy placebo dose) daily.

Primary: Investigator’s Assessment of Clinical Success at the Post Treatment Evaluation Visit - ITT

End point title	Investigator’s Assessment of Clinical Success at the Post Treatment Evaluation Visit - ITT

End point description:

Clinical success defined as resolution/near resolution of disease specific signs and symptoms, absence/near resolution of baseline systemic signs of infection, and no further antibiotic therapy required for treatment of primary acute bacterial skin and skin structure infection (ABSSSI) lesion. A count of responders: subjects classified by the investigator as clinical successes. The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Primary

End point timeframe:

Post-Treatment Evaluation (7-14 days after the End of Therapy)

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: participants	292	293		

Statistical analyses

Statistical analysis title	Analysis for Clinical Success at PTE - ITT

Statistical analysis description:

Non-inferiority test of the Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg

Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Risk difference (RD)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	5.1

Notes:

[1] - A two-sided 95% CI was calculated for the observed differences in the clinical success rates at the PTE Visit (after the infusion of study drug) using the method of Miettinen and Nurminen with adjustment for clinical syndrome and geographical region. Non-inferiority was concluded if the lower limit of the 95% CI was greater than -10%.

Primary: Investigator's Assessment of Clinical Success at the Post Treatment Evaluation Visit – CE-PTE

End point title	Investigator's Assessment of Clinical Success at the Post Treatment Evaluation Visit – CE-PTE

End point description:

Clinical success defined as resolution/near resolution of disease specific signs and symptoms, absence/near resolution of baseline systemic signs of infection, and no further antibiotic therapy required for treatment of primary ABSSSI lesion. A count of responders: subjects classified by the investigator as clinical successes. The analysis population is the clinically evaluable at PTE (CE-PTE) analysis set including data from all randomized subjects receiving minimal study therapy, completed EOT and PTE Investigator's assessments, no concomitant systemic antibiotic therapy through PTE, and no confounding events or factors.

End point type	Primary

End point timeframe:

Post-Treatment Evaluation (7-14 days after the End of Therapy)

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	280		
Units: participants	268	269		

Statistical analyses

Statistical analysis title	Analysis for Clinical Success at PTE - CE-PTE

Statistical analysis description:

Non-inferiority test of the Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg

Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Risk difference (RD)
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	0

Notes:

[2] - A two-sided 95% CI was calculated for the observed differences in the clinical success rates at the PTE Visit (after the infusion of study drug) using the method of Miettinen and Nurminen with adjustment for clinical syndrome and geographical region. Non-inferiority was concluded if the lower limit of the 95% CI was greater than -10%.

Secondary: The Early Clinical Response Rate - ITT

End point title	The Early Clinical Response Rate - ITT

End point description:

A count of responders: subjects with no increase in lesion surface area from baseline. The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Secondary

End point timeframe:

48-72 hours after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: participants	283	276		

Statistical analyses

Statistical analysis title	Analysis for The Early Clinical Response - ITT

Statistical analysis description:

Non-inferiority test of the Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Risk difference (RD)
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	8.2

Notes:

[3] - A two-sided 95% Confidence Interval (CI) was calculated for the observed differences in the early clinical response rates at 48 to 72 Hours after the first infusion of study drug using the method of Miettinen and Nurminen without stratification. Non-inferiority was concluded if the lower limit of the 95% CI was greater than -10%.

Secondary: Clinical Response at the End of Therapy Visit - ITT

End point title	Clinical Response at the End of Therapy Visit - ITT

End point description:

A count of responders: subjects with no increase in lesion surface area from baseline. The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Secondary

End point timeframe:

Day 11 after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: participants	289	294		

Statistical analyses

Statistical analysis title	Analysis for Clinical Response at the EOT - ITT

Statistical analysis description:

Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Risk difference (RD)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	4.1

Notes:

[4] - A two-sided 95% CI was calculated for the observed differences in the clinical response rates at 11 Days after the first infusion of study drug using the method of Miettinen and Nurminen without stratification.

Secondary: Investigator’s Assessment of Clinical Response at the 48-72 Hour Visit- ITT

End point title	Investigator’s Assessment of Clinical Response at the 48-72 Hour Visit- ITT

End point description:

A count of responders: subjects with clinical improvement defined as improvement in overall clinical status. The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Secondary

End point timeframe:

48-72 hours after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: participants	304	302		

Statistical analyses

Statistical analysis title	Analysis for Clinical Response at 48-72 hours -ITT

Statistical analysis description:

Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Risk difference (RD)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	5.5

Notes:

[5] - A two-sided 95% CI was calculated for the observed differences in the clinical response rates at 48-72 hours after first infusion of study drug using the method of Miettinen and Nurminen without stratification.

Secondary: Investigator’s Assessment of Clinical Response at the Day 7 Visit- ITT

End point title	Investigator’s Assessment of Clinical Response at the Day 7 Visit- ITT

End point description:

A count of responders: subjects with clinical improvement defined as improvement in overall clinical status. The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Secondary

End point timeframe:

Day 7 after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: participants	309	308		

Statistical analyses

Statistical analysis title	Analysis for Clinical Response at Day 7 -ITT

Statistical analysis description:

Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg
Number of subjects included in analysis	666
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Risk difference (RD)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	4.9

Notes:

[6] - A two-sided 95% CI was calculated for the observed differences in the clinical response rates at 7 Days after the first infusion of study drug using the method of Miettinen and Nurminen without stratification.

Secondary: Investigator’s Assessment of Clinical Response at the EOT Visit-CE-EOT

End point title	Investigator’s Assessment of Clinical Response at the EOT Visit-CE-EOT

End point description:

A count of responders: subjects classified by the investigator as clinical successes. The analysis population is the clinically evaluable at PTE (CE-EOT) analysis set including data from all randomized subjects receiving minimal study therapy, completed EOT Investigator's assessment, no concomitant systemic antibiotic therapy through EOT, and no confounding events or factors.

End point type	Secondary

End point timeframe:

Day 11 after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	293		
Units: participants	281	284		

Statistical analyses

Statistical analysis title	Analysis for Clinical Response at EOT –CE-EOT

Statistical analysis description:

Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Risk difference (RD)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	1.2

Notes:

[7] - A two-sided 95% CI was calculated for the observed differences in the clinical response rates at 11 Days after the first infusion of study drug using the method of Miettinen and Nurminen without stratification.

Secondary: Clinical Response at the End of Therapy Visit - CE-EOTUS

End point title	Clinical Response at the End of Therapy Visit - CE-EOTUS

End point description:

A count of responders: subjects with no increase in lesion surface area from baseline. The analysis population is the clinically evaluable at EOT using programmatic assessment of response, a United States FDA objective (CE-EOTUS) analysis set including data from all randomized subjects receiving minimal study therapy, completed EOT Investigator's assessment, no concomitant systemic antibiotic therapy through EOT, and no confounding events or factors.

End point type	Secondary

End point timeframe:

Day 11 after first dose of study drug

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	299		
Units: participants	272	280		

Statistical analyses

Statistical analysis title	Analysis for Clinical Response at EOT - CE-EOTUS

Statistical analysis description:

Risk difference which corresponds to the tedizolid (TR-701 FA) responder rate minus the linezolid responder rate.

Comparison groups	TR-701 FA 200 mg v Linezolid 600 mg

Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Risk difference (RD)
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	0.3

Notes:

[8] - A two-sided 95% CI was calculated for the observed differences in the clinical response rates at 11 Days after the first infusion of study drug using the method of Miettinen and Nurminen without stratification.

Secondary: Change From Baseline in Patient-reported Pain via the Total Faces Rating Scale, by Study Visit - ITT

End point title	Change From Baseline in Patient-reported Pain via the Total Faces Rating Scale, by Study Visit - ITT

End point description:

The mean change in total faces rating scale (FRS) is presented by Study Visit. The assessment was made at 6 time points. One visit per subject on Day 2 and Day 3, only 1 visit total for Days 4-6, only 1 visit total for Days 7-9, only 1 visit total for Days 10-13, and 1 visit after Day 14. Data displayed for Day 2, Day 4-6, Day 7-9, and Day 10-13. Baseline is the last assessment made before first dose of study drug. The FRS is a 10 point scale where 0 is no pain, 4 is hurts little more, and 10 is the worst pain "you can imagine". The analysis population is the ITT analysis set including data from all randomized subjects.

End point type	Secondary

End point timeframe:

Multiple: Day 2, Day 4-6, Day 7-9, Day 10-13

End point values	TR-701 FA 200 mg	Linezolid 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	332	334		
Units: units on a scale				
geometric mean (standard deviation)				
Day 2 (n=325, 319)	-1.7 (± 2.05)	-2.1 (± 2.29)		
Day 4-6 (n=162, 165)	-3.1 (± 2.67)	-3.3 (± 2.56)		
Day 7-9 (n=304, 302)	-4.9 (± 2.89)	-4.9 (± 2.96)		
Day 10-13 (n=296, 292)	-5.4 (± 2.8)	-5.6 (± 2.84)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Collected from signing of the ICF through the late follow-up visit (up to 38 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	TR-701 FA 200 mg
Reporting group description:	
Subjects were to be randomized to receive TR-701 FA 200 mg once daily for 6 days, followed by 4 days of placebo treatment. Subjects received 3 infusions or 3 tablets of study treatment (1 active dose and 2 double dummy placebo doses) daily.	
Reporting group title	Linezolid 600 mg
Reporting group description:	
Subjects were to be randomized to receive IV to oral linezolid 600 mg every 12 hours for 10 days. Subjects received 3 infusions or 3 tablets of study treatment (2 active doses and 1 double dummy placebo dose) daily.	

Serious adverse events	TR-701 FA 200 mg	Linezolid 600 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 331 (2.11%)	9 / 327 (2.75%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
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	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 331 (0.00%)	2 / 327 (0.61%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis tuberculous			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 331 (0.00%)	1 / 327 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 331 (0.30%)	0 / 327 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TR-701 FA 200 mg	Linezolid 600 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 331 (17.52%)	67 / 327 (20.49%)	
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 331 (6.04%)	22 / 327 (6.73%)	
occurrences (all)	20	28	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	11 / 331 (3.32%)	17 / 327 (5.20%)	
occurrences (all)	11	17	
Nausea			
subjects affected / exposed	26 / 331 (7.85%)	36 / 327 (11.01%)	
occurrences (all)	27	39	
Vomiting			
subjects affected / exposed	10 / 331 (3.02%)	17 / 327 (5.20%)	
occurrences (all)	11	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 October 2012	Protocol Amendment 6 changed the definition of responder in the primary efficacy endpoint to a ≥20% reduction in lesion area and no fever component. Protocol Amendment 6 was reviewed by the US FDA and agreement that the Special Protocol Assessment was still intact.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Analyses for this study were conducted using 2 statistical plans, 1 for the US FDA and 1 for the EMA, to address differing guidance on the development of antibacterials. These differences are reflected in the EudraCT and clinicaltrials.gov records.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25421472