Clinical trial results:
A Randomized, Double-Blinded, Active-Controlled Study of CB-183,315 in Patients With Clostridium Difficile Associated Diarrhea

Summary

EudraCT number	2012-000252-34
Trial protocol	SE BE DE CZ PL ES AT GB IT HU
Global end of trial date	20 March 2015

Results information

Result version number	v1
This version publication date	16 March 2016
First version publication date	16 March 2016

Trial information

Trial identification

Sponsor protocol code	4261-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01597505
WHO universal trial number (UTN)	-
Other trial identifiers	Cubist Pharmaceuticals Holdings LLC: LCD-CDAD-10-07

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, 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	20 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

606 participants with Clostridium Difficile Associated Diarrhea (CDAD) participated in this study and received either oral vancomycin or CB-183,315 (surotomycin) in a blinded fashion. Treatment lasted for 10 days and participants were followed up for at least 40 days and a maximum of 100 days. The purpose of this study was to evaluate how well surotomycin treats CDAD as compared to vancomycin.

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	16 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Canada: 122
Country: Number of subjects enrolled	Czech Republic: 28
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 267
Worldwide total number of subjects	606
EEA total number of subjects	205

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)	307
From 65 to 84 years	253
85 years and over	46

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Males and females aged 18 years or older with diarrhea at risk for CDAD were enrolled in this study

Period 1

Period 1 title	Intent to Treat (ITT) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Surotomycin

Arm description:

250 mg Surotomycin over-encapsulated tablet administered orally, twice daily for a daily total dose of 500 mg; and Placebo over-encapsulated tablet administered orally, twice daily for 10 days

Arm type	Experimental
Investigational medicinal product name	Surotomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

250 mg Surotomycin over-encapsulated tablet administered orally, twice daily for a daily total dose of 500 mg, for 10 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for Surotomycin over-encapsulated tablet administered orally, twice daily for 10 days

Arm title	Vancomycin

Arm description:

125 mg Vancomycin over-encapsulated tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days

Arm type	Active comparator
Investigational medicinal product name	Vancomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

125 mg Vancomycin over-encapsulated capsule administered orally, four times daily for a daily total dose of 500 mg, for 10 days

Number of subjects in period 1	Surotomycin	Vancomycin
Started	308	298
Treated	305	286
Completed	261	253
Not completed	47	45
Physician decision	5	-
Consent withdrawn by subject	10	18
Not Treated	3	12
Unspecified	5	6
Lost to follow-up	4	2
Missing	1	-
Adverse event, non-fatal + serious fatal	19	7

Baseline characteristics

Reporting groups	
Reporting group title	Surotomycin
Reporting group description:	
250 mg Surotomycin over-encapsulated tablet administered orally, twice daily for a daily total dose of 500 mg; and Placebo over-encapsulated tablet administered orally, twice daily for 10 days	
Reporting group title	Vancomycin
Reporting group description:	
125 mg Vancomycin over-encapsulated tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days	

Reporting group values	Surotomycin	Vancomycin	Total
Number of subjects	308	298	606
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	158	149	307
From 65-84 years	131	122	253
85 years and over	19	27	46
Age Continuous Units: years			
arithmetic mean	61.5	61.8	
standard deviation	± 17.5	± 18.4	-
Gender Categorical Units: Subjects			
Female	185	175	360
Male	123	123	246

End points

End points reporting groups

Reporting group title	Surotomycin
Reporting group description:	
250 mg Surotomycin over-encapsulated tablet administered orally, twice daily for a daily total dose of 500 mg; and Placebo over-encapsulated tablet administered orally, twice daily for 10 days	
Reporting group title	Vancomycin
Reporting group description:	
125 mg Vancomycin over-encapsulated tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days	
Subject analysis set title	Surotomycin
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
250 mg Surotomycin tablet administered orally, twice daily for a daily total dose of 500 mg, for 10 days	
Subject analysis set title	Vancomycin
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
125 mg Vancomycin tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days	
Subject analysis set title	Surotomycin
Subject analysis set type	Safety analysis
Subject analysis set description:	
250 mg Surotomycin tablet administered orally, twice daily for a daily total dose of 500 mg, for 10 days	
Subject analysis set title	Vancomycin
Subject analysis set type	Safety analysis
Subject analysis set description:	
125 mg Vancomycin tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days	

Primary: Adjusted percentage of participants with a clinical outcome of cure at the end of treatment (EOT)

End point title	Adjusted percentage of participants with a clinical outcome of cure at the end of treatment (EOT)
End point description:	
A clinical outcome of cure at EOT was determined by resolution of diarrhea, defined as ≤ 2 loose stools per 24-hour period for at least 2 consecutive days and the lack of need for additional antibiotics to treat the current CDAD episode after completion of the study treatment period. Participants requiring a collection device were considered to have resolution of diarrhea when the volume of stool (over a 24-hour period) was decreased by 75% as compared to baseline or the participant was no longer passing liquid stool. The estimated adjusted percentage was a weighted average across all strata, constructed using Mehrotra-Railkar continuity-corrected minimum risk (MRc) stratum weights. The population analyzed is the Microbiological Modified Intent-To-Treat (mMITT) population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized.	
End point type	Primary
End point timeframe:	
Up to 13 days	

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: Percentage of participants				
number (confidence interval 95%)	79 (73.9 to 83.2)	83.6 (78.8 to 87.4)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

The 95% confidence interval (CI) were stratified Wilson intervals for the treatment group percentages and a stratified Newcombe interval for the treatment difference, constructed using the MRc stratum weights.

Comparison groups	Vancomycin v Surotomycin
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage of participants
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1.9

Notes:

[1] - Difference: Surotomycin minus Vancomycin. For surotomycin to be non-inferior to vancomycin the lower bound of a 2-sided 95% CI for the difference between treatment groups had to be ≥ -10%.

Primary: Percentage of participants with at least one adverse event (AE)

End point title	Percentage of participants with at least one adverse event

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. AEs may be new events or may be pre-existing conditions that have become aggravated or have worsened in severity or frequency; or may be clinically significant changes from baseline in physical examination, laboratory tests, or other diagnostic investigation (e.g. laboratory results, x-ray findings). The analyzed population consisted of all randomized participants who received any amount of study drug.

End point type	Primary

End point timeframe:

Up to Day 50

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses for this end point were neither planned nor performed.

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	305	286		
Units: Percentage of participants				
number (not applicable)	48.5	55.2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with at least one serious adverse event (SAE)

End point title	Percentage of participants with at least one serious adverse event (SAE)[3]

End point description:

A serious adverse event is any adverse experience occurring at any dose that results in any of the following outcomes: either death; a life-threatening experience, referring to a situation in which the participant was at risk of death at the time of the event; it does not refer to an event which might have caused death if it were more severe; requires in-patient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability or incapacity; is a congenital anomaly or birth defect; or is considered to be an important medical event. The analyzed population consisted of all randomized participants who received any amount of study drug.

End point type	Primary

End point timeframe:

Up to Day 50

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses for this end point were neither planned nor performed.

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	305	286		
Units: Percentage of participants				
number (not applicable)	14.4	12.9		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants who discontinued treatment due to an AE

End point title	Percentage of participants who discontinued treatment due to an AE[4]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. AEs may be new events or may be pre-existing conditions that have become aggravated or have worsened in severity or frequency; or may be clinically significant changes from baseline in physical examination, laboratory tests, or other diagnostic investigation (e.g. laboratory results, x-ray

findings). The analyzed population consisted of all randomized participants who received any amount of study drug.

End point type	Primary

End point timeframe:

Up to Day 13

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses for this end point were neither planned nor performed.

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	305	286		
Units: Percentage of participants				
number (not applicable)	5.6	2.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical response over time measured by those without treatment failure, recurrence, death, or lost to follow-up

End point title	Number of participants with clinical response over time measured by those without treatment failure, recurrence, death, or lost to follow-up

End point description:

Clinical response over time, is measured as the number of participants without failure events (survivors) through the end of therapy (reported for Day 14) and from end of therapy to Day 40 (reported for Day 41). The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized

End point type	Secondary

End point timeframe:

Up to Day 41

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: Participants				
number (not applicable)				
Day 14	227	231		
Day 41	147	151		

Statistical analyses

Statistical analysis title	Surotomycin v Vancomycin

Statistical analysis description:

Log-rank test of equality of survival times, stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1)

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.832 [5]
Method	Log rank test

Notes:

[5] - Significance cut-off = 0.05

Secondary: Adjusted percentage of participants with sustained clinical response at the end of study (Days 40 - 50)

End point title	Adjusted percentage of participants with sustained clinical response at the end of study (Days 40 - 50)

End point description:

Sustained clinical response at the end of study was achieved by participants who had a clinical outcome of cure at the end of treatment (Days 40-50) and did not experience a recurrence of CDAD, did not die, were not lost to follow-up, and did not have end of study visit prior to Day 40. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

30 days after last dose of study drug: up to Day 50

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: Percentage of participants				
number (confidence interval 95%)	60.6 (55 to 66)	61.4 (55.9 to 66.8)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

The 95% CI was stratified Wilson intervals for the treatment group percentages and a stratified Newcombe interval for the treatment difference, constructed using the MRc stratum weights. Stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1).

Comparison groups	Surotomycin v Vancomycin

Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Difference in percentage of participants
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	7.1

Notes:

[6] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Adjusted percentage of participants with sustained clinical response at Day 24

End point title	Adjusted percentage of participants with sustained clinical response at Day 24

End point description:

Sustained clinical response at Day 24 was defined as participants who had a clinical outcome of cure at Day 24, who did not experience a recurrence of CDAD, did not die, were not lost to follow-up. Only the first failure event was counted per participant. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed was the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Day 24

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: Percentage of participants				
number (confidence interval 95%)	66.6 (61.1 to 71.8)	66.1 (60.5 to 71.3)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

The 95% CI was stratified Wilson intervals for the treatment group percentages and a stratified Newcombe interval for the treatment difference, constructed using the MRc stratum weights. Stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1).

Comparison groups	Surotomycin v Vancomycin

Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Difference in percentage of participants
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	8.3

Notes:

[7] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Adjusted percentage of participants with recurrence of CDAD at end of study (Days 40 to 50)

End point title	Adjusted percentage of participants with recurrence of CDAD at end of study (Days 40 to 50)

End point description:

Participants with recurrences were defined as those who were cured at the end of therapy and had a recurrence or were lost to follow-up, died or had a Day 40 -50 contact prior to Day 40. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

30 days after last dose of study drug: up to Day 50

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: Percentage of participants				
number (confidence interval 95%)	17.7 (13.8 to 22.4)	21.2 (16.9 to 26.1)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

The 95% CI was stratified Wilson intervals for the treatment group percentages and a stratified Newcombe interval for the treatment difference, constructed using the MRc stratum weights. Stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1).

Comparison groups	Surotomycin v Vancomycin

Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Difference in percentage of participants
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	3

Notes:

[8] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Time to Resolution of Diarrhea

End point title	Time to Resolution of Diarrhea

End point description:

Time to resolution of diarrhea with =< 2 unformed bowel movements (UBM) per 24-hour period was calculated as the date/time of last UBM minus the date/time of the first dose of study drug. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Up to Day 13

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	290	280		
Units: days				
median (confidence interval 95%)	2.8 (2.2 to 3.3)	3 (2.2 to 3.3)		

Statistical analyses

Statistical analysis title	Surotomycin v Vancomycin

Statistical analysis description:

Log-rank test of equality of survival times, stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1)

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.431 [9]
Method	Log-rank test

Notes:

[9] - Significance cut-off = 0.05

Secondary: Time to reappearance of diarrhea from end of treatment to the end of study (days 40 to 50)

End point title	Time to reappearance of diarrhea from end of treatment to the end of study (days 40 to 50)

End point description:

Time to reappearance of diarrhea with >= 3 UBM per 24-hour period was calculated as the last date/time of study drug dose to the date/time of first reappearance of 3 or more UBMs among participants who were cured. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized; and includes cures at end of study only. The Number At Risk is the number of participants who entered the interval without having a reappearance of diarrhea. Results were shown as "0" because median time to reappearance and the 95% Confidence Interval (CI) could not be determined.

End point type	Secondary

End point timeframe:

Up to day 50

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	229	234		
Units: Days				
median (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Surotomycin v Vancomycin

Statistical analysis description:

Log-rank test of equality of survival times, stratified by age group (< 75, >= 75 years) and number of CDAD episodes (0, >= 1)

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011 [10]
Method	Log-rank test

Notes:

[10] - Significance cut-off = 0.05

Secondary: Adjusted percentage of participants with a clinical response at the end of treatment for infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline

End point title	Adjusted percentage of participants with a clinical response at the end of treatment for infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline

End point description:

Clinical response corresponded to a clinical outcome of cure at the end of treatment, and was achieved by participants who did not fail treatment, did not die, or were not lost to follow-up at the end of treatment. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received

any amount of study drug, based on the treatment to which they were randomized. The Number At Risk is the number of participants with infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline.

End point type	Secondary

End point timeframe:

Up to Day 13

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	59	67		
Units: Percentage of participants				
number (confidence interval 95%)	88.5 (75.8 to 92.4)	86.3 (76.2 to 92.6)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

Analyses were performed separately for each indicated strain or subgroup. Treatment group percentages were stratified by age group (< 75, ≥ 75) and number of previous CDAD episodes (0, ≥ 1). The 95% CIs were stratified Wilson intervals for the treatment group percentages.

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority[11]
Parameter estimate	Difference in percentage of participants
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.7
upper limit	14.8

Notes:

[11] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Adjusted percentage of participants Per Protocol 1 population with a clinical response at the end of treatment

End point title	Adjusted percentage of participants Per Protocol 1 population with a clinical response at the end of treatment

End point description:

Clinical response corresponded to a clinical outcome of cure at the end of treatment, and was achieved by participants who did not fail treatment, did not die, or were not lost to follow-up at the end of treatment. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the Per Protocol 1 (PP1) population composed of participants from the mMITT population, according to the actual treatment they received; without any protocol deviations from enrollment through 2 days after end of treatment, which could affect the efficacy conclusions.

End point type	Secondary

End point timeframe:

Up to Day 13

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252	243		
Units: Percentage of participants				
number (confidence interval 95%)	89.1 (84.5 to 92.2)	91.5 (87.2 to 94.3)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

Treatment group proportions were stratified by age group (< 75, ≥ 75) and number of previous CDAD episodes (0, ≥1). The 95% CIs were stratified Wilson intervals for the treatment group proportions.

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	superiority[12]
Parameter estimate	Difference in percentage of participants
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	3

Notes:

[12] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Adjusted percentage of participants with a sustained clinical response at the end of study (Days 40 - 50) for infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline

End point title	Adjusted percentage of participants with a sustained clinical response at the end of study (Days 40 - 50) for infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline

End point description:

Sustained clinical response at the end of study was achieved by participants who had a clinical outcome of cure at the end of treatment (Days 40-50) and did not experience a recurrence of CDAD, did not die, were not lost to follow-up, and did not have end of study visit prior to Day 40. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the mMITT population consisting of all randomized participants who had a confirmed diagnosis of CDAD regardless of whether they received any amount of study drug, based on the treatment to which they were randomized. The Number At Risk is the number of participants with infections deemed to be caused by the C. difficile BI/NAP1/027 strain at baseline.

End point type	Secondary

End point timeframe:

Up to Day 50

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	59	67		
Units: Percentage of participants				
number (confidence interval 95%)	66.1 (53.6 to 76.7)	51.5 (40.5 to 63.1)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

Analyses were performed separately for each indicated strain or subgroup. Treatment group percentages were stratified by age group (< 75, ≥ 75) and number of previous CDAD episodes (0, ≥ 1). The 95% CIs were stratified Wilson intervals for the treatment group percentages.

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority[13]
Parameter estimate	Difference in percentage of participants
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	30.7

Notes:

[13] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Secondary: Adjusted percentage of participants from the Per Protocol 2 population with a sustained clinical response at the end of study (Days 40 - 50)

End point title	Adjusted percentage of participants from the Per Protocol 2 population with a sustained clinical response at the end of study (Days 40 - 50)

End point description:

Sustained clinical response at the end of study was achieved by participants who had a clinical outcome of cure at the end of treatment (Days 40-50) and did not experience a recurrence of CDAD, did not die, were not lost to follow-up, and did not have end of study visit prior to Day 40. Only the first failure event per participant was counted. The estimated adjusted percentage was a weighted average across all strata, constructed using MRc stratum weights. The population analyzed is the Per Protocol 2 (PP2) population composed of cures and failures from the PP1 population. Additionally, to be included in the PP2 population, PP1 participants who were cured at end of treatment must not have had any protocol deviations which could affect the assessment of recurrence and have had follow-up contact through at least Day 40.

End point type	Secondary

End point timeframe:

Up to Day 50

End point values	Surotomycin	Vancomycin		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	233	227		
Units: Percentage of participants				
number (confidence interval 95%)	70.8 (64.8 to 76.2)	66.5 (60.6 to 72.2)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants

Statistical analysis description:

Treatment group percentages were stratified by age group (< 75, ≥ 75) and number of previous CDAD episodes (0, ≥ 1). The 95% CIs were stratified Wilson intervals for the treatment group percentages.

Comparison groups	Surotomycin v Vancomycin
Number of subjects included in analysis	460
Analysis specification	Pre-specified
Analysis type	superiority[14]
Parameter estimate	Difference in percentage of participants
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	12.7

Notes:

[14] - Difference: Surotomycin - Vancomycin. For surotomycin to be considered superior to vancomycin the lower bound of the 2-sided 95% CI had to be > 0%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected up to Day 13; only SAEs and drug related AEs were collected thereafter 30 days after end of treatment (up to Day 50)

Adverse event reporting additional description:

All randomized participants who received any amount of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Surotomycin

Reporting group description:

250 mg Surotomycin over-encapsulated tablet administered orally, twice daily for a daily total dose of 500 mg; and Placebo over-encapsulated tablet administered orally, twice daily for 10 days

Reporting group title	Vancomycin

Reporting group description:

125 mg Vancomycin over-encapsulated tablet administered orally, four times daily for a daily total dose of 500 mg, for 10 days

Serious adverse events	Surotomycin	Vancomycin	
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 305 (14.43%)	37 / 286 (12.94%)	
number of deaths (all causes)	18	9	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
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	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 305 (0.33%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pyrexia			
subjects affected / exposed	1 / 305 (0.33%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sudden cardiac death			
subjects affected / exposed	2 / 305 (0.66%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 305 (0.33%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Dyspnoea exertional			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
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	0 / 305 (0.00%)	1 / 286 (0.35%)	
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	1 / 305 (0.33%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	

Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	3 / 305 (0.98%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
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	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (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	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonic convulsion			

subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 305 (0.98%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	2 / 305 (0.66%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal ulcer perforation			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatorenal syndrome			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	1 / 305 (0.33%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Systemic lupus erythematosus			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 305 (0.33%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			

subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal peritonitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 305 (0.98%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pseudomembranous colitis			

subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 305 (0.66%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Strongyloidiasis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 305 (0.33%)	2 / 286 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 305 (0.33%)	3 / 286 (1.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 286 (0.35%)	
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 / 305 (0.00%)	1 / 286 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Surotomycin	Vancomycin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 305 (12.46%)	38 / 286 (13.29%)	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 305 (3.93%)	18 / 286 (6.29%)	
occurrences (all)	13	21	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	16 / 305 (5.25%)	6 / 286 (2.10%)	
occurrences (all)	20	6	
Nausea			
subjects affected / exposed	20 / 305 (6.56%)	21 / 286 (7.34%)	
occurrences (all)	23	21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2012	Amendment 1: Addition of objective and endpoint to assess health economic outcomes
15 May 2013	Amendment 2: Addition of other glycopeptides (in addition to vancomycin) and fidaxomixin to list of disallowed concurrent medications. Pharmacokinetic sampling times further defined with tolerance times added. Statistical text revised to provide additional information on general methodology and clarity regarding efficacy endpoints and analyses

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported