Clinical trial results:
A Phase IIIb/IV Randomized, Controlled, Open-Label, Parallel Group Study to Compare the Efficacy of Vancomycin Therapy to Extended Duration Fidaxomicin Therapy in the Sustained Clinical Cure of Clostridium difficile Infection in an Older Population

Summary

EudraCT number	2013-004619-31
Trial protocol	SE FI GB CZ DK DE IT GR SI HU IE AT BE PT HR
Global end of trial date	05 May 2016

Results information

Result version number	v1
This version publication date	14 May 2017
First version publication date	14 May 2017

Trial information

Trial identification

Sponsor protocol code	2819-MA-1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02254967
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe Ltd.
Sponsor organisation address	2000 Hillswood Drive, Chertsey Surey, United Kingdom, KT16 0RS
Public contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd., astellas.resultsdisclosure.@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe Ltd., astellas.resultsdisclosure.@astellas.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	05 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of fidaxomicin extended pulsed (EPFX) in the treatment of Clostridium difficile (C. difficile) infection (CDI) in male and female patients aged 60 years and older compared with standard vancomycin therapy.

Protection of trial subjects:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the fed ral, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 November 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	Austria: 4
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Croatia: 9
Country: Number of subjects enrolled	Czech Republic: 27
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Greece: 45
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Romania: 45
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Slovenia: 10
Country: Number of subjects enrolled	Spain: 14

Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Turkey: 7
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	364
EEA total number of subjects	338

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)	55
From 65 to 84 years	245
85 years and over	64

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 86 clinical sites in 21 countries in Europe and Asia. Randomization was stratified by CDI severity (severe or non-severe), presence or absence of cancer, age (≥ 75 years or < 75 years) and number of previous recurrences (0, 1, 2) in the 3 months prior to the study.

Pre-assignment

Screening details:

Females and males of ≥ 60 years of age with CDI confirmed by clinical symptoms (either > 3 UBMs or ≥ 200 mL of unformed stool [for patients having rectal collection devices] in the 24 hours prior to randomization and CDI test confirmed positive for presence of C. difficile toxin A/B in stool (within 48 hours prior to randomization) were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Fidaxomicin Extended Pulsed Regimen (EPFX)

Arm description:

Participants received 200 mg fidaxomicin from day 1 to day 5 twice daily, followed by a 1-day gap (day 6) before starting alternate day dosing of 1 tablet of fidaxomicin 200 mg once daily from day 7 to day 25.

Arm type	Experimental
Investigational medicinal product name	Fidaxomicin extended pulsed
Investigational medicinal product code	ASP2819, OPT-80
Other name	DIFICLIR™, DIFICID
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 200 mg of immediate-release fidaxomicin tablets orally in the morning and evening from day 1-5 twice daily and alternate day dosing from day 7-25 once daily.

Arm title	Vancomycin

Arm description:

Participants received 125 mg vancomycin from day 1 to day 10, 4 times daily.

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

Dosage and administration details:

Participants received 125 mg of vancomycin 4 times daily (with a time interval of 6 hours) at the same time each day from day 1 to day 10.

Number of subjects in period 1	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin
Started	183	181
Treated	181	181
Completed	132	125
Not completed	51	56
Randomized but Never Received/Dispensed Study Drug	2	-
Physician Decision	7	2
Death	29	36
Lost to Follow-up	6	9
Miscellaneous	1	2
Withdrawal by Patient	6	7

Baseline characteristics

Reporting groups	
Reporting group title	Fidaxomicin Extended Pulsed Regimen (EPFX)
Reporting group description:	
Participants received 200 mg fidaxomicin from day 1 to day 5 twice daily, followed by a 1-day gap (day 6) before starting alternate day dosing of 1 tablet of fidaxomicin 200 mg once daily from day 7 to day 25.	
Reporting group title	Vancomycin
Reporting group description:	
Participants received 125 mg vancomycin from day 1 to day 10, 4 times daily.	

Reporting group values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin	Total
Number of subjects	183	181	364
Age categorical Units: Subjects			
< 75 years	85	82	167
≥ 75 years	98	99	197
Age continuous Units: years			
arithmetic mean	75.2	74.9	
standard deviation	± 8.4	± 8.9	-
Gender categorical Units:			
Male	72	79	151
Female	111	102	213
CDI Severity at Baseline Units: Subjects			
Severe	66	67	133
Non-severe	117	114	231
Number of Previous Recurrences in the 3 Months prior to Randomization Units: Subjects			
0 recurrences	146	142	288
1 recurrence	27	29	56
2 recurrences	10	10	20
Cancer Status Units: Subjects			
Presence	40	37	77
Absence	143	144	287

End points

End points reporting groups

Reporting group title	Fidaxomicin Extended Pulsed Regimen (EPFX)
Reporting group description:	
Participants received 200 mg fidaxomicin from day 1 to day 5 twice daily, followed by a 1-day gap (day 6) before starting alternate day dosing of 1 tablet of fidaxomicin 200 mg once daily from day 7 to day 25.	
Reporting group title	Vancomycin
Reporting group description:	
Participants received 125 mg vancomycin from day 1 to day 10, 4 times daily.	

Primary: Percentage of Participants with a Sustained Clinical Cure of CDI at 30 Days after End of Treatment

End point title	Percentage of Participants with a Sustained Clinical Cure of CDI at 30 Days after End of Treatment
End point description:	
Sustained clinical cure was defined as an assessment of clinical response at test of cure (TOC; day 12 for vancomycin and day 27 or 12 for EPFX arm) and no recurrence of CDI from TOC until time of assessment. Clinical response was determined by the investigator based on the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) criteria at TOC. Treatment response was present when either stool frequency decreases or stool consistency improved and parameters of disease severity (clinical, laboratory, radiological) improved and no new signs of severe disease developed. The analysis population was the modified Full Analysis Set (mFAS), which consisted of randomized participants who received at least 1 dose of study drug and had confirmed CDI in the 24 hours prior to randomization and CDI test confirmed positive for presence of C. difficile toxin A or B in stool 48 hours prior to randomization.	
End point type	Primary
End point timeframe:	
Day 40 (for vancomycin) and day 55 (for EPFX)	

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	179		
Units: percentage of participants				
number (confidence interval 95%)	70.1 (63.3 to 76.8)	59.2 (52 to 66.4)		

Statistical analyses

Statistical analysis title	Treatment Difference
Statistical analysis description:	
This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.	

Comparison groups	Vancomycin v Fidaxomicin Extended Pulsed Regimen (EPFX)
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	20.7

Notes:

[1] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Secondary: Percentage of Participants with a Sustained Clinical Cure of CDI at Day 40, Day 55 and Day 90

End point title	Percentage of Participants with a Sustained Clinical Cure of CDI at Day 40, Day 55 and Day 90

End point description:

Sustained clinical cure was defined as an assessment of clinical response at test of cure (TOC; day 12 for vancomycin and day 27 or 12 for EPFX arm) and no recurrence of CDI from TOC until time of assessment. Clinical response was determined by the investigator based on the ESCMID criteria at TOC. Treatment response was present when either stool frequency decreases or stool consistency improved and parameters of disease severity (clinical, laboratory, radiological) improved and no new signs of severe disease developed. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Day 40, 55, 90

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	179		
Units: percentage of participants				
number (confidence interval 95%)				
Day 40	75.1 (68.8 to 81.5)	59.2 (52 to 66.4)		
Day 55	70.1 (63.3 to 76.8)	55.3 (48 to 62.6)		
Day 90	65.5 (58.5 to 72.5)	51.4 (44.1 to 58.7)		

Statistical analyses

Statistical analysis title	Treatment Difference (Day 40)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.3
upper limit	25.5

Notes:

[2] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Statistical analysis title	Treatment Difference (Day 55)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	14.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	24.7

Notes:

[3] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Statistical analysis title	Treatment Difference (Day 90)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin

Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	14.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	24.3

Notes:

[4] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Secondary: Percentage of Participants with a Clinical Response of CDI at Day 12

End point title	Percentage of Participants with a Clinical Response of CDI at Day 12

End point description:

Clinical response was determined by the investigator based on the ESCMID criteria (i.e., Treatment response was present when either stool frequency decreases or stool consistency improved and parameters of disease severity [clinical, laboratory, radiological] improved and no new signs of severe disease developed. Treatment response should have been daily observed and evaluated after at least three days, assuming that the participant was not worsening on treatment) at TOC. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Day 12

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	179		
Units: percentage of participants				
number (confidence interval 95%)	80.2 (74.4 to 86.1)	82.1 (76.5 to 87.7)		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin

Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.721 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	6.2

Notes:

[5] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Secondary: Number of Participants with a Relapse on Day 90 as Determined by Whole Genome Sequencing of C. Difficile Isolates

End point title	Number of Participants with a Relapse on Day 90 as Determined by Whole Genome Sequencing of C. Difficile Isolates

End point description:

For participants with a recurrence after TOC, whole genome sequencing of isolates was performed on paired samples from day 1 and the day of the confirmed recurrence. Relapse was defined as paired isolates from a single recurrent participant with ≤ 2 single nucleotide variations (SNVs). Only participants who had a recurrence (45) and had paired samples available for whole sequencing from baseline and at time of recurrence are included in the analysis. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Baseline through day 90

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	9		
Units: participants				
number (not applicable)	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Clinical Response of CDI at 2 Days after End of Treatment

End point title	Percentage of Participants with a Clinical Response of CDI at 2 Days after End of Treatment

End point description:

Clinical response was determined by the investigator based on the ESCMID criteria (i.e., Treatment response was present when either stool frequency decreases or stool consistency improved and parameters of disease severity [clinical, laboratory, radiological] improved and no new signs of severe disease developed. Treatment response should have been daily observed and evaluated after at least three days, assuming that the patient was not worsening on treatment) at TOC. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Day 12, 27

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	179		
Units: percentage of participants				
number (confidence interval 95%)	78 (71.9 to 84.1)	82.1 (76.5 to 87.7)		

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.399 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	4.1

Notes:

[6] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Secondary: Time to Resolution of Diarrhea

End point title	Time to Resolution of Diarrhea

End point description:

Time to resolution of diarrhea was defined as the time elapsing (in hours rounded up from minutes > 30) from the start of treatment (time of first dose of study drug) to resolution of diarrhea (time of the

last unformed bowel movement [UBM] the day prior to the first of 2 consecutive days of ≤ 3 UBMs, > 50% reduction in number of stools or > 75% reduction in volume of liquid stool) that are sustained through to TOC. Participants without a resolution of diarrhea on day 25 (600 hours) for EPFX or day 10 (240 hours) for standard vancomycin were censored on day 25 or 10. Participants who discontinued early before resolution of diarrhea were also censored on the day of discontinuation. Participants with no UBM records were excluded from the analysis. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Up to day 25

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	174		
Units: hours				
median (confidence interval 95%)				
Percentile 50	34 (25 to 49)	22 (10 to 30)		

Statistical analyses

Statistical analysis title	Comparison of Survival Curves

Statistical analysis description:

The comparison of the difference of the 2 treatment groups was done using a stratified Wilcoxon-Gehan test, stratified by CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068 [7]
Method	Stratified Wilcoxon-Gehan test

Notes:

[7] - Stratified by CDI severity, presence or absence of cancer, age group (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Statistical analysis title	Hazard Ratio

Statistical analysis description:

From the Cox proportional hazards model with covariates for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066 [8]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.01

Notes:

[8] - Adjusted for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Secondary: Percentage of Participants with a Recurrence of CDI at Day 40, Day 55 and Day 90

End point title	Percentage of Participants with a Recurrence of CDI at Day 40, Day 55 and Day 90

End point description:

Recurrence of CDI was defined as participants with clinical response at TOC with re-establishment of diarrhea after TOC to an extent (judged by the requency of passed UBMs) that is greater than the frequency recorded on day 10 for vancomycin arm or day 25 for EPFX arm (2 days prior to TOC), confirmed by a CDI test positive for Toxin A/B and requiring further CDI therapy. The analysis population was the mFAS.

End point type	Secondary

End point timeframe:

Day 40, 55, 90

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	179		
Units: percentage of participants				
number (confidence interval 95%)				
Day 40	1.7 (0 to 3.6)	16.8 (11.3 to 22.2)		
Day 55	4 (1.1 to 6.8)	17.9 (12.3 to 23.5)		
Day 90	6.2 (2.7 to 9.8)	19 (13.2 to 24.7)		

Statistical analyses

Statistical analysis title	Treatment Difference (Day 40)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin

Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	-15.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.9
upper limit	-9.3

Notes:

[9] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Statistical analysis title	Treatment Difference (Day 55)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	-13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.2
upper limit	-7.6

Notes:

[10] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Statistical analysis title	Treatment Difference (Day 90)

Statistical analysis description:

This analysis was the difference between the rates (EPFX – vancomycin) and the associated 95% CI around the difference.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment difference
Point estimate	-12.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.5
upper limit	-6

Notes:

[11] - P-value was adjusted for the randomization factors (CDI severity [severe or non-severe], presence or absence of cancer, age [≥ 75 years or < 75 years] and number of previous recurrences [0, 1, and 2]).

Secondary: Time to Recurrence of CDI after End of Active Treatment

End point title	Time to Recurrence of CDI after End of Active Treatment

End point description:

Time to recurrence of CDI was defined as the time in days from clinical response until onset of recurrence of CDI for participants who responded at TOC. Participants who completed the study but did not show recurrence of CDI were censored on day 90, and participants who discontinued early were censored on the day of discontinuation. The analysis population was the mFAS. Due to the low number of participants with a recurrence, median and 95% CI could not be estimated and are denoted as "99999."

End point type	Secondary

End point timeframe:

From day 10 up to day 90

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	147		
Units: days				
median (confidence interval 95%)				
Percentile 50	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Comparison of Survival Curves

Statistical analysis description:

The comparison of the difference of the 2 treatment groups was done using a stratified Wilcoxon-Gehan test, stratified by CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [12]
Method	Stratified Wilcoxon-Gehan test

Notes:

[12] - Stratified by CDI severity, presence or absence of cancer, age group (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Statistical analysis title	Hazard Ratio

Statistical analysis description:

From the Cox proportional hazards model with covariates for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [13]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.52

Notes:

[13] - Adjusted for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Secondary: Disease-free Survival After Day 10

End point title	Disease-free Survival After Day 10

End point description:

Disease-free survival was defined as the time in days a participant did not have symptoms of diarrhea from day 10 up to day 90 for participants who responded at TOC. Participants who completed the study but did not show symptoms of diarrhea were censored at day 90, and participants who discontinued early were censored at the day of discontinuation. The analysis population was mFAS. Due to the low number of participants with symptoms of diarrhea, median and 95% CI could not estimated and are denoted as "99999."

End point type	Secondary

End point timeframe:

From day 10 up to day 90

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	147		
Units: days				
median (confidence interval 95%)				
Percentile 50	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Comparison of Survival Curves

Statistical analysis description:

The comparison of the difference of the 2 treatment groups was done using a stratified Wilcoxon-Gehan test, stratified by CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [14]
Method	Stratified Wilcoxon-Gehan test

Notes:

[14] - Stratified by CDI severity, presence or absence of cancer, age group (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Statistical analysis title	Hazard Ratio

Statistical analysis description:

From the Cox proportional hazards model with covariates for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Comparison groups	Fidaxomicin Extended Pulsed Regimen (EPFX) v Vancomycin
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [15]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.5

Notes:

[15] - Adjusted for treatment, CDI severity, presence or absence of cancer, age (≥ 75 or < 75 years) and number of previous recurrences (0, 1 or 2) in the 3 months prior to the study.

Secondary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events

End point description:

Safety was assessed by adverse events (AEs), which included abnormalities identified during a medical test (e.g. laboratory tests, vital signs, electrocardiogram, etc.) if the abnormality induced clinical signs or symptoms, needed active intervention, interruption or discontinuation of study medication or was clinically significant. A serious AE (SAE) was an event resulting in death, persistent or significant disability/incapacity or congenital anomaly or birth defect, was life-threatening, required or prolonged hospitalization or was considered medically important. The analysis population was the Safety Analysis Set (SAF), which consisted of all randomized participants who took at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

From first dose of study drug to end of study (up to 90 days)

End point values	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	181		
Units: participants				
AEs	121	128		
Drug-related AEs	14	9		
Deaths	28	36		
SAEs	68	78		
Drug-related SAEs	3	6		
AEs Leading to Discontinuation of Study Drug	14	5		
Drug-related AEs Leading to Discont. of Study Drug	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug to end of study (up to 90 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Fidaxomicin Extended Pulsed Regimen (EPFX)
Reporting group description:	
Participants received 200 mg fidaxomicin from day 1 to day 5 twice daily, followed by a 1-day gap (day 6) before starting alternate day dosing of 1 tablet of fidaxomicin 200 mg once daily from day 7 to day 25.	
Reporting group title	Vancomycin
Reporting group description:	
Participants received 125 mg vancomycin from day 1 to day 10, 4 times daily.	

Serious adverse events	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin	
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 181 (37.57%)	78 / 181 (43.09%)	
number of deaths (all causes)	28	36	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bile duct cancer recurrent			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm malignant			

subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphoma			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to central nervous system			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to gastrointestinal tract			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis			
subjects affected / exposed	2 / 181 (1.10%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic carcinoma of the bladder			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic gastric cancer			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple myeloma			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal neoplasm			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematoma			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Aortic valve replacement			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotracheal intubation			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrectomy			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	3 / 181 (1.66%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 3	
Fatigue			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incorrect product storage			
subjects affected / exposed	2 / 181 (1.10%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Multi-organ failure			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 181 (0.55%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Treatment failure			
subjects affected / exposed	0 / 181 (0.00%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 181 (1.10%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Aspiration			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 181 (0.55%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	2 / 181 (1.10%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 181 (0.55%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 181 (1.10%)	4 / 181 (2.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Culture positive			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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			
Cardiac valve rupture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Clavicle fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 181 (0.00%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medication error			
subjects affected / exposed	0 / 181 (0.00%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 181 (1.10%)	0 / 181 (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	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	3 / 181 (1.66%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Cardiac failure			
subjects affected / exposed	3 / 181 (1.66%)	8 / 181 (4.42%)	
occurrences causally related to treatment / all	0 / 3	1 / 8	
deaths causally related to treatment / all	0 / 2	1 / 3	
Cardiac failure acute			

subjects affected / exposed	2 / 181 (1.10%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	2 / 181 (1.10%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial ischaemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tachyarrhythmia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Convulsion			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Somnolence			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	2 / 181 (1.10%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 181 (0.00%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 181 (1.10%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis microscopic			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 181 (1.10%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disbacteriosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia, obstructive			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			

subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 181 (0.55%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematochezia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 181 (0.00%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic failure			
subjects affected / exposed	0 / 181 (0.00%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hepatorenal syndrome			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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	3 / 181 (1.66%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial pyelonephritis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac valve abscess			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Citrobacter sepsis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			
subjects affected / exposed	5 / 181 (2.76%)	18 / 181 (9.94%)	
occurrences causally related to treatment / all	0 / 6	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis enterococcal			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia bacteraemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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	0 / 181 (0.00%)	3 / 181 (1.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			

subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
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	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 181 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nosocomial infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	2 / 181 (1.10%)	7 / 181 (3.87%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 4	
Pneumonia staphylococcal			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 181 (0.00%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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	1 / 181 (0.55%)	9 / 181 (4.97%)	
occurrences causally related to treatment / all	0 / 1	1 / 9	
deaths causally related to treatment / all	0 / 1	1 / 6	
Septic shock			
subjects affected / exposed	3 / 181 (1.66%)	2 / 181 (1.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Skin infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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 / 181 (0.55%)	0 / 181 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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			
subjects affected / exposed	1 / 181 (0.55%)	4 / 181 (2.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 181 (0.55%)	11 / 181 (6.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 181 (0.55%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 181 (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	Fidaxomicin Extended Pulsed Regimen (EPFX)	Vancomycin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 181 (4.42%)	10 / 181 (5.52%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 181 (4.42%)	10 / 181 (5.52%)	
occurrences (all)	9	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported