Clinical trial results:
A Phase 3, Multicenter, Investigator-blind, Randomized, Parallel Group Study to Investigate the Safety and Efficacy of Fidaxomicin Oral Suspension or Tablets Taken q12h, and Vancomycin Oral Liquid or Capsules Taken q6h, for 10 Days in Pediatric Subjects with Clostridium difficile-associated Diarrhea

Summary

EudraCT number	2013-000508-40
Trial protocol	DE BE SK PL IT ES HU FR
Global end of trial date	07 March 2018

Results information

Result version number	v2 (current)
This version publication date	18 June 2020
First version publication date	15 September 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	2819-CL-0202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02218372
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: SUNSHINE

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe B.V.
Sponsor organisation address	Sylviusweg 62, Leiden, Netherlands, 2333 BE
Public contact	Clinical Trial Disclosure, Astellas Pharma Europe B.V., astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe B.V., astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000636-PIP01-09
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2018
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 investigate the clinical response to fidaxomicin granules for oral suspension or tablets and vancomycin oral liquid or capsules of pediatric participants with Clostridium Difficile-Associated Diarrhea (CDAD) from birth to < 18 years of age.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, 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 federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2015
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	Belgium: 7
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	United States: 57
Worldwide total number of subjects	148
EEA total number of subjects	90

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)	30
Children (2-11 years)	89
Adolescents (12-17 years)	29
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pediatric participants with clostridium difficile-associated diarrhea (CDAD) were enrolled in this multicenter study.

Pre-assignment

Screening details:

Eligible participants who met inclusion criteria and none of the exclusion criteria were enrolled, 159 participants were assessed for eligibility of whom 148 were randomized. Participants were randomized to either fidaxomicin or vancomycin in a 2:1 ratio, stratified by age group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Fidaxomicin

Arm description:

Participants from birth to < 6 years of age received weight based doses of fidaxomicin oral suspension (32 mg/kg/day with a maximum dose of 400 mg/day divided in 2 doses) 2 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 200 mg fidaxomicin tablet 2 times daily for 10 days.

Arm type	Experimental
Investigational medicinal product name	Fidaxomicin oral suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants from birth to < 6 years of age received weight based doses of fidaxomicin oral suspension (32 mg/kg/day with a maximum dose of 400 mg/day, divided in 2 doses) 2 times daily for 10 days.

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

Dosage and administration details:

Participants aged ≥ 6 years to < 18 years of age received a 200 mg fidaxomicin tablet 2 times daily for 10 days.

Arm title	Vancomycin

Arm description:

Participants from birth to < 6 years of age received weight based doses of vancomycin oral liquid (40 mg/kg/day with a maximum dose of 500 mg/day divided in 4 doses) 4 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 125 mg vancomycin capsule 4 times daily for 10 days.

Arm type	Active comparator

Investigational medicinal product name	Vancomycin oral liquid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Participants from birth to < 6 years of age received weight based doses of vancomycin oral liquid (40 mg/kg/day with a maximum dose of 500 mg/day divided in 4 doses) 4 times daily for 10 days.

Investigational medicinal product name	Vancomycin capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants aged ≥ 6 years to < 18 years of age received a 125 mg vancomycin capsule 4 times daily for 10 days.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Double blinding of the study drug for this pediatric study population was not feasible, given dosing constraints, the study was investigator-blinded only.

Number of subjects in period 1	Fidaxomicin	Vancomycin
Started	100	48
Treated	98	44
Completed	95	42
Not completed	5	6
Randomized but did not receive treatment	2	3
Miscellaneous	2	1
Adverse event	1	1
Withdrawal by Parent/Guardian	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Fidaxomicin
Reporting group description:	
Participants from birth to < 6 years of age received weight based doses of fidaxomicin oral suspension (32 mg/kg/day with a maximum dose of 400 mg/day divided in 2 doses) 2 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 200 mg fidaxomicin tablet 2 times daily for 10 days.	
Reporting group title	Vancomycin
Reporting group description:	
Participants from birth to < 6 years of age received weight based doses of vancomycin oral liquid (40 mg/kg/day with a maximum dose of 500 mg/day divided in 4 doses) 4 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 125 mg vancomycin capsule 4 times daily for 10 days.	

Reporting group values	Fidaxomicin	Vancomycin	Total
Number of subjects	100	48	148
Age categorical Units: Subjects			
Age continuous			
The baseline analysis set consisted of the Intent-to-treat (ITT) population. The ITT analysis set consisted of all randomized participants, irrespective of a participant having received a study drug (fidaxomicin or vancomycin) or not.			
Units: months			
arithmetic mean	79.7	77.5	
standard deviation	± 61.8	± 59.2	-
Gender categorical Units: Subjects			
Female	41	21	62
Male	59	27	86
Race Units: Subjects			
WHITE	83	36	119
BLACK OR AFRICAN AMERICAN	6	5	11
ASIAN	2	0	2
OTHER	4	1	5
MISSING	5	6	11
Ethnicity Units: Subjects			
HISPANIC OR LATINO	12	5	17
NOT HISPANIC OR LATINO	82	37	119
MISSING	6	6	12

End points

End points reporting groups

Reporting group title	Fidaxomicin

Reporting group description:

Participants from birth to < 6 years of age received weight based doses of fidaxomicin oral suspension (32 mg/kg/day with a maximum dose of 400 mg/day divided in 2 doses) 2 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 200 mg fidaxomicin tablet 2 times daily for 10 days.

Reporting group title	Vancomycin

Reporting group description:

Participants from birth to < 6 years of age received weight based doses of vancomycin oral liquid (40 mg/kg/day with a maximum dose of 500 mg/day divided in 4 doses) 4 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 125 mg vancomycin capsule 4 times daily for 10 days.

Subject analysis set title	Fidaxomin all formulations
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received either fidaxomicin oral suspension or tablet formulation.

Subject analysis set title	Fidaxomicin oral suspension
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received fidaxomicin oral suspension formulation.

Subject analysis set title	Fidaxomicin tablets
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received fidaxomicin tablets formulation.

Subject analysis set title	Vancomycin oral liquid
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received vancomycin oral liquid formulation.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all randomized participants who received at least 1 dose of study drug. In the FAS, participants were allocated to the treatment arm corresponding to the study medication that the participant was randomized to (treatment allocation as randomized).

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAF consisted of all randomized participants who received at least 1 study drug dose. In the SAF, participants were allocated to the treatment arm corresponding to study drug first administered (fidaxomicin or vancomycin), even if it differed from the treatment randomized to.

Primary: Percentage of Participants with Confirmed Clinical Response (CCR) at End of Treatment (EOT) +2 Days

End point title	Percentage of Participants with Confirmed Clinical Response (CCR) at End of Treatment (EOT) +2 Days

End point description:

Initial clinical response (ICR) for ages from birth to < 2 years was defined as absence of watery diarrhea for 2 consecutive treatment days, remaining well until study drug discontinuation. ICR for ages ≥ 2 years to < 18 years was defined as improvement in number and character of bowel movements as determined by < 3 unformed bowel movements (UBMs) per day for 2 consecutive treatment days, remaining well until study drug discontinuation. CCR was defined for both age groups as not requiring further CDAD therapy within 2 days after study drug completion, and was reported with a positive (Yes)

or negative (No) outcome. Resolution of diarrhea was assessed during interviews of participant/parent/legal guardian, supplemented by review of personal records (if hospitalized) and checked for presence of watery diarrhea (ages from birth to < 2 years) or number of UBMs (for ages ≥ 2 years to < 18 years). The analysis population consisted of the FAS.

End point type	Primary

End point timeframe:

Up to day 12

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: percentage of participants				
number (confidence interval 95%)	77.6 (68.0 to 85.4)	70.5 (54.8 to 83.2)		

Statistical analyses

Statistical analysis title	Adjusted Difference of CCR at EOT + 2 Days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified Cochran-Mantel-Haenszel (CMH) method. Newcombe 95% confidence intervals (CIs) presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	23.9

Secondary: Percentage of Participants with Sustained Clinical Response (SCR) at EOT +9 Days

End point title	Percentage of Participants with Sustained Clinical Response (SCR) at EOT +9 Days

End point description:

SCR at EOT + 9 days was defined as CCR (EOT + 2 days) without CDAD recurrence until assessment at EOT +9 days during the follow-up period. Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic Clostridium difficile (C. difficile) in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. FAS population (participants with CCR at EOT +2 days).

End point type	Secondary
End point timeframe:	
Up to day 19	

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	94.7 (87.1 to 98.5)	77.4 (58.9 to 90.4)		

Statistical analyses

Statistical analysis title	Adjusted Difference of SCR at EOT +9 days
Statistical analysis description:	
Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.	
Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	34.2

Secondary: Percentage of Participants with Global Cure (GC) at EOT +9 Days

End point title	Percentage of Participants with Global Cure (GC) at EOT +9 Days
End point description:	
GC was reported as a positive (Yes) or negative (No) outcome and was calculated using SCR and ICR/CCR values according to the following conditions: ● if ICR/CCR=Yes and SCR=Yes, then Global Cure was Yes. ● if ICR/CCR=Yes and SCR =No, then Global Cure was No. ● if ICR/CCR=No (SCR not assessed), then Global Cure was No. ● if ICR/CCR=Missing (SCR not assessed), then Global Cure was set to No. No multiple imputation method (MI) was used for global cure at EOT + 9 days. The analysis population consisted of the FAS.	
End point type	Secondary
End point timeframe:	
Up to day 19	

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: percentage of participants				
number (confidence interval 95%)	75.5 (65.8 to 83.6)	54.5 (38.8 to 69.6)		

Statistical analyses

Statistical analysis title	Adjusted Difference of GC at EOT +9 days

Statistical analysis description:

Adjusted treatment difference of rates was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	21.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	37.7

Secondary: Percentage of Participants with Recurrence of CDAD at EOT +9 Days

End point title	Percentage of Participants with Recurrence of CDAD at EOT +9 Days

End point description:

Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 19

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	5.3 (1.5 to 12.9)	22.6 (9.6 to 41.1)		

Statistical analyses

Statistical analysis title	Adjusted Diff. of CDAD Recurrence at EOT +9 days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	-16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.2
upper limit	-1.8

Secondary: Percentage of Participants with SCR at EOT +16 Days

End point title	Percentage of Participants with SCR at EOT +16 Days

End point description:

SCR at EOT + 16 days was defined as CCR (EOT + 2 days) without CDAD recurrence until assessment at EOT + 16 days during the follow-up period. Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 26

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	89.5 (80.3 to 95.3)	71.0 (52.0 to 85.8)		

Statistical analyses

Statistical analysis title	Adjusted Difference of SCR at EOT +16 days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	35.6

Secondary: Percentage of Participants with GC at EOT +16 Days

End point title	Percentage of Participants with GC at EOT +16 Days

End point description:

GC was reported as a positive (Yes) or negative (No) outcome and was calculated using SCR and ICR/CCR values according to the following conditions: ● if ICR/CCR=Yes and SCR=Yes, then Global Cure was Yes. ● if ICR/CCR=Yes and SCR =No, then Global Cure was No. ● if ICR/CCR=No (SCR not assessed), then Global Cure was No. ● if ICR/CCR=Missing (SCR not assessed), then Global Cure was set to No. No multiple imputation method (MI) was used for global cure at EOT + 16 days. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Up to day 26

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: percentage of participants				
number (confidence interval 95%)	71.4 (61.4 to 80.1)	52.3 (36.7 to 67.5)		

Statistical analyses

Statistical analysis title	Adjusted Difference of GC at EOT +16 days

Statistical analysis description:

Adjusted treatment difference of rates was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	19.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	35.9

Secondary: Percentage of Participants with Recurrence of CDAD at EOT +16 Days

End point title	Percentage of Participants with Recurrence of CDAD at EOT +16 Days

End point description:

Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 26

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	7.9 (3.0 to 16.4)	25.8 (11.9 to 44.6)		

Statistical analyses

Statistical analysis title	Adjusted Diff. of CDAD Recurrence at EOT +16 days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	-17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.6
upper limit	-1.9

Secondary: Percentage of Participants with SCR at EOT +23 Days

End point title	Percentage of Participants with SCR at EOT +23 Days

End point description:

SCR at EOT + 23 days was defined as CCR (EOT + 2 days) without CDAD recurrence until assessment at EOT + 16 days during the follow-up period. Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 33

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	85.5 (75.6 to 92.5)	71.0 (52.0 to 85.8)		

Statistical analyses

Statistical analysis title	Adjusted Difference of SCR at EOT +23 days
Statistical analysis description:	
Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.	
Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	34.5

Secondary: Percentage of Participants with GC at EOT +23 Days

End point title	Percentage of Participants with GC at EOT +23 Days
End point description:	
GC was reported as a positive (Yes) or negative (No) outcome and was calculated using SCR and ICR/CCR values according to the following conditions: ● if ICR/CCR=Yes and SCR=Yes, then Global Cure was Yes. ● if ICR/CCR=Yes and SCR =No, then Global Cure was No. ● if ICR/CCR=No (SCR not assessed), then Global Cure was No. ● if ICR/CCR=Missing (SCR not assessed), then Global Cure was set to No. No multiple imputation method (MI) was used for global cure at EOT + 23 days. The analysis population consisted of the FAS.	
End point type	Secondary
End point timeframe:	
Up to day 33	

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: percentage of participants				
number (confidence interval 95%)	68.4 (58.2 to 77.4)	50.0 (34.6 to 65.4)		

Statistical analyses

Statistical analysis title	Adjusted Difference of GC at EOT +23 days

Statistical analysis description:

Adjusted treatment difference of rates was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	18.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	35.3

Secondary: Percentage of Participants with Recurrence of CDAD at EOT +23 Days

End point title	Percentage of Participants with Recurrence of CDAD at EOT +23 Days

End point description:

Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 33

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	11.8 (5.6 to 21.3)	29.0 (14.2 to 48.0)		

Statistical analyses

Statistical analysis title	Adjusted Diff. of CDAD Recurrence at EOT +23 days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe

95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	-15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.5
upper limit	0.5

Secondary: Percentage of Participants with SCR at End of Study (EOS) (EOT +30 Days)

End point title	Percentage of Participants with SCR at End of Study (EOS) (EOT +30 Days)

End point description:

SCR at EOS was defined as CCR (EOT + 2 days) without CDAD recurrence until assessment at EOS (EOT + 30 days) during the follow-up period. Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 40

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	85.5 (75.6 to 92.5)	71.0 (52.0 to 85.8)		

Statistical analyses

Statistical analysis title	Adjusted Difference of SCR at EOS (EOT +30 days)

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	34.5

Secondary: Percentage of Participants with GC at EOS (EOT +30 Days)

End point title	Percentage of Participants with GC at EOS (EOT +30 Days)

End point description:

GC was reported as a positive (Yes) or negative (No) outcome and was calculated using SCR and ICR/CCR values according to the following conditions: ● if ICR/CCR=Yes and SCR=Yes, then Global Cure was Yes. ● if ICR/CCR=Yes and SCR =No, then Global Cure was No. ● if ICR/CCR=No (SCR not assessed), then Global Cure was No. ● if ICR/CCR=Missing (SCR not assessed), then Global Cure was set to No. Global Cure at EOT +30 days was derived using MI in case ICR/CCR=Missing (SCR not assessed) following Rubin's multiple imputation method. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Up to day 40

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: percentage of participants				
number (confidence interval 95%)	68.4 (58.2 to 77.4)	50.0 (34.6 to 65.4)		

Statistical analyses

Statistical analysis title	Adjusted Difference of GC at EOS (EOT +30 days)

Statistical analysis description:

Adjusted treatment difference of rates was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	18.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	35.3

Secondary: Percentage of Participants with Recurrence of CDAD at EOS (EOT +30 Days)

End point title	Percentage of Participants with Recurrence of CDAD at EOS (EOT +30 Days)

End point description:

Recurrence for ages from birth to < 2 years was defined as re-establishment of watery diarrhea after CCR to an extent that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. Recurrence for ages ≥ 2 years < 18 years was defined as re-establishment of diarrhea after CCR to an extent (as measured by the frequency of UBMs) that was greater than that noted on the last day of study drug with positive direct or indirect testing for the presence of toxigenic C. difficile in stool and that, in the investigator's opinion, required retreatment with CDAD anti-infective therapy. The analysis population consisted of the FAS (participants with CCR at EOT +2 days).

End point type	Secondary

End point timeframe:

Up to day 40

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: percentage of participants				
number (confidence interval 95%)	11.8 (5.6 to 21.3)	29.0 (14.2 to 48.0)		

Statistical analyses

Statistical analysis title	Adj. Diff. of CDAD Recurrence at EOS/EOT +30 days

Statistical analysis description:

Adjusted treatment difference of proportions was calculated using a stratified CMH method. Newcombe 95% CIs presented for adjusted treatment difference.

Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	adjusted treatment difference
Point estimate	-15.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.5
upper limit	0.5

Secondary: Time to Resolution of Diarrhea (TTROD)

End point title	Time to Resolution of Diarrhea (TTROD)

End point description:

TTROD for ages from birth < 2 years was defined as time elapsing (hours rounded up from minutes > 30) from treatment start (time of first study drug dose) to diarrhea resolution (time of last episode of watery diarrhea the day prior to the first of 2 consecutive days without watery diarrhea sustained through EOT). TTROD for ages ≥ 2 years to < 18 years was defined as time elapsing (hours rounded up from minutes > 30) from treatment start (time of first dose) to diarrhea resolution (time of the last UBM the day prior to the first of 2 consecutive days of < 3 UBMs sustained through EOT). TTROD by Kaplan-Meier Method. Those who completed treatment but did not show diarrhea resolution until EOT were censored at Day 10/240 hours. Those who did not complete treatment, discontinued earlier but did not show diarrhea resolution until disc. day were censored at disc. (days converted to hours). Those whose diarrhea did not continue after first dose were included with a TTROD of 1 hour. FAS.

End point type	Secondary

End point timeframe:

Up to day 10

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: hours				
median (confidence interval 95%)	58 (29.0 to 122.0)	97 (42.0 to 146.0)		

Statistical analyses

Statistical analysis title	Time to resolution of diarrhea
Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.579
Method	Logrank

Secondary: Time to Recurrence of CDAD for Participants with CCR at EOT +2 Days

End point title	Time to Recurrence of CDAD for Participants with CCR at EOT +2 Days

End point description:

Time to recurrence was defined as the time (days) from CCR until the onset of recurrence. Time to recurrence of CDAD by Kaplan-Meier Method. Data for median was estimated and the 95% CI could not be estimated due to low event rate. Data not evaluable denoted as "99999." Although median time was evaluable (25 days for the fidaxomicin arm and 26 days for the vancomycin arm) "99999" was entered to bypass system validation error, since 95% CI was not evaluable and system requires "99999" to be entered for data not available (the median values are not between the low and high values of "99999". The analysis population consisted of the FAS (participants with CCR at EOT +2 days). Participants with CCR at EOT+2 days, who completed the follow-up period but did not experience a recurrence of CDAD were censored at EOT+30 days and those who did not complete the follow-up period and discontinued during this period and did not experience a recurrence of CDAD were censored at day of discontinuation.

End point type	Secondary

End point timeframe:

Up to day 40

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	31		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Time to recurrence of CDAD
Comparison groups	Fidaxomicin v Vancomycin
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.023
Method	Logrank

Secondary: Number of Participants with Adverse Events (AEs)

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

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a study drug or who had undergone study procedures which did not necessarily have a causal relationship with this treatment. This included abnormal laboratory tests, vital signs, electrocardiogram data or physical examinations that were defined as AEs if the abnormality induced clinical signs or symptoms, required active intervention, interruption or discontinuation of study drug or was clinically significant in the investigator's opinion. The following standard with 3 grades was used to measure the severity of AEs, including abnormal clinical laboratory values: • Mild: No disruption of normal daily activities • Moderate: Affected normal daily activities • Severe: Inability to perform daily activities. A treatment-emergent adverse event (TEAE) was defined as an AE observed after starting administration of the test drug/comparative drug. The analysis population consisted of the SAF.

End point type	Secondary

End point timeframe:

From the first dose of study drug administration up to 30 days after EOT (up to day 40)

End point values	Fidaxomicin	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	44		
Units: participants				
TEAE	72	33		
Drug-related TEAE	7	5		
Serious TEAE	24	12		
Drug-related Serious TEAE	0	0		
Moderate TEAE	39	14		
Drug-related Moderate TEAE	4	1		
Mild TEAE	56	30		
Drug-related Mild TEAE	3	4		
TEAE Leading to Death	3	0		
Drug-related TEAE Leading to Death	0	0		
TEAE leading to Withdrawal of Treatment (Tx)	1	1		
Drug-related TEAE Leading to Withdrawal of Tx	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Fidaxomicin

End point title	Plasma Concentrations of Fidaxomicin

End point description:

Drug concentration was derived from the blood samples collected. The analysis population consisted of the pharmacokinetics analysis set (PKAS). The PKAS consisted of all participants randomized to fidaxomicin, having received at least 1 dose of fidaxomicin and having at least 1 valid measurement of plasma concentration or fecal concentration of fidaxomicin or its main metabolite OP-1118. N is the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Within 30 minutes predose and 1 to 5 hours postdose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	98	67	31	
Units: ng/mL				
arithmetic mean (standard deviation)				
Predose (Arm 1 N=82, Arm 2 N=55, Arm 3 N=27)	20.17 (± 40.16)	15.26 (± 20.43)	30.16 (± 63.27)	
Postdose (Arm 1 N=81, Arm 2 N=53, Arm 3 N=28)	39.41 (± 62.15)	34.60 (± 57.79)	48.53 (± 69.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Metabolite OP-1118

End point title	Plasma Concentrations of Metabolite OP-1118

End point description:

Drug concentration was derived from the blood samples collected. The analysis population consisted of the PKAS. N is the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Within 30 minutes predose and 1 to 5 hours postdose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	98	67	31	
Units: ng/mL				
arithmetic mean (standard deviation)				
Predose (Arm 1 N=82, Arm 2 N=55, Arm 3 N=27)	63.04 (± 171.97)	42.18 (± 76.76)	105.54 (± 277.67)	
Postdose (Arm 1 N=81, Arm 2 N=53, Arm 3 N=28)	116.64 (± 259.10)	102.38 (± 245.19)	143.63 (± 286.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolite-to-Parent Ratio (MPRconc)

End point title	Metabolite-to-Parent Ratio (MPRconc)

End point description:

Drug concentration was derived from the blood samples collected. The analysis population consisted of the PKAS. N is the number of participants with available data at each time point.

End point type	Secondary

End point timeframe:

Within 30 minutes predose and 1 to 5 hours postdose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	98	67	31	
Units: ratio				
arithmetic mean (standard deviation)				
Predose (Arm 1 N=82, Arm 2 N=55, Arm 3 N=27)	3.18 (± 1.42)	3.24 (± 1.46)	3.05 (± 1.35)	
Postdose (Arm 1 N=81, Arm 2 N=53, Arm 3 N=28)	2.86 (± 1.18)	2.95 (± 1.23)	2.69 (± 1.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Fecal Concentrations of Fidaxomicin

End point title	Fecal Concentrations of Fidaxomicin

End point description:

Drug concentration was derived from the stool samples collected. The analysis population consisted of the PKAS.

End point type	Secondary

End point timeframe:

Within 24 hours of a dose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	47	27	
Units: µg/g				
arithmetic mean (standard deviation)				
Postdose	2685.56 (± 2476.92)	2969.87 (± 2713.58)	2190.63 (± 1948.68)	

Statistical analyses

No statistical analyses for this end point

Secondary: Fecal Concentrations of Metabolite OP-1118

End point title	Fecal Concentrations of Metabolite OP-1118

End point description:

Drug concentration was derived from the stool samples collected. The analysis population consisted of the PKAS.

End point type	Secondary

End point timeframe:

Within 24 hours of a dose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	73	46	27	
Units: µg/g				
arithmetic mean (standard deviation)	889.23 (± 817.83)	789.15 (± 728.58)	1059.73 (± 941.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: MPRconc Within 24 Hours of a Dose

End point title	MPRconc Within 24 Hours of a Dose

End point description:

Drug concentration was derived from the stool samples collected. The analysis population consisted of the PKAS.

End point type	Secondary

End point timeframe:

Within 24 hours of a dose taken between day 5 and day 10

End point values	Fidaxomin all formulations	Fidaxomicin oral suspension	Fidaxomicin tablets	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	72	45	27	
Units: ratio				
arithmetic mean (standard deviation)				
Postdose	0.43 (± 0.31)	0.32 (± 0.19)	0.63 (± 0.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptance of Formulation (Palatability Assessment) in All Participants at First Administration of Study Drug and at Day 7

End point title	Acceptance of Formulation (Palatability Assessment) in All Participants at First Administration of Study Drug and at Day 7

End point description:

Acceptance of formulation was evaluated in all participants who received fidaxomicin oral suspension and vancomycin oral liquid (i.e., participants from birth to =< 6 years and participants > 6 years unable to swallow tablets) by means of a five-point rating scale (awful, poor, fair, good, excellent) by unblinded staff if hospitalized, and by the participant/parents/legal guardian when at home. The analysis population consisted of the FAS.

End point type	Secondary

End point timeframe:

Days 1 and 7

End point values	Fidaxomicin oral suspension	Vancomycin oral liquid		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	30		
Units: participants				
Day 1 Awful	4	5		
Day 1 Poor	6	3		
Day 1 Fair	13	6		
Day 1 Good	19	7		
Day 1 Excellent	13	4		
Day 1 Missing	12	5		
Day 7 Awful	2	3		
Day 7 Poor	5	5		
Day 7 Fair	8	5		
Day 7 Good	21	9		
Day 7 Excellent	16	3		
Day 7 Missing	15	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug administration up to 30 days after EOT (up to day 40)

Adverse event reporting additional description:

The total number of deaths (all causes) includes deaths reported after time frame above.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Fidaxomicin

Reporting group description:

Participants from birth to < 6 years of age received weight based doses of fidaxomicin oral suspension (32 mg/kg/day with a maximum dose of 400 mg/day, divided in 2 doses) 2 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 200 mg fidaxomicin tablet 2 times daily for 10 days.

Reporting group title	Vancomycin

Reporting group description:

Participants from birth to < 6 years of age received weight based doses of vancomycin oral liquid (40 mg/kg/day with a maximum dose of 500 mg/day divided in 4 doses) 4 times daily for 10 days. Participants aged ≥ 6 years to < 18 years of age received a 125 mg vancomycin capsule 4 times daily for 10 days.

Serious adverse events	Fidaxomicin	Vancomycin	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 98 (24.49%)	12 / 44 (27.27%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	3	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant ascites			

subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Radiotherapy			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (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			
Mucosal inflammation			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (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	2 / 98 (2.04%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food allergy			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			

subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Heart rate irregular			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Mitochondrial encephalomyopathy			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (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			
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 98 (3.06%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (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 pain lower			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			

subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
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 / 98 (1.02%)	0 / 44 (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 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
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	2 / 98 (2.04%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial diarrhoea			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			

subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal sepsis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex meningoencephalitis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scedosporium infection			
subjects affected / exposed	0 / 98 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 98 (2.04%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 98 (2.04%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	Vancomycin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 98 (36.73%)	21 / 44 (47.73%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 98 (8.16%)	0 / 44 (0.00%)	
occurrences (all)	11	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 98 (11.22%)	8 / 44 (18.18%)	
occurrences (all)	18	11	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 98 (5.10%)	9 / 44 (20.45%)	
occurrences (all)	6	11	
Constipation			
subjects affected / exposed	5 / 98 (5.10%)	1 / 44 (2.27%)	
occurrences (all)	6	1	
Diarrhoea			
subjects affected / exposed	7 / 98 (7.14%)	4 / 44 (9.09%)	
occurrences (all)	7	5	
Vomiting			
subjects affected / exposed	7 / 98 (7.14%)	6 / 44 (13.64%)	
occurrences (all)	8	8	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 98 (3.06%)	3 / 44 (6.82%)	
occurrences (all)	3	3	
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	3 / 98 (3.06%)	3 / 44 (6.82%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2014	The changes include: ● Throughout the protocol, the age ranges '< 6 months of age' were changed to 'from birth'. Nonsubstantial changes were made to the protocol: ● To update the contract research organization (CRO) contact for reporting SAEs and contact details of clinical research contact; ● To add text on the coadministration of P-glycoprotein inhibitor to the introduction; ● To add the term palatability to study objectives; ● To update the number of study sites to approximately 65 to 80 sites; ● To move palatability from exploratory endpoint to secondary endpoint, and replace cultures with samples in the exploratory microbiology endpoint; ● To update statistical methodology (several sections); ● To update the schedule of assessments, changing 'Follow-up visit' to 'Follow-up TC'; ● To update the timeframe for positive detection of CDAD, changing it from within 48 hours to within 72 hours prior to randomization; ● To update the risk-benefit assessment, adding text on children < 6 months of age and on hypersensitivity reactions; ● To add weight-based dosing instruction of the fidaxomicin oral suspension and the vancomycin oral liquid; ● To update the specified AEs of interest and add lack of efficacy to the special situation events; and ● To include edits for consistency and other minor administrative-type corrections.
21 July 2015	The changes include: ● Inclusion criterion No. 2 was amended to specify that in the US, subjects could only be included if aged ≥ 6 months to < 18 years. Nonsubstantial changes were made to the protocol: ● To update safety reporting, removing reporting to delegated CRO only for North American sites; ● To update contact details for the clinical research contact; ● To extend the planned study period based on expected recruitment rate; ● To update/revise study design to investigate subjects from birth instead of ≥ 6 months, with the exception of the US; ● To update/revise study design to administer fidaxomicin tablets to subjects aged ≥ 6 years instead of from birth; ● To update concomitant treatment, including the most recent use of fidaxomicin or any macrolide antibiotic to be recorded in the electronic Case Report Form (eCRF); ● To update discontinuation of individual subjects, updating the terminology in alignment with new process for protocol deviation; ● To include instructional text related to reporting certain events as AEs based on local requirements; and ● To include edits for consistency and other minor administrative-type corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported