Clinical trial results:
Rectal Bacteriotherapy, Faecal microbiota transplantation or oral vancomycin for the treatment of recurrent Clostridium Difficile infection: A randomised controlled trial

Summary

EudraCT number	2015-003062-82
Trial protocol	DK
Global end of trial date	18 September 2019

Results information

Result version number	v1 (current)
This version publication date	01 May 2021
First version publication date	01 May 2021
Summary attachment (see zip file)	Table of all AEs and SAEs in the trial (AEs and SAEs_table of all.pdf)

Trial information

Trial identification

Sponsor protocol code	RBI/FMT-CDI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02774382
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Medicine, Zealand University Hospital
Sponsor organisation address	Lykkebækvej 1, Køge, Denmark, 4600
Public contact	Clinical Trial Information, Department of Medicine, Zealand University Hospital, Køge, Denmark, +45 23345235, aala@regionsjaelland.dk
Scientific contact	Clinical Trial Information, Department of Medicine, Zealand University Hospital, Køge, Denmark, +45 47322405, aala@regionsjaelland.dk

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	18 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2019
Global end of trial reached?	Yes
Global end of trial date	18 September 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the treatment effect of rectal bacteriotherapy instillation (RBI) and faecal microbiota transplantation /FMT) against the standard antibotic treatment with vancomycin for patients with recurrent Clostridium Difficile infection in a randomised controlled trial

Protection of trial subjects:

All participants gave written informed consent. The Regional Committee of Health Research Ethics (SJ-478),
the Danish Medicines Agency (2015-003062-82) and The Danish Data Protection Agency (REG-103-2015) approved the study. We conducted the trial according to the Helsinki Declaration II and to the principles of Good Clinical Practice. An external party monitored the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 98
Worldwide total number of subjects	98
EEA total number of subjects	98

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)	27
From 65 to 84 years	55

85 years and over	16

Subject disposition

Recruitment

Recruitment details:

We assessed the eligibility of all consecutive individuals with a positive test for C difficile from all clinical microbiological laboratories in eastern Denmark from May 2017 - December 2018 at Zealand University Hospital and from June 2017 - March 2019 at Hvidovre University hospital. Predefined inclusion- and exclusion criteria were used.

Pre-assignment

Screening details:

We screened 1020 persons with a repeated positive CD test within 90 days, yet only included 98. Exclusion were primarily due to the person being asymptomatic at the time of testing or not being able to give informed consent. Furthermore, some were excluded due to having other GI-disease with diarrhoea or declined to participate

Period 1

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

Blinding implementation details:

Computer-generated stratified randomisation in blocks of six was used with allocation concealment in sealed opaque envelopes with sequential
numbers for each stratum. An independent party conducted the block size, randomisation code and packing of envelopes. The trial personnel were blinded to this process. After allocation, the trial was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Faecal microbiota transplantation (FMT)

Arm description:

Participants were pre-treated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 36 hours prior to FMT.
Frozen donor stool from a donor stool bank was administered by rectal enema once, but with a possibility to repeat it up to two times
within 14 days after the first infusion. The indication for repetition was ongoing or new-onset diarrhoea (≥3 loose or liquid stools per day), as judged by a trial physician, without new testing for C difficile. We used a different donor when repeating FMTs.

Arm type	Active comparator
Investigational medicinal product name	Donor stool (not considered a medicinal product)
Investigational medicinal product code	
Other name	FMT
Pharmaceutical forms	Gastroenteral solution, Rectal suspension
Routes of administration	Gastroenteral use, Rectal use

Dosage and administration details:

Frozen donor stool from a donor stool bank. One product consists of 50 g stool, 150 mL NaCl and 20 mL glycerol (85%). It was administered by rectal enema once, but with a possibility to repeat it up to two times within 14 days after the first infusion. The indication for repetition was ongoing or new-onset diarrhoea (≥3 loose or liquid stools per day), as judged by a trial physician, without new testing for C difficile. We used a different donor when repeating FMTs.

Arm title	Rectal bacteriotherapy (RBT)

Arm description:

The standardised laboratory-based bacterial mixture used for rectal bacteriotherapy consisted of 12

bacterial strains suspended in 200 ml isotonic saline with concentrations of 5 × 10-10 bacteria of each strain. Included strains:
Escherichia coli MT-1108-1, Escherichia coli MT-1109, Enterococcus cassiliflavus, Enterococcus gallinarum, Bacteroides thetaiotaomicron, Bacteroides ovatus, Bacteroides vulgatus, Clostridium bifermentans, Clostridium innocuum, Coprobacillus cateniformis, LactobacilIus rhamnosus, LactobacilIus gasserii.
Participants were pretreated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 12 hours prior to RBT.
RBT was administered by rectal enema with three infusions on three consecutive days for all participants in this group.

Arm type	Experimental
Investigational medicinal product name	Rectal bacteriotherapy
Investigational medicinal product code	
Other name	RBT
Pharmaceutical forms	Rectal suspension
Routes of administration	Rectal use

Dosage and administration details:

The bacterial mixture used for rectal bacteriotherapy consisted of 12 bacterial strains suspended in 200 ml isotonic saline with concentrations of 5 × 10-10 bacteria of each strain. Included strains: Escherichia coli MT-1108-1, Escherichia coli MT-1109, Enterococcus cassiliflavus, Enterococcus gallinarum, Bacteroides thetaiotaomicron, Bacteroides ovatus, Bacteroides vulgatus, Clostridium bifermentans, Clostridium innocuum, Coprobacillus cateniformis, LactobacilIus rhamnosus, LactobacilIus gasserii.
RBT was administered by rectal enema with three infusions on three consecutive days for all participants in this group.

Arm title	Oral vancomycin (control)

Arm description:

All participants in the vancomycin group received monotherapy with oral capsule vancomycin 125 mg four times daily for 14 days.
Furthermore, participants with ≥2 recurrences of CDI were treated with additionally 5 weeks of tapering as recommended in guidelines.
The tapering regimen included oral vancomycin 125 mg twice daily for 1 week, 125 mg once daily for 1 week, 125 mg every other day for 1 week and 125 mg every third day for 2 weeks.

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

Dosage and administration details:

All participants in the vancomycin group received monotherapy with oral capsule vancomycin 125 mg four times daily for 14 days.
Furthermore, participants with ≥2 recurrences of CDI were treated with additionally 5 weeks of tapering as recommended in guidelines.
The tapering regimen included oral vancomycin 125 mg twice daily for 1 week, 125 mg once daily for 1 week, 125 mg every other day for 1 week and 125 mg every third day for 2 weeks.

Number of subjects in period 1	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)
Started	34	33	31
Completed	34	31	31
Not completed	0	2	0
Consent withdrawn by subject	-	1	-
Concomitant non-C difficile-related disease	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Faecal microbiota transplantation (FMT)

Reporting group description:

Participants were pre-treated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 36 hours prior to FMT.
Frozen donor stool from a donor stool bank was administered by rectal enema once, but with a possibility to repeat it up to two times
within 14 days after the first infusion. The indication for repetition was ongoing or new-onset diarrhoea (≥3 loose or liquid stools per day), as judged by a trial physician, without new testing for C difficile. We used a different donor when repeating FMTs.

Reporting group title	Rectal bacteriotherapy (RBT)

Reporting group description:

The standardised laboratory-based bacterial mixture used for rectal bacteriotherapy consisted of 12 bacterial strains suspended in 200 ml isotonic saline with concentrations of 5 × 10-10 bacteria of each strain. Included strains:
Escherichia coli MT-1108-1, Escherichia coli MT-1109, Enterococcus cassiliflavus, Enterococcus gallinarum, Bacteroides thetaiotaomicron, Bacteroides ovatus, Bacteroides vulgatus, Clostridium bifermentans, Clostridium innocuum, Coprobacillus cateniformis, LactobacilIus rhamnosus, LactobacilIus gasserii.
Participants were pretreated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 12 hours prior to RBT.
RBT was administered by rectal enema with three infusions on three consecutive days for all participants in this group.

Reporting group title	Oral vancomycin (control)

Reporting group description:

All participants in the vancomycin group received monotherapy with oral capsule vancomycin 125 mg four times daily for 14 days.
Furthermore, participants with ≥2 recurrences of CDI were treated with additionally 5 weeks of tapering as recommended in guidelines.
The tapering regimen included oral vancomycin 125 mg twice daily for 1 week, 125 mg once daily for 1 week, 125 mg every other day for 1 week and 125 mg every third day for 2 weeks.

Reporting group values	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)
Number of subjects	34	33	31
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median	75	67	76
full range (min-max)	47 to 96	36 to 87	33 to 94

Gender categorical Units: Subjects			
Female	20	19	14
Male	14	14	17
Toxin profile Units: Subjects			
Only toxine B (and A)	23	20	15
Both binary toxin and toxine B (and A)	9	10	14
CD027 (incl. toxine B, A and binary toxin)	2	3	2
Hospital admission at inclusion Units: Subjects			
Admitted	6	7	7
Not admitted	28	26	24
Number of recurrences of CDI Units: number			
median	1	1	1
full range (min-max)	1 to 6	1 to 4	1 to 5
Charlson Comorbidity Index Units: NA			
median	2	2	2
full range (min-max)	0 to 7	0 to 6	0 to 6

Reporting group values	Total		
Number of subjects	98		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	53		
Male	45		
Toxin profile Units: Subjects			
Only toxine B (and A)	58		
Both binary toxin and toxine B (and A)	33		

CD027 (incl. toxine B, A and binary toxin)	7		
Hospital admission at inclusion Units: Subjects			
Admitted	20		
Not admitted	78		
Number of recurrences of CDI Units: number			
median			
full range (min-max)	-		
Charlson Comorbidity Index Units: NA			
median			
full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Faecal microbiota transplantation (FMT)

Reporting group description:

Participants were pre-treated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 36 hours prior to FMT.
Frozen donor stool from a donor stool bank was administered by rectal enema once, but with a possibility to repeat it up to two times
within 14 days after the first infusion. The indication for repetition was ongoing or new-onset diarrhoea (≥3 loose or liquid stools per day), as judged by a trial physician, without new testing for C difficile. We used a different donor when repeating FMTs.

Reporting group title	Rectal bacteriotherapy (RBT)

Reporting group description:

The standardised laboratory-based bacterial mixture used for rectal bacteriotherapy consisted of 12 bacterial strains suspended in 200 ml isotonic saline with concentrations of 5 × 10-10 bacteria of each strain. Included strains:
Escherichia coli MT-1108-1, Escherichia coli MT-1109, Enterococcus cassiliflavus, Enterococcus gallinarum, Bacteroides thetaiotaomicron, Bacteroides ovatus, Bacteroides vulgatus, Clostridium bifermentans, Clostridium innocuum, Coprobacillus cateniformis, LactobacilIus rhamnosus, LactobacilIus gasserii.
Participants were pretreated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 12 hours prior to RBT.
RBT was administered by rectal enema with three infusions on three consecutive days for all participants in this group.

Reporting group title	Oral vancomycin (control)

Reporting group description:

All participants in the vancomycin group received monotherapy with oral capsule vancomycin 125 mg four times daily for 14 days.
Furthermore, participants with ≥2 recurrences of CDI were treated with additionally 5 weeks of tapering as recommended in guidelines.
The tapering regimen included oral vancomycin 125 mg twice daily for 1 week, 125 mg once daily for 1 week, 125 mg every other day for 1 week and 125 mg every third day for 2 weeks.

Primary: Clinical cure within 90 days

End point title	Clinical cure within 90 days

End point description:

Clinical cure was defined as absence of C. difficile infection (i.e. absence of diarrhoea or diarrhoea with a negative C difficile test), within 90 days after ended treatment.

End point type	Primary

End point timeframe:

Within 90 days after ended treatment

End point values	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	31	
Units: Number				
Clinical cure	26	16	14	

Attachments (see zip file)	Clinical cure rate/Primary endpoint, figure for EudraCT.jpg

Statistical analyses

Statistical analysis title	Comparison of primary end point
Comparison groups	Faecal microbiota transplantation (FMT) v Rectal bacteriotherapy (RBT) v Oral vancomycin (control)
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	25
upper limit	75

Secondary: 180-day mortality

End point title	180-day mortality
End point description: All-cause mortality	
End point type	Secondary
End point timeframe: 180 days after ended treatment	

End point values	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	31	
Units: Number				
Dead of all-causes at 180-days follow-up	2	4	7	

Attachments (see zip file)	All-cause mortality at 180-days follow-up/Secondary endpoint,

Statistical analyses

Statistical analysis title	Odds ratio
Comparison groups	Faecal microbiota transplantation (FMT) v Rectal bacteriotherapy (RBT) v Oral vancomycin (control)
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	25
upper limit	75

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion to 14 days after ended treatment

Assessment type	Systematic

Dictionary used

Dictionary name	NA
Dictionary version	NA

Reporting groups

Reporting group title	Faecal microbiota transplantation (FMT)

Reporting group description:

Participants were pre-treated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 36 hours prior to FMT.
Frozen donor stool from a donor stool bank was administered by rectal enema once, but with a possibility to repeat it up to two times
within 14 days after the first infusion. The indication for repetition was ongoing or new-onset diarrhoea (≥3 loose or liquid stools per day), as judged by a trial physician, without new testing for C difficile. We used a different donor when repeating FMTs.

Reporting group title	Rectal bacteriotherapy (RBT)

Reporting group description:

The standardised laboratory-based bacterial mixture used for rectal bacteriotherapy consisted of 12 bacterial strains suspended in 200 ml isotonic saline with concentrations of 5 × 10-10 bacteria of each strain. Included strains:
Escherichia coli MT-1108-1, Escherichia coli MT-1109, Enterococcus cassiliflavus, Enterococcus gallinarum, Bacteroides thetaiotaomicron, Bacteroides ovatus, Bacteroides vulgatus, Clostridium bifermentans, Clostridium innocuum, Coprobacillus cateniformis, LactobacilIus rhamnosus, LactobacilIus gasserii.
Participants were pretreated with oral vancomycin 125 mg four times a day for 7-14 days. This was discontinued 12 hours prior to RBT.
RBT was administered by rectal enema with three infusions on three consecutive days for all participants in this group.

Reporting group title	Oral vancomycin (control)

Reporting group description:

All participants in the vancomycin group received monotherapy with oral capsule vancomycin 125 mg four times daily for 14 days.
Furthermore, participants with ≥2 recurrences of CDI were treated with additionally 5 weeks of tapering as recommended in guidelines.
The tapering regimen included oral vancomycin 125 mg twice daily for 1 week, 125 mg once daily for 1 week, 125 mg every other day for 1 week and 125 mg every third day for 2 weeks.

Serious adverse events	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)	3 / 31 (9.68%)	6 / 31 (19.35%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Chest pain	Additional description: Unknown cause		

subjects affected / exposed	0 / 34 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope	Additional description: Syncope leading to a car crash, happening after hemodialysis		
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Dizziness	Additional description: Severe, leading to hospitalization. Occurred before FMT, during pre-treatment with oral vancomycin.		
subjects affected / exposed	1 / 34 (2.94%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 34 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema	Additional description: Oedema, dyspnoea and fever		
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death	Additional description: Of unknown cause - the participant had anaemia and a possible insufficiently treated e.coli bacteriaemia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urosepsis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Faecal microbiota transplantation (FMT)	Rectal bacteriotherapy (RBT)	Oral vancomycin (control)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 34 (94.12%)	29 / 31 (93.55%)	21 / 31 (67.74%)
General disorders and administration site conditions			
Fever or feeling feverish after treatment			
subjects affected / exposed	3 / 34 (8.82%)	3 / 31 (9.68%)	0 / 31 (0.00%)
occurrences (all)	3	3	0
Dizziness during treatment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Hypotension during treatment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Defecation urge during procedure			
subjects affected / exposed	20 / 34 (58.82%)	5 / 31 (16.13%)	0 / 31 (0.00%)
occurrences (all)	20	5	0
Abdominal pain or discomfort during procedure or active treatment			

subjects affected / exposed	15 / 34 (44.12%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	15	1	2
Faecal incontinence during procedure			
subjects affected / exposed	8 / 34 (23.53%)	3 / 31 (9.68%)	0 / 31 (0.00%)
occurrences (all)	8	3	0
Borborygmi during procedure			
subjects affected / exposed	7 / 34 (20.59%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	7	1	0
Nausea or vomiting during procedure or active treatment			
subjects affected / exposed	5 / 34 (14.71%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	5	0	3
Bloating after treatment			
subjects affected / exposed	14 / 34 (41.18%)	19 / 31 (61.29%)	0 / 31 (0.00%)
occurrences (all)	14	19	0
Abdominal pain or discomfort after treatment			
subjects affected / exposed	17 / 34 (50.00%)	24 / 31 (77.42%)	2 / 31 (6.45%)
occurrences (all)	17	24	2
Flatulence after treatment			
subjects affected / exposed	7 / 34 (20.59%)	3 / 31 (9.68%)	0 / 31 (0.00%)
occurrences (all)	7	3	0
Diarrhoae after treatment			
subjects affected / exposed	10 / 34 (29.41%)	22 / 31 (70.97%)	3 / 31 (9.68%)
occurrences (all)	10	22	3
Borborygmi after treatment			
subjects affected / exposed	4 / 34 (11.76%)	10 / 31 (32.26%)	0 / 31 (0.00%)
occurrences (all)	4	10	0
Nausea or vomiting after treatment			
subjects affected / exposed	4 / 34 (11.76%)	5 / 31 (16.13%)	0 / 31 (0.00%)
occurrences (all)	4	5	0
Bloating during treatment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Loss of appetite			

subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Constipation			
subjects affected / exposed	4 / 34 (11.76%)	2 / 31 (6.45%)	1 / 31 (3.23%)
occurrences (all)	4	2	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea during treatment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Itching or rash during treatment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Infections and infestations			
Urinary tract infections			
subjects affected / exposed	1 / 34 (2.94%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	1	0

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

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

A interim analysis was performed for the first 90 participants. When the reported results were apparent, including the mortality data, the study was terminated due to futility and ethical concerns—even though the Haybittle-Peto boundary was not met

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33694229

http://www.ncbi.nlm.nih.gov/pubmed/31273647