Clinical trial results:
A Phase 2, Randomized, Open-Label, Active-Controlled Clinical Study to Investigate the Safety and Efficacy of SMT19969 (200 mg BID) for 10 days Compared with Fidaxomicin (200 mg BID) for 10 days for the Treatment of Clostridium difficile Infection (CDI)

Summary

EudraCT number	2013-005483-25
Trial protocol	GB CZ
Global end of trial date	08 August 2016

Results information

Result version number	v1 (current)
This version publication date	25 October 2017
First version publication date	25 October 2017

Trial information

Trial identification

Sponsor protocol code	SMT19969/C003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02784002
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Summit (Oxford) Limited
Sponsor organisation address	136a Eastern Avenue, Milton Park, Abingdon, United Kingdom, OX14 4SB
Public contact	Clinical Operations, Summit (Oxford) Limited, 0044 1235443939, codify@summitplc.com
Scientific contact	Clinical Operations, Summit (Oxford) Limited, 0044 1235443939, codify@summitplc.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2016
Global end of trial reached?	Yes
Global end of trial date	08 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of 10 days of dosing with ridinilazole (200mg BID) compared to fidaxomicin (200mg BID) in the treatment of subjects with CDI

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH 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. Summit 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	19 February 2015
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	United Kingdom: 12
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	27
EEA total number of subjects	16

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)	11

From 65 to 84 years	14
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only subjects with signs and symptoms consistent with CDI and a positive local diagnostic result for C. difficile and who met all
inclusion/exclusion criteria were randomized to one of the 2 treatment groups. Four subjects failed screening for not meeting an inclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ridinilazole

Arm description:

Subjects in this group received ridinilazole 200 mg BID for 10 days

Arm type	Experimental
Investigational medicinal product name	Ridinilazole
Investigational medicinal product code	SMT19969
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

For the entire 10 day treatment period subjects were asked to take 2 doses (capsules) of study drug each day. One capsule every 12 hours.

Arm title	Fidaxomicin

Arm description:

Subjects in this group received fidaxomicin 200 mg BID for 10 days

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

Dosage and administration details:

For the entire 10 day treatment period subjects will be asked to take 2 doses (tablets) of study drug each day. One tablet every 12 hours.

Number of subjects in period 1	Ridinilazole	Fidaxomicin
Started	14	13
Completed	12	10
Not completed	2	3
Consent withdrawn by subject	1	1
Physician decision	-	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	27	27	
Age categorical Units: Subjects			
<65	11	11	
65 to <75	8	8	
>=75	8	8	
Age continuous Units: years			
arithmetic mean	67.3		
standard deviation	± 15.37	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	16	16	
History of recurrent CDI in the last 12 months Units: Subjects			
none	20	20	
1 previous	7	7	
Baseline Severity - Modified ESCMID scale Units: Subjects			
Mild	18	18	
Moderate	7	7	
Severe	2	2	
Prior antibiotic treatments for current CDI occurence Units: Subjects			
Vancomycin	7	7	
Metronidazole	6	6	
Fidaxomicin	3	3	
Vancomycin + Metronidazole	2	2	
None	9	9	

Subject analysis sets	
Subject analysis set title	Ridinilazole
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects from ridinilazole arm	
Subject analysis set title	Fidaxomicin
Subject analysis set type	Intention-to-treat

Subject analysis set description:
Subjects from fidaxomicin arm

Reporting group values	Ridinilazole	Fidaxomicin	
Number of subjects	14	13	
Age categorical Units: Subjects			
<65	4	7	
65 to <75	6	2	
>=75	4	4	
Age continuous Units: years			
arithmetic mean	68.1	66.3	
standard deviation	± 17.82	± 12.89	
Gender categorical Units: Subjects			
Female	7	4	
Male	7	9	
History of recurrent CDI in the last 12 months Units: Subjects			
none	10	10	
1 previous	4	3	
Baseline Severity - Modified ESCMID scale Units: Subjects			
Mild	9	9	
Moderate	3	4	
Severe	2	0	
Prior antibiotic treatments for current CDI occurence Units: Subjects			
Vancomycin	4	3	
Metronidazole	4	2	
Fidaxomicin	1	2	
Vancomycin + Metronidazole	0	2	
None	5	4	

End points

End points reporting groups

Reporting group title	Ridinilazole
Reporting group description:	
Subjects in this group received ridinilazole 200 mg BID for 10 days	
Reporting group title	Fidaxomicin
Reporting group description:	
Subjects in this group received fidaxomicin 200 mg BID for 10 days	
Subject analysis set title	Ridinilazole
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects from ridinilazole arm	
Subject analysis set title	Fidaxomicin
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects from fidaxomicin arm	

Primary: Safety as assessed by the number of adverse events and SAEs reported during the study

End point title	Safety as assessed by the number of adverse events and SAEs reported during the study[1]

End point description:

The primary endpoint was the occurrence of adverse events and SAEs reported during the study.
Treatment-emergent adverse events (TEAEs) were adverse events that started or increased in severity on or after the first dose of study drug.
Adverse events were reported as study drug related (DR) if the Investigator judged them as at least possibly related to study drug.

End point type	Primary

End point timeframe:

From first dose of study drug to 30 days after last dose of study drug (up to 40 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The data were summarised and no statistical analyses were performed.

End point values	Ridinilazole	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: Subjects				
Deaths	1	1		
Number of subjects with TEAEs	14	11		
Maximum Severity: Mild	4	6		
Maximum Severity: Moderate	5	2		
Maximum Severity: Severe	5	3		
Number of subjects with DR TEAEs	3	1		
DR Maximum Severity: Mild	0	0		
DR Maximum Severity: Moderate	2	1		
DR Maximum Severity: Severe	1	0		
Number of subjects with serious TEAEs	4	3		
Number of subjects with serious DR TEAEs	1	0		

Number of discontinuations due to TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Sustained Clinical Response

End point title	Sustained Clinical Response

End point description:

Sustained clinical response was defined as clinical cure at test-of-cure (TOC) and no recurrence of CDI within 30 days post end of treatment (EOT).
Clinical cure at TOC was assessed by the investigator and was defined as the resolution of diarrhoea (<=3 UBMs in a 24-hour period or 200 mL unformed stool for subjects using rectal collection devices) while on treatment that was maintained until TOC (Day 12).
Recurrence was defined as a new episode of diarrhoea between TOC and End of Study (Day 40 [ie, 30 days post-EOT]) that resulted in the subject receiving antimicrobial treatment active against C. difficile prior to EOS.

End point type	Secondary

End point timeframe:

Till 30 days post End of Treatment (EOT)

End point values	Ridinilazole	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: Percentage				
number (confidence interval 95%)				
Success Rate (%)	50 (23 to 77)	46.2 (19.2 to 74.9)		

Statistical analyses

Statistical analysis title	Comparison of Success Rates

Statistical analysis description:

95% CI was obtained based on the stratified (<75 and ≥ 75 years of age) Miettinen and Nurminen method.

Comparison groups	Fidaxomicin v Ridinilazole
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Difference (Ridinilazole - Fidaxomicin)
Point estimate	2.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.8
upper limit	36.7

Notes:

[2] - Estimated difference (Ridinilazole - Fidaxomicin) between percentage success rates.

Secondary: Investigator-assessed Clinical Response at Test-of-Cure (TOC)

End point title	Investigator-assessed Clinical Response at Test-of-Cure (TOC)

End point description:

Clinical cure at TOC was assessed by the investigator and was defined as the resolution of diarrhoea (<= 3 UBMs in a 24-hour period or 200 mL unformed stool for subjects using rectal collection devices) while on treatment that was maintained until TOC (Day 12).

End point type	Secondary

End point timeframe:

Day 12, test-of-cure (TOC) 48 hours after last treatment

End point values	Ridinilazole	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: Percentage				
number (confidence interval 95%)				
Success Rate (%)	85.7 (57.2 to 98.2)	61.5 (31.6 to 86.1)		

Statistical analyses

Statistical analysis title	Comparison of Success Rates

Statistical analysis description:

95% CI was obtained based on the stratified (<75 and ≥ 75 years of age) Miettinen and Nurminen method.

Comparison groups	Ridinilazole v Fidaxomicin
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Difference (Ridinilazole - Fidaxomicin)
Point estimate	21.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	52.7

Notes:

[3] - Estimated difference (Ridinilazole - Fidaxomicin) between percentage success rates.

Secondary: Ridinilazole plasma Concentrations (Sparse Sampling)

End point title	Ridinilazole plasma Concentrations (Sparse Sampling)[4]

End point description:

Values below the limit of quantification (0.1 ng/mL) have been taken as 0 in the calculations.

End point type	Secondary

End point timeframe:

Sparse samples collected till Day 12. Samples could be taken on Day 1 or Day 2, as well as Days 5, 10 and 12.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only Ridinilazole treated subjects would have Ridinilazole concentrations.

End point values	Ridinilazole			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: ng/mL				
median (full range (min-max))				
Day 1/2 - 4 hours post-dose	0 (0 to 0.279)			
Day 5 - 4 hours post-dose	0.162 (0 to 0.515)			
Day 10 (EOT) - 4 hours post-dose	0.149 (0 to 0.418)			
Day 12 (TOC)	0 (0 to 0.157)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ridinilazole Faecal Concentrations (Sparse Sampling)

End point title	Ridinilazole Faecal Concentrations (Sparse Sampling)[5]

End point description:

Values below the limit of quantification (20.0 mcg/g) have been taken as 0 in the calculations.

End point type	Secondary

End point timeframe:

Sparse samples collected till Day 12.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only Ridinilazole treated subjects would have Ridinilazole concentrations.

End point values	Ridinilazole			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: µg/g				
median (full range (min-max))				
Screening	0 (0 to 0)			
Day 5	530 (0 to 5570)			

Day 10 (EOT) Day 12 (TOC)	1060 (169 to 2400) 47 (0 to 2790)			

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 30 days after last dose of study drug (up to 40 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Ridinilazole
Reporting group description:	
Subjects in this group received ridinilazole 200 mg BID for 10 days	
Reporting group title	Fidaxomicin
Reporting group description:	
Subjects in this group received fidaxomicin 200 mg BID for 10 days	

Serious adverse events	Ridinilazole	Fidaxomicin	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	3 / 13 (23.08%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute coronary syndrome			

subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
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			
Bone marrow failure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lobar pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (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: 0 %

Non-serious adverse events	Ridinilazole	Fidaxomicin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	10 / 13 (76.92%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Catheter site haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Lung consolidation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Psychiatric disorders			

Disorientation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood albumin decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Blood potassium decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pus in stool			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Arthropod sting			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Sunburn			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Laceration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	3	2	

Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Eye pruritus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 14 (35.71%)	2 / 13 (15.38%)	
occurrences (all)	8	2	
Diarrhoea			
subjects affected / exposed	3 / 14 (21.43%)	1 / 13 (7.69%)	
occurrences (all)	4	1	
Frequent bowel movements			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	4	
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Flatulence			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Haematochezia			

subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Tongue ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Haematemesis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rectal discharge			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Blister			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Renal injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Urosepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Genital candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 14 (21.43%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Dehydration			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Gout			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Hypophosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Hypomagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 13 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2015	The main changes to the protocol are: - Removing reference to a modified ITT. - The Intensive PK sampling was changed from required to optional with only a sparse PK sampling required. - Location for the clinical study was expanded to Europe. - Allows a subject to have legal representative provide consent if they are unable to due to their medical condition. - Allows for positive CDI diagnostics to be within the 72 hours prior to randomization instead of 48 hours. - Widened visit windows for Day 5, 7, 10 and 12.
30 March 2016	The changes to the protocol are summarised below: - Removal of reference to the faecal test by Glutamate Dehydrogenase due to inclusion of sites from outside Europe. This has been replaced by a requirement for a positive diagnostic result. This affects inclusion criteria number 2 and the recurrence definition. - Inclusion of Alere C Diff Quik Check to determine free toxin status at baseline and recurrence. - Removal of cytokine analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported