# 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<br>Units: Subjects | | | |
| <65 | 11 | 11 | |
| 65 to <75 | 8 | 8 | |
| >=75 | 8 | 8 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 67.3 | | |
| standard deviation | ± 15.37 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 11 | 11 | |
| Male | 16 | 16 | |
| History of recurrent CDI in the last 12 months<br>Units: Subjects | | | |
| none | 20 | 20 | |
| 1 previous | 7 | 7 | |
| Baseline Severity - Modified ESCMID scale<br>Units: Subjects | | | |
| Mild | 18 | 18 | |
| Moderate | 7 | 7 | |
| Severe | 2 | 2 | |
| Prior antibiotic treatments for current CDI occurence<br>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:<br>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<br>Units: Subjects | | | |
| <65 | 4 | 7 | |
| 65 to <75 | 6 | 2 | |
| >=75 | 4 | 4 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 68.1 | 66.3 | |
| standard deviation | ± 17.82 | ± 12.89 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 4 | |
| Male | 7 | 9 | |
| History of recurrent CDI in the last 12 months<br>Units: Subjects | | | |
| none | 10 | 10 | |
| 1 previous | 4 | 3 | |
| Baseline Severity - Modified ESCMID scale<br>Units: Subjects | | | |
| Mild | 9 | 9 | |
| Moderate | 3 | 4 | |
| Severe | 2 | 0 | |
| Prior antibiotic treatments for current CDI occurence<br>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)<br><br>Day 12 (TOC) | 1060 (169 to 2400)<br><br>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<br>occurrences (all) | 1 / 14 (7.14%)<br>1 | 0 / 13 (0.00%)<br>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:<br>- Removing reference to a modified ITT.<br>- The Intensive PK sampling was changed from required to optional with only a sparse PK sampling required.<br>- Location for the clinical study was expanded to Europe.<br>- Allows a subject to have legal representative provide consent if they are unable to due to their medical condition.<br>- Allows for positive CDI diagnostics to be within the 72 hours prior to randomization instead of 48 hours.<br>- Widened visit windows for Day 5, 7, 10 and 12. |
| 30 March 2016 | The changes to the protocol are summarised below:<br>- 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.<br>- Inclusion of Alere C Diff Quik Check to determine free toxin status at baseline and recurrence.<br>- Removal of cytokine analysis. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported