Clinical trial results:
A Phase 3, randomized, double-blind, active controlled study to compare the efficacy and safety of ridinilazole (200 mg, bid) for 10 days with vancomycin (125 mg, qid) for 10 days in the treatment of Clostridium difficile infection (CDI).

Summary

EudraCT number	2017-001642-10
Trial protocol	EE LV LT BE DE CZ ES FR RO
Global end of trial date	19 November 2021

Results information

Result version number	v1 (current)
This version publication date	06 December 2022
First version publication date	06 December 2022

Trial information

Trial identification

Sponsor protocol code	SMT19969/C005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03595566
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Summit Therapeutics
Sponsor organisation address	2882 sand hill road suite 106, menlo park, United States, 94025
Public contact	Clinical Operations, Summit (Oxford) Limited, 0044 1235443939, ridinilazolephase3studies@summitplc.com
Scientific contact	Clinical Operations, Summit (Oxford) Limited, 0044 1235443939, ridinilazolephase3studies@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	08 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of 10 days dosing with ridinilazole (200 mg bid) with vancomycin (125 mg qid) in the treatment of patients with CDI

Protection of trial subjects:

Patients will be assigned a unique identifier by the Sponsor. Any patient records or datasets that are transferred to the Sponsor will contain the identifier only; patient names or any information which would make the patient identifiable will not be transferred. The patient must be informed that his/her personal study-related data will be used by the Sponsor in accordance with local data protection law. Data protection laws governing the trial include EU GDPR and any local regulation as applicable. The level of disclosure must also be explained to the patient. The patient must be informed that his/her medical records may be examined by the Sponsor, Clinical Quality Assurance auditors or other authorized personnel appointed by the Sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities. Unscheduled telephone calls and/or visits may be conducted if necessary, for the patient's safety and to ensure dosing and diary completion per protocol. Safety procedures during this clinical trial consist of vital signs, physical examinations, and laboratory assessments. More detailed information about the known and expected benefits and risks and reasonably expected adverse events of ridinilazole may be found in the Investigator's Brochure including the Reference Safety Information (RSI). Prompt notification by the Investigator to the Sponsor of a SAE is essential so that legal obligations and ethical responsibilities towards the safety of patients and the safety of a study treatment under clinical investigation are met.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2018
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 States: 175
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	Mexico: 17
Country: Number of subjects enrolled	Brazil: 13
Country: Number of subjects enrolled	Chile: 5
Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Peru: 1
Country: Number of subjects enrolled	Israel: 32
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	New Zealand: 5

Country: Number of subjects enrolled	Belarus: 98
Country: Number of subjects enrolled	Spain: 60
Country: Number of subjects enrolled	Hungary: 58
Country: Number of subjects enrolled	Georgia: 54
Country: Number of subjects enrolled	Bulgaria: 45
Country: Number of subjects enrolled	Romania: 44
Country: Number of subjects enrolled	Greece: 18
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Latvia: 15
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Korea, Republic of: 19
Worldwide total number of subjects	759
EEA total number of subjects	284

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)	429
From 65 to 84 years	330
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study recruitment comprises a screening visit, a 10-day treatment period (beginning on the day of screening or the following day) and a 90-day follow-up period. Randomization will occur after confirmation of eligibility is established with reference to the protocol inclusion and exclusion criteria.

Pre-assignment

Screening details:

All screening evaluations must be completed and reviewed to confirm that potential patients meet all eligibility criteria. The Investigator or site staff will maintain a screening log to confirm eligibility or record reasons for screening failure. Total subjects screened: 1369. Total Screen Failed: 610.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

To maintain the blind, a double-dummy approach for study treatment will be employed. Vancomycin will be encapsulated within a Size 0 Swedish Orange, hard gelatin, and immediate release capsule. There will be a matching vancomycin placebo. Ridinilazole is presented as a coated tablet. There will be a matching ridinilazole placebo. The study drug and packaging will be manufactured in such a way that patients and study site staff will not know to which arm a patient has been assigned.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ridinilazole

Arm description:

ridinilazole (200 mg bid)

Arm type	Experimental
Investigational medicinal product name	Ridinilazole 200mg, Coated Tablet
Investigational medicinal product code	308362-25-6
Other name	2,2'-di(pyridin-4-yl)-1H,1'H-5,5'-bi(benzimidazole), 2,2'-bis(4-pyridyl)-3H,3'H-5,5'-bibenzimidazole, 2-pyridin-4-yl-6-(2-pyridin-4-yl-3H-benzimidazol
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage 200mg, Coated Tablet, oral administration

Arm title	Vancomycin

Arm description:

vancomycin (125 mg qid)

Arm type	Active comparator
Investigational medicinal product name	Over Encapsulated Vancomycin 125mg, Capsules
Investigational medicinal product code	1404-90-6
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Dosage 125mg, Capsules, oral administration

Number of subjects in period 1	Ridinilazole	Vancomycin
Started	378	381
Completed	316	329
Not completed	62	52
Adverse event, serious fatal	24	22
Physician decision	3	2
Consent withdrawn by subject	22	10
Adverse event, non-fatal	2	5
Other	5	5
Sponsor Decision	-	1
Lost to follow-up	6	7

Baseline characteristics

Reporting groups	
Reporting group title	Ridinilazole
Reporting group description: ridinilazole (200 mg bid)	
Reporting group title	Vancomycin
Reporting group description: vancomycin (125 mg qid)	

Reporting group values	Ridinilazole	Vancomycin	Total
Number of subjects	378	381	759
Age categorical Units: Subjects			
Adults (18-64 years)	213	216	429
Adults (65 years+)	165	165	330
Age continuous Units: years			
log mean	59.1	59.7	
standard deviation	± 17.81	± 17.37	-
Gender categorical Units: Subjects			
Female	216	230	446
Male	162	151	313
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	11	10	21
Black or African American	10	16	26
White	341	336	677
Other	8	8	16
Unknown	3	6	9
Disclosure Not Permitted per Regulation	4	5	9
Ethnicity Units: Subjects			
Hispanic or Latino	42	60	102
Not Hispanic or Latino	327	310	637
Unknown	3	6	9
Disclosure Not Permitted per Regulation	6	5	11
Region Units: Subjects			
US/Canada	98	107	205
Europe	230	222	452
Latin America	13	24	37
Other	37	28	65

BMI			
Units: kg/(height in meters)^2			
log mean	26.69	26.39	
standard deviation	± 5.772	± 5.728	-

End points

End points reporting groups	
Reporting group title	Ridinilazole
Reporting group description: ridinilazole (200 mg bid)	
Reporting group title	Vancomycin
Reporting group description: vancomycin (125 mg qid)	

Primary: Sustained Clinical Response (SCR)	
End point title	Sustained Clinical Response (SCR)
End point description: Defined as Clinical Response and no Recurrence of CDI Through 30 Days Post End of Treatment (EOT).	
End point type	Primary
End point timeframe: Day 40	

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	375		
Units: Subjects				
SCR based on Clinical Cure	238	225		
SCR based on Clinical Cure Failure	132	150		

Statistical analyses

Statistical analysis title	Primary endpoint statistical analysis
Statistical analysis description: SCR is defined as Clinical Response and no recurrence of CDI through 30 days post EOT. Subjects who exited study prior to Study Day 40 or received other CDI antimicrobial treatments between Study Days 2 and 45 are considered as SCR failures.	
Comparison groups	Ridinilazole v Vancomycin
Number of subjects included in analysis	745
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4672
Method	Cochran-Mantel-Haenszel

Secondary: Gut Microbiota β-diversity (Bray-Curtis) Index in Stool Samples From Baseline to EOT

End point title	Gut Microbiota β-diversity (Bray-Curtis) Index in Stool Samples From Baseline to EOT

End point description:

Gut Microbiota β-diversity (Bray-Curtis) Index in Stool Samples From Baseline to EOT

End point type	Secondary

End point timeframe:

Day 10

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	280		
Units: number				
arithmetic mean (confidence interval 95%)				
Baseline to EOT	0.7 (0.68 to 0.72)	0.81 (0.79 to 0.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response

End point title	Clinical Response

End point description:

defined as •less than 3 unformed bowel movements (UBMs) for consecutive days and maintained through EOT without further CDI treatment at EOT + 2 days, or •the investigator’s assessment that the subject no longer needs specific CDI antimicrobial treatment after completion of the course of study medication.

End point type	Secondary

End point timeframe:

Day 12

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	375		
Units: subjects				
Clinical Response	320	346		
Clinical Response Failure	50	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Cure

End point title	Clinical Cure

End point description:

defined as the resolution of diarrhea (<3 UBMs in the 1-day period immediately prior to EOT, that is maintained for 2 days after EOT).

End point type	Secondary

End point timeframe:

Day 12

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	375		
Units: subjects				
Clinical Cure	275	292		
Clinical Cure Failure	95	83		

Statistical analyses

No statistical analyses for this end point

Secondary: Sustained Clinical Response over 60 days

End point title	Sustained Clinical Response over 60 days

End point description:

defined as Clinical Response and no recurrence of CDI through 60 days post EOT

End point type	Secondary

End point timeframe:

Day 70

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	375		
Units: subjects				
Sustained Clinical Response 60 Days Post EOT	262	258		
Sustained Clinical Response 60 Days Post EOT Fail	108	117		

Statistical analyses

No statistical analyses for this end point

Secondary: Sustained Clinical Response over 90 days

End point title	Sustained Clinical Response over 90 days

End point description:

defined as Clinical Response and no recurrence of CDI through 90 days post EOT

End point type	Secondary

End point timeframe:

Day 100

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	375		
Units: subjects				
Sustained Clinical Response 90 Days Post EOT	259	249		
Sustained Clinical Response 90 Days Post EOT Fail	111	126		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to EOT of the relative abundance of the 3 main bile acid groups (conjugated primary, primary and secondary bile acids)

End point title	Change from baseline to EOT of the relative abundance of the 3 main bile acid groups (conjugated primary, primary and secondary bile acids)

End point description:

Change from baseline to EOT of the relative abundance of the 3 main bile acid groups (conjugated primary, primary and secondary bile acids)

End point type	Secondary

End point timeframe:

Day 10

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	378	381		
Units: number				
log mean (standard deviation)				
Baseline	33.34 (± 35.68)	30.25 (± 34.13)		

End of Treatment	38.13 (± 39.63)	7.87 (± 22.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to EOT of the Microbiota α-diversity (Shannon) Index in Stool Samples

End point title	Change From Baseline to EOT of the Microbiota α-diversity (Shannon) Index in Stool Samples

End point description:

Percentage of change From Baseline to EOT of the Microbiota α-diversity (Shannon) Index in Stool Samples

End point type	Secondary

End point timeframe:

Day 10

End point values	Ridinilazole	Vancomycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	280		
Units: percentage				
arithmetic mean (confidence interval 95%)				
Baseline to EOT	37.06 (6.01 to 68.11)	-7.32 (-16.61 to 1.97)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	VANCOMYCIN 125 MG
Reporting group description: -	
Reporting group title	RIDINILAZOLE 200 MG
Reporting group description: -	

Serious adverse events	VANCOMYCIN 125 MG	RIDINILAZOLE 200 MG	
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 377 (15.12%)	63 / 374 (16.84%)	
number of deaths (all causes)	24	25	
number of deaths resulting from adverse events	24	25	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia	Additional description: Acute lymphocytic leukaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chondrosarcoma metastatic	Additional description: Chondrosarcoma metastatic		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal cancer metastatic	Additional description: Oesophageal cancer metastatic		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer	Additional description: Prostate cancer		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Extremity necrosis	Additional description: Extremity necrosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemodynamic instability	Additional description: Haemodynamic instability		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis	Additional description: Hypertensive crisis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death	Additional description: Death		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Multiple organ dysfunction syndrome	Additional description: Multiple organ dysfunction syndrome		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Systemic inflammatory response syndrome	Additional description: Systemic inflammatory response syndrome		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity	Additional description: Drug hypersensitivity		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema	Additional description: Acute pulmonary oedema		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma	Additional description: Asthma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration	Additional description: Pneumonia aspiration		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism	Additional description: Pulmonary embolism		

subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Psychiatric disorders			
Disorientation	Additional description: Disorientation		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental poisoning	Additional description: Accidental poisoning		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall	Additional description: Fall		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication	Additional description: Post procedural complication		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Postoperative respiratory failure	Additional description: Postoperative respiratory failure		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpericardiotomy syndrome	Additional description: Postpericardiotomy syndrome		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture	Additional description: Wrist fracture		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction	Additional description: Acute myocardial infarction		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure	Additional description: Cardiac failure		
subjects affected / exposed	4 / 377 (1.06%)	3 / 374 (0.80%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cardiac failure congestive	Additional description: Cardiac failure congestive		
subjects affected / exposed	3 / 377 (0.80%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardio-respiratory arrest	Additional description: Cardio-respiratory arrest		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiogenic shock	Additional description: Cardiogenic shock		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy	Additional description: Ischaemic cardiomyopathy		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Left ventricular failure	Additional description: Left ventricular failure		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles	Additional description: Ventricular extrasystoles		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident	Additional description: Cerebrovascular accident		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic stroke	Additional description: Ischaemic stroke		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolic encephalopathy	Additional description: Metabolic encephalopathy		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack	Additional description: Transient ischaemic attack		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (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			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic uraemic syndrome	Additional description: Haemolytic uraemic syndrome		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia	Additional description: Iron deficiency anaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia	Additional description: Normochromic normocytic anaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic vein thrombosis	Additional description: Splenic vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere's disease	Additional description: Meniere's disease		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (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 upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis ischaemic	Additional description: Colitis ischaemic		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Duodenitis	Additional description: Duodenitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterocolitis haemorrhagic	Additional description: Enterocolitis haemorrhagic		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterocutaneous fistula	Additional description: Enterocutaneous fistula		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal haemorrhage	Additional description: Gastrointestinal haemorrhage		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haematochezia	Additional description: Haematochezia

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome	Additional description: Irritable bowel syndrome		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome	Additional description: Mallory-Weiss syndrome		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon	Additional description: Megacolon		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis	Additional description: Mesenteric vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal motility disorder	Additional description: Oesophageal motility disorder		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute	Additional description: Cholecystitis acute		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis	Additional description: Portal vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer	Additional description: Decubitus ulcer		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease	Additional description: Chronic kidney disease		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Haematuria	Additional description: Haematuria		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy	Additional description: Nephropathy		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal failure	Additional description: Renal failure		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus	Additional description: Systemic lupus erythematosus		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection	Additional description: Clostridium difficile infection		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

COVID-19	Additional description: COVID-19		
subjects affected / exposed	4 / 377 (1.06%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia	Additional description: COVID-19 pneumonia		
subjects affected / exposed	3 / 377 (0.80%)	7 / 374 (1.87%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 3	
Diverticulitis	Additional description: Diverticulitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema	Additional description: Empyema		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterobacter infection	Additional description: Enterobacter infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis	Additional description: Enterococcal sepsis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia infection	Additional description: Escherichia infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis	Additional description: Escherichia sepsis		

subjects affected / exposed	3 / 377 (0.80%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia urinary tract infection	Additional description: Escherichia urinary tract infection		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HCoV-OC43 infection	Additional description: HCoV-OC43 infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer	Additional description: Infected skin ulcer		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection	Additional description: Klebsiella infection		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis	Additional description: Klebsiella sepsis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Osteomyelitis	Additional description: Osteomyelitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: Pneumonia		

subjects affected / exposed	2 / 377 (0.53%)	8 / 374 (2.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 2	
Postoperative wound infection	Additional description: Postoperative wound infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Proteus infection	Additional description: Proteus infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pseudomembranous colitis	Additional description: Pseudomembranous colitis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis	Additional description: Pseudomonal sepsis		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock	Additional description: Septic shock		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Staphylococcal sepsis	Additional description: Staphylococcal sepsis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenotrophomonas sepsis	Additional description: Stenotrophomonas sepsis		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection	Additional description: Streptococcal infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Trichosporon infection	Additional description: Trichosporon infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	3 / 377 (0.80%)	2 / 374 (0.53%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	4 / 377 (1.06%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis	Additional description: Diabetic ketoacidosis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia	Additional description: Hyperkalaemia		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	VANCOMYCIN 125 MG	RIDINILAZOLE 200 MG	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	158 / 377 (41.91%)	159 / 374 (42.51%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain	Additional description: Cancer pain		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Colon adenoma	Additional description: Colon adenoma		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Pancreatic carcinoma	Additional description: Pancreatic carcinoma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Squamous cell carcinoma	Additional description: Squamous cell carcinoma		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Axillary vein thrombosis	Additional description: Axillary vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Bleeding varicose vein	Additional description: Bleeding varicose vein		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Circulatory collapse	Additional description: Circulatory collapse		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Haematoma	Additional description: Haematoma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	3 / 377 (0.80%)	6 / 374 (1.60%)	
occurrences (all)	3	6	
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Jugular vein thrombosis	Additional description: Jugular vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Phlebitis	Additional description: Phlebitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	3 / 377 (0.80%)	3 / 374 (0.80%)	
occurrences (all)	3	4	
Catheter site pain	Additional description: Catheter site pain		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Chills	Additional description: Chills		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Discomfort	Additional description: Discomfort		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Drug intolerance	Additional description: Drug intolerance		

subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Drug withdrawal syndrome	Additional description: Drug withdrawal syndrome		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 377 (0.27%)	3 / 374 (0.80%)	
occurrences (all)	1	3	
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Pain	Additional description: Pain		
subjects affected / exposed	0 / 377 (0.00%)	3 / 374 (0.80%)	
occurrences (all)	0	3	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	7 / 377 (1.86%)	8 / 374 (2.14%)	
occurrences (all)	8	13	
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Social circumstances			
Immobile	Additional description: Immobile		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			

Intermenstrual bleeding	Additional description: Intermenstrual bleeding		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Pelvic pain	Additional description: Pelvic pain		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pruritus	Additional description: Vulvovaginal pruritus		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure	Additional description: Acute respiratory failure		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Asthma	Additional description: Asthma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Atelectasis	Additional description: Atelectasis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Cough	Additional description: Cough		
subjects affected / exposed	2 / 377 (0.53%)	4 / 374 (1.07%)	
occurrences (all)	2	4	
Dry throat	Additional description: Dry throat		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 377 (0.00%)	4 / 374 (1.07%)	
occurrences (all)	0	4	
Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hydrothorax	Additional description: Hydrothorax		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Hypoxia	Additional description: Hypoxia		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Lower respiratory tract congestion	Additional description: Lower respiratory tract congestion		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Nasal septum deviation	Additional description: Nasal septum deviation		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Rales	Additional description: Rales		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Respiratory tract congestion	Additional description: Respiratory tract congestion		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Sinus polyp	Additional description: Sinus polyp		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Vasomotor rhinitis	Additional description: Vasomotor rhinitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Anxiety	Additional description: Anxiety		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	
Confusional state	Additional description: Confusional state		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Delirium	Additional description: Delirium		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Depression	Additional description: Depression		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences (all)	2	1	
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 377 (0.00%)	7 / 374 (1.87%)	
occurrences (all)	0	7	
Panic disorder	Additional description: Panic disorder		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Poor quality sleep	Additional description: Poor quality sleep		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		

subjects affected / exposed	4 / 377 (1.06%)	1 / 374 (0.27%)	
occurrences (all)	4	1	
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	6 / 377 (1.59%)	1 / 374 (0.27%)	
occurrences (all)	6	1	
Bacteroides test positive	Additional description: Bacteroides test positive		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Blood albumin decreased	Additional description: Blood albumin decreased		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Blood creatinine abnormal	Additional description: Blood creatinine abnormal		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 377 (0.00%)	3 / 374 (0.80%)	
occurrences (all)	0	3	
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Blood pressure increased	Additional description: Blood pressure increased		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	

Blood uric acid increased	Additional description: Blood uric acid increased		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Cytomegalovirus test positive	Additional description: Cytomegalovirus test positive		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Haematocrit decreased	Additional description: Haematocrit decreased		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Heart rate increased	Additional description: Heart rate increased		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Hepatic enzyme increased	Additional description: Hepatic enzyme increased		
subjects affected / exposed	4 / 377 (1.06%)	2 / 374 (0.53%)	
occurrences (all)	4	2	
Laboratory test abnormal	Additional description: Laboratory test abnormal		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Platelet count increased	Additional description: Platelet count increased		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Protein total decreased	Additional description: Protein total decreased		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Pus in stool	Additional description: Pus in stool		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	3	0	
White blood cell count increased	Additional description: White blood cell count increased		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	

Injury, poisoning and procedural complications			
Animal scratch	Additional description: Animal scratch		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Arteriovenous fistula site haematoma	Additional description: Arteriovenous fistula site haematoma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Contusion	Additional description: Contusion		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Epicondylitis	Additional description: Epicondylitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Facial bones fracture	Additional description: Facial bones fracture		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Fall	Additional description: Fall		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Haemodialysis complication	Additional description: Haemodialysis complication		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	4	
Iliotibial band syndrome	Additional description: Iliotibial band syndrome		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Ligament sprain	Additional description: Ligament sprain		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Limb injury	Additional description: Limb injury		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Neck injury	Additional description: Neck injury		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Post procedural haematoma	Additional description: Post procedural haematoma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Thermal burn	Additional description: Thermal burn		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Urinary tract stoma complication	Additional description: Urinary tract stoma complication		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Vaccination complication	Additional description: Vaccination complication		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	4	0	
Cardiac disorders			
Angina pectoris	Additional description: Angina pectoris		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Aortic valve incompetence	Additional description: Aortic valve incompetence		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 377 (0.00%)	3 / 374 (0.80%)	
occurrences (all)	0	3	
Cardiac failure congestive	Additional description: Cardiac failure congestive		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Burning sensation	Additional description: Burning sensation		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Diabetic neuropathy	Additional description: Diabetic neuropathy		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Dizziness	Additional description: Dizziness		
subjects affected / exposed	4 / 377 (1.06%)	6 / 374 (1.60%)	
occurrences (all)	5	6	
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Headache	Additional description: Headache		
subjects affected / exposed	12 / 377 (3.18%)	8 / 374 (2.14%)	
occurrences (all)	12	9	
Hepatic encephalopathy	Additional description: Hepatic encephalopathy		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	2	
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Neuralgia	Additional description: Neuralgia		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	2	
Presyncope	Additional description: Presyncope		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Somnolence	Additional description: Somnolence		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Syncope	Additional description: Syncope		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	9 / 377 (2.39%)	8 / 374 (2.14%)	
occurrences (all)	10	8	
Eosinophilia	Additional description: Eosinophilia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia	Additional description: Iron deficiency anaemia		
subjects affected / exposed	3 / 377 (0.80%)	2 / 374 (0.53%)	
occurrences (all)	3	2	
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences (all)	2	1	
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Neutrophilia	Additional description: Neutrophilia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Normochromic normocytic anaemia	Additional description: Normochromic normocytic anaemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Normocytic anaemia	Additional description: Normocytic anaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Vertigo	Additional description: Vertigo		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Eye disorders			
Cataract	Additional description: Cataract		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Conjunctival haemorrhage	Additional description: Conjunctival haemorrhage		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Diplopia	Additional description: Diplopia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Macular oedema	Additional description: Macular oedema		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Presbyopia	Additional description: Presbyopia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Retinal vein thrombosis	Additional description: Retinal vein thrombosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 377 (0.00%)	4 / 374 (1.07%)	
occurrences (all)	0	5	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	9 / 377 (2.39%)	8 / 374 (2.14%)	
occurrences (all)	9	10	
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Abdominal pain upper	Additional description: Abdominal pain upper		

subjects affected / exposed	1 / 377 (0.27%)	5 / 374 (1.34%)	
occurrences (all)	1	5	
Abdominal tenderness	Additional description: Abdominal tenderness		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Anal incontinence	Additional description: Anal incontinence		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Ascites	Additional description: Ascites		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Colitis	Additional description: Colitis		
subjects affected / exposed	1 / 377 (0.27%)	3 / 374 (0.80%)	
occurrences (all)	1	3	
Colon dysplasia	Additional description: Colon dysplasia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Constipation	Additional description: Constipation		
subjects affected / exposed	3 / 377 (0.80%)	6 / 374 (1.60%)	
occurrences (all)	3	6	
Crohn's disease	Additional description: Crohn's disease		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Dental caries	Additional description: Dental caries		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	42 / 377 (11.14%)	42 / 374 (11.23%)	
occurrences (all)	49	46	
Duodenitis	Additional description: Duodenitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Dyspepsia	Additional description: Dyspepsia		

subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	
Epiploic appendagitis	Additional description: Epiploic appendagitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Faeces discoloured	Additional description: Faeces discoloured		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Flatulence	Additional description: Flatulence		
subjects affected / exposed	1 / 377 (0.27%)	3 / 374 (0.80%)	
occurrences (all)	1	4	
Food poisoning	Additional description: Food poisoning		
subjects affected / exposed	3 / 377 (0.80%)	1 / 374 (0.27%)	
occurrences (all)	3	1	
Frequent bowel movements	Additional description: Frequent bowel movements		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Gastrointestinal hypermotility	Additional description: Gastrointestinal hypermotility		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Glossitis	Additional description: Glossitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Haematemesis	Additional description: Haematemesis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Haematochezia	Additional description: Haematochezia		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	
Haemorrhoidal haemorrhage	Additional description: Haemorrhoidal haemorrhage		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Haemorrhoids	Additional description: Haemorrhoids		

subjects affected / exposed	5 / 377 (1.33%)	1 / 374 (0.27%)	
occurrences (all)	5	1	
Irritable bowel syndrome	Additional description: Irritable bowel syndrome		
subjects affected / exposed	2 / 377 (0.53%)	2 / 374 (0.53%)	
occurrences (all)	2	3	
Nausea	Additional description: Nausea		
subjects affected / exposed	5 / 377 (1.33%)	14 / 374 (3.74%)	
occurrences (all)	5	15	
Oral mucosal erythema	Additional description: Oral mucosal erythema		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Peptic ulcer	Additional description: Peptic ulcer		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 377 (0.27%)	6 / 374 (1.60%)	
occurrences (all)	1	7	
Hepatobiliary disorders			
Drug-induced liver injury	Additional description: Drug-induced liver injury		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hepatic cytolysis	Additional description: Hepatic cytolysis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hepatitis	Additional description: Hepatitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	

Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Decubitus ulcer	Additional description: Decubitus ulcer		
subjects affected / exposed	3 / 377 (0.80%)	1 / 374 (0.27%)	
occurrences (all)	3	1	
Dermatitis	Additional description: Dermatitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Ecchymosis	Additional description: Ecchymosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Erythema	Additional description: Erythema		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Macule	Additional description: Macule		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Night sweats	Additional description: Night sweats		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Pruritus	Additional description: Pruritus		
subjects affected / exposed	0 / 377 (0.00%)	3 / 374 (0.80%)	
occurrences (all)	0	3	
Rash	Additional description: Rash		

subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Rash papular	Additional description: Rash papular		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	2	
Toxic skin eruption	Additional description: Toxic skin eruption		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 377 (0.27%)	2 / 374 (0.53%)	
occurrences (all)	1	2	
Chronic kidney disease	Additional description: Chronic kidney disease		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Cystitis haemorrhagic	Additional description: Cystitis haemorrhagic		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Haematuria	Additional description: Haematuria		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Micturition urgency	Additional description: Micturition urgency		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Nephropathy	Additional description: Nephropathy		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Neurogenic bladder	Additional description: Neurogenic bladder		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	

Renal colic	Additional description: Renal colic		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Renal cyst	Additional description: Renal cyst		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Renal failure	Additional description: Renal failure		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Renal impairment	Additional description: Renal impairment		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Urinary tract obstruction	Additional description: Urinary tract obstruction		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	7 / 377 (1.86%)	1 / 374 (0.27%)	
occurrences (all)	9	1	
Arthritis reactive	Additional description: Arthritis reactive		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Arthritis	Additional description: Arthritis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Back pain	Additional description: Back pain		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences (all)	2	1	
Bursitis	Additional description: Bursitis		

subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Chest wall haematoma	Additional description: Chest wall haematoma		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Haematoma muscle	Additional description: Haematoma muscle		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Myalgia	Additional description: Myalgia		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Oligoarthritis	Additional description: Oligoarthritis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Osteoporosis	Additional description: Osteoporosis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Rheumatoid arthritis	Additional description: Rheumatoid arthritis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis	Additional description: Spinal osteoarthritis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Asymptomatic COVID-19	Additional description: Asymptomatic COVID-19		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	

Bacteraemia	Additional description: Bacteraemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Bacteriuria	Additional description: Bacteriuria		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Candida infection	Additional description: Candida infection		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Chronic sinusitis	Additional description: Chronic sinusitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Clostridium difficile colitis	Additional description: Clostridium difficile colitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
COVID-19	Additional description: COVID-19		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Cystitis	Additional description: Cystitis		
subjects affected / exposed	2 / 377 (0.53%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Escherichia urinary tract infection	Additional description: Escherichia urinary tract infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	

Fungal infection	Additional description: Fungal infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Gastritis viral	Additional description: Gastritis viral		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Helicobacter gastritis	Additional description: Helicobacter gastritis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Helicobacter infection	Additional description: Helicobacter infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Herpes simplex	Additional description: Herpes simplex		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Infected dermal cyst	Additional description: Infected dermal cyst		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Influenza	Additional description: Influenza		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Intervertebral discitis	Additional description: Intervertebral discitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Large intestine infection	Additional description: Large intestine infection		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences (all)	2	1	
Laryngitis	Additional description: Laryngitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	3 / 377 (0.80%)	1 / 374 (0.27%)	
occurrences (all)	3	1	
Oesophageal candidiasis	Additional description: Oesophageal candidiasis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	

Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Otitis media	Additional description: Otitis media		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Pharyngotonsillitis	Additional description: Pharyngotonsillitis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 377 (0.27%)	1 / 374 (0.27%)	
occurrences (all)	1	1	
Pneumonia bacterial	Additional description: Pneumonia bacterial		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis chronic	Additional description: Pyelonephritis chronic		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Renal cyst infection	Additional description: Renal cyst infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Salmonellosis	Additional description: Salmonellosis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	

Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Staphylococcal infection	Additional description: Staphylococcal infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Torulopsis infection	Additional description: Torulopsis infection		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Tracheitis	Additional description: Tracheitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	3 / 377 (0.80%)	2 / 374 (0.53%)	
occurrences (all)	3	2	
Upper respiratory tract infection bacterial	Additional description: Upper respiratory tract infection bacterial		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	2	0	
Urinary tract candidiasis	Additional description: Urinary tract candidiasis		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	5 / 377 (1.33%)	7 / 374 (1.87%)	
occurrences (all)	5	8	
Urinary tract infection staphylococcal	Additional description: Urinary tract infection staphylococcal		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Viral infection	Additional description: Viral infection		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Viral rhinitis	Additional description: Viral rhinitis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal candidiasis	Additional description: Vulvovaginal candidiasis		

subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection	Additional description: Vulvovaginal mycotic infection		
subjects affected / exposed	2 / 377 (0.53%)	1 / 374 (0.27%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	4 / 377 (1.06%)	5 / 374 (1.34%)	
occurrences (all)	4	5	
Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Electrolyte imbalance	Additional description: Electrolyte imbalance		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 377 (0.00%)	3 / 374 (0.80%)	
occurrences (all)	0	3	
Hypoglycaemia	Additional description: Hypoglycaemia		
subjects affected / exposed	0 / 377 (0.00%)	2 / 374 (0.53%)	
occurrences (all)	0	2	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	3 / 377 (0.80%)	9 / 374 (2.41%)	
occurrences (all)	3	10	
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	5 / 377 (1.33%)	1 / 374 (0.27%)	
occurrences (all)	5	1	

Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Iron deficiency	Additional description: Iron deficiency		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Lactic acidosis	Additional description: Lactic acidosis		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Magnesium deficiency	Additional description: Magnesium deficiency		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	
Pseudohyponatraemia	Additional description: Pseudohyponatraemia		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	1 / 377 (0.27%)	0 / 374 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	0 / 377 (0.00%)	1 / 374 (0.27%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2020	Amendment 4; Protocol Version 5.0 • Addition of a microbiome secondary objective and endpoint • Investigator assessment of clinical cure and sustained clinical response moved from exploratory to secondary endpoints • Day 40 visit window amended from ±3 days to +5 days • Allowance of a negative Free Toxin Test (FTT) to be repeated once at baseline and for suspected recurrence • Addition of a CCNA for patients with a negative FTT for suspected recurrence • Revision of exclusion criteria 6 (immunosuppressed patients) • Additional section to further clarify exclusion criteria 6 (immunosuppressed patients) • Clarification of exclusion criteria 7 (prior antimicrobial treatment) • Revision of exclusion criteria 8 (antitoxin antibodies) • Revision of exclusion criterion 9 in line with changes made to the potentially confounding medication section • Additional instructions for administration of study treatment • Revisions and reorganization of potential confounding medications for clarity and to reflect clinical practice • Allowance for telephone consent to conduct a Free Toxin Test where the test is not standard of care • Revision of the requirement for an eDiary from up to Day 100 to up to Day 40 • Allowance of the Investigator, or a 3rd party vendor where available, to call the patient daily as an alternative to the eDiary • Addition of weekly calls to the patient post Day 40 to check for diarrhea/suspected recurrence • Stool sampling instructions added • Medical history requirements were updated and clarified Allowance for a FTT to be conducted without patient consent on a stool sample collected per standard of care for diagnostic purposes • Updates to the statistical analysis section to align with protocol changes made • Adverse event assessment of causality revised from 4 possible grades (probable, possible, unlikely, not related) to 2 possible grades (related, not related)

03 September 2020	Amendment 5; Protocol Version 6 • Added allowance for screening and Day 100 visits to be completed over the phone. • Added the option to conduct the physical exam at screening or baseline. If conducted at screening, the vital sign assessment must still be repeated at baseline. Added allowance for baseline visit to be completed at home with assistance from site staff or a home healthcare vendor approved by sponsor with the addition of video conferencing for certain procedures. • Added allowance for Day 12, Day 40, and any recurrence visit(s) to be completed at home synchronously over video conference with site staff and with the addition of a home healthcare vendor where required by the Investigator. • Added allowance for consent to be captured electronically (eConsent) or via email, printing, signing, scanning to site as back-up. • Added instruction that the ECG does not need to be completed at baseline if patient's most recent ECG was normal and was completed in the 12 months prior. • Added instruction that the urine and blood samples, including PK, may be collected at patient's home by site staff or home healthcare vendor. Urine and blood samples (except PK sampling) may alternately be completed by other qualified person at alternate location, where needed. • Clarified in footnote 16 that either site or 3rd party vendor may contact patient daily to collect dosing and bowel movement information until Day 40 • Modified risk/benefit assessment section to include COVID-19 pandemic and added risk mitigation language
03 February 2021	Amendment 6; Protocol Version 7 • Revised exclusion criterion 4 to improve clarity and readability, to add pancreatectomy to the examples of prohibited gastrointestinal tract surgery, and to clarify that cholecystectomy is not prohibited. • Deleted exclusion criterion 6 and corresponding Section 5.2.1 (immunosuppressed patients). • Revised exclusion criteria 7, 8, and 9 for clarity and readability (prior/concomitant therapy) • Revised exclusion criterion 12 to provide additional examples of conditions that would make a patient unsuitable for inclusion in the study and to improve clarity and readability.
21 June 2021	Amendment 7; Protocol Version 8.0 • Modified the definition of Sustained Clinical Response (Sections 1.1 and 3). • Updated secondary and exploratory endpoints including microbiome, bile acid, and antibiotic susceptibility endpoints (Sections 1.1, 3 and 9).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported