Clinical trial results:
A Phase 3, Randomized, Double-blind, Active-controlled Noninferiority Study Evaluating the Efficacy, Safety, and Tolerability of Cefepime/VNRX-5133 in Adults with Complicated Urinary Tract Infections, Including Acute Pyelonephritis.

Summary

EudraCT number	2018-001451-13
Trial protocol	LV CZ HU BG HR RO
Global end of trial date	14 December 2021

Results information

Result version number	v1 (current)
This version publication date	19 October 2023
First version publication date	19 October 2023

Trial information

Trial identification

Sponsor protocol code	VNRX-5133-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03840148
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Venatorx Pharmaceuticals, Inc.
Sponsor organisation address	74 E. Swedesford Road, Suite 100, Malvern, PA, United States, 19355
Public contact	Clinical Research, Venatorx Pharmaceuticals, Inc., +1 (610) 644-8935, contact@Venatorx.com
Scientific contact	Clinical Research, Venatorx Pharmaceuticals, Inc., +1 (610) 644-8935, contact@Venatorx.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	14 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2021
Global end of trial reached?	Yes
Global end of trial date	14 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of cefepime/VNRX 5133 compared with meropenem with respect to both per patient microbiologic eradication and symptomatic resolution of all urinary tract infection (UTI)-core symptoms (or return to pre morbid baseline) at the Test of Cure (TOC) visit

Protection of trial subjects:

1. Conducted under Good Clinical Practice (GCP)
2. Ethics Committee/Institutional Review Board approval
3. Informed consent
4. Safety monitoring / DSMB

Background therapy:

None.

Evidence for comparator: -

Actual start date of recruitment	07 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Romania: 62
Country: Number of subjects enrolled	Croatia: 8
Country: Number of subjects enrolled	Bulgaria: 153
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Latvia: 57
Country: Number of subjects enrolled	United States: 44
Country: Number of subjects enrolled	Serbia: 17
Country: Number of subjects enrolled	Russian Federation: 76
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	Ukraine: 95
Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	China: 49
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	Peru: 22
Worldwide total number of subjects	661
EEA total number of subjects	310

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)	412
From 65 to 84 years	234
85 years and over	15

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult patients with complicated urinary tract infection, including acute pyelonephritis.

Period 1

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

Blinding implementation details:

All study drugs were prepared at the study site by an unblinded pharmacist or designee. Prepared study drug and placebo IV bags and IV tubing were blinded with sleeves to maintain the blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cefepime-taniborbactam

Arm description:

Patients randomized to cefepime-taniborbactam received meropenem placebo intravenous (IV) immediately followed by cefepime-taniborbactam (2 g/0.5 g IV q8h). Meropenem placebo was administered via IV pump over 30 minutes. Cefepime-taniborbactam was administered via IV pump over a 2-hour period

Arm type	Experimental
Investigational medicinal product name	Cefepime-Taniborbactam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2g/cefepime vial and 0.5g/taniborbactam vial individually reconstituted and combined in 250 mL 0.9% sodium chloride IV

Arm title	Meropenem

Arm description:

Patients randomized to receive meropenem received cefepime-taniborbactam placebo intravenous (IV) immediately following meropenem (1 g IV every 8 hours). Meropenem was infused over 30 minutes. Cefepime-taniborbactam placebo was administered via IV pump over a 2-hour period.

Arm type	Active comparator
Investigational medicinal product name	Meropenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 g/vial; reconstituted and added to 50 mL 0.9% sodium chloride

Number of subjects in period 1	Cefepime-taniborbactam	Meropenem
Started	441	220
Completed	426	214
Not completed	15	6
Adverse event, serious fatal	1	-
Consent withdrawn by subject	6	2
Physician decision	2	-
COVID-19 related	2	-
Lost to follow-up	1	1
Reason not provided	3	3

Baseline characteristics

Reporting groups

Reporting group title	Cefepime-taniborbactam

Reporting group description:

Patients randomized to cefepime-taniborbactam received meropenem placebo intravenous (IV) immediately followed by cefepime-taniborbactam (2 g/0.5 g IV q8h). Meropenem placebo was administered via IV pump over 30 minutes. Cefepime-taniborbactam was administered via IV pump over a 2-hour period

Reporting group title	Meropenem

Reporting group description:

Patients randomized to receive meropenem received cefepime-taniborbactam placebo intravenous (IV) immediately following meropenem (1 g IV every 8 hours). Meropenem was infused over 30 minutes. Cefepime-taniborbactam placebo was administered via IV pump over a 2-hour period.

Reporting group values	Cefepime-taniborbactam	Meropenem	Total
Number of subjects	441	220	661
Age categorical Units: Subjects			
<65 years	275	137	412
65 to 75 years	111	56	167
>75 years	55	27	82
Age continuous Units: years			
arithmetic mean	56.2	55.8	
standard deviation	± 17.43	± 18.15	-
Gender categorical Units: Subjects			
Female	248	115	363
Male	193	105	298

Subject analysis sets

Subject analysis set title	microITT Analysis Population: Cefepime-taniborbactam
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The microbiological intent-to-treat (microITT) analysis population consisted of all patients in the intent-to-treat analysis population who:
− Had a positive study entry (ie, baseline) urine culture defined as ≥10^5 colony forming unit/mL of a gram-negative pathogen(s) against which both cefepime-taniborbactam and meropenem had antibacterial activity, and
− Had no more than 2 microorganisms identified in the study entry (ie, baseline) culture regardless of colony count.

Subject analysis set title	microITT analysis population: Meropenem
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The microbiological intent-to-treat (microITT) analysis population consisted of all patients in the intent-to-treat analysis population who:
− Had a positive study entry (ie, baseline) urine culture defined as ≥10^5 colony forming unit/mL of a gram-negative pathogen(s) against which both cefepime-taniborbactam and meropenem had antibacterial activity, and

– Had no more than 2 microorganisms identified in the study entry (ie, baseline) culture regardless of colony count.

Reporting group values	microITT Analysis Population: Cefepime-taniborbactam	microITT analysis population: Meropenem	
Number of subjects	293	143	
Age categorical Units: Subjects			
<65 years	180	90	
65 to 75 years	72	35	
>75 years	41	18	
Age continuous Units: years			
arithmetic mean	56.5	55.8	
standard deviation	± 17.64	± 17.93	
Gender categorical Units: Subjects			
Female	161	69	
Male	132	74	

End points

End points reporting groups

Reporting group title	Cefepime-taniborbactam

Reporting group description:

Patients randomized to cefepime-taniborbactam received meropenem placebo intravenous (IV) immediately followed by cefepime-taniborbactam (2 g/0.5 g IV q8h). Meropenem placebo was administered via IV pump over 30 minutes. Cefepime-taniborbactam was administered via IV pump over a 2-hour period

Reporting group title	Meropenem

Reporting group description:

Patients randomized to receive meropenem received cefepime-taniborbactam placebo intravenous (IV) immediately following meropenem (1 g IV every 8 hours). Meropenem was infused over 30 minutes. Cefepime-taniborbactam placebo was administered via IV pump over a 2-hour period.

Subject analysis set title	microITT Analysis Population: Cefepime-taniborbactam
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The microbiological intent-to-treat (microITT) analysis population consisted of all patients in the intent-to-treat analysis population who:
− Had a positive study entry (ie, baseline) urine culture defined as ≥10^5 colony forming unit/mL of a gram-negative pathogen(s) against which both cefepime-taniborbactam and meropenem had antibacterial activity, and
− Had no more than 2 microorganisms identified in the study entry (ie, baseline) culture regardless of colony count.

Subject analysis set title	microITT analysis population: Meropenem
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The microbiological intent-to-treat (microITT) analysis population consisted of all patients in the intent-to-treat analysis population who:
− Had a positive study entry (ie, baseline) urine culture defined as ≥10^5 colony forming unit/mL of a gram-negative pathogen(s) against which both cefepime-taniborbactam and meropenem had antibacterial activity, and
− Had no more than 2 microorganisms identified in the study entry (ie, baseline) culture regardless of colony count.

Primary: Composite (Microbiological and Clinical) Response at Test of Cure

End point title	Composite (Microbiological and Clinical) Response at Test of Cure

End point description:

The primary endpoint was the demonstration of microbiological success (any gram negative bacterial pathogens found at study entry are eradicated to <10^3 colony forming units per milliliter [CFU/mL] on urine culture) and the demonstration of symptomatic clinical success (symptomatic resolution or return to pre-morbid baseline of all UTI-core symptoms, no new symptoms, patient is alive, and patient has not received additional antibacterial therapy for cUTI) at TOC in the microbiological intent-to-
treat (microITT) population.

End point type	Primary

End point timeframe:

Tested at Test of Cure visit (Day 19 to 23).

End point values	microITT Analysis Population: Cefepime-taniborbactam	microITT analysis population: Meropenem		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	293	143		
Units: subjects				
Composite Success	207	83		
Composite Failure	73	53		
Composite Indeterminate	13	7		

Statistical analyses

Statistical analysis title	Composite Success Response Rate

Statistical analysis description:

95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.

Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0088 [1]
Method	Miettinen and Nurminen
Parameter estimate	Response Rate Difference
Point estimate	12.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	22.2

Notes:

[1] - P-value for superiority test presented whenever the lower confidence interval is greater than 0 for the primary endpoint analysis

Secondary: Composite, Microbiological, and Symptomatic Clinical Success at End of Treatment

End point title	Composite, Microbiological, and Symptomatic Clinical Success at End of Treatment

End point description:

Composite Success: The proportion of patients with both microbiological success and symptomatic clinical]success at EOT in the extended microITT population.

Microbiological Success: Demonstration that the bacterial pathogen found at study entry (≥10^5 CFU/mL) is eradicated to <10^3 CFU/mL at EOT in the microITT population.

Clinical Success: "Symptomatic resolution or return to pre-morbid baseline of all UTI-core symptoms patient is alive, and patient has not received additional antibacterial therapy for cUTI) at EOT in the microITT population.

End point type	Secondary

End point timeframe:

End of treatment (within 24 hours after last dose).

End point values	microITT Analysis Population: Cefepime-taniborbactam	microITT analysis population: Meropenem		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	293	143		
Units: participants				
Composite Success	261	123		
Microbiological Success	284	139		
Symptomatic Clinical Success	265	127		

Statistical analyses

Statistical analysis title	Composite Success at End of Treatment
Statistical analysis description: 95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.	
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	10.4

Statistical analysis title	Microbiological Success at End of Treatment
Statistical analysis description: 95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.	
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	4.1

Statistical analysis title	Symptomatic Clinical Success at End of Treatment

Statistical analysis description:

95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.

Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	8.5

Secondary: Composite, Microbiological, and Symptomatic Clinical Success at Late Follow Up

End point title	Composite, Microbiological, and Symptomatic Clinical Success at Late Follow Up

End point description:

Composite Success: The proportion of patients with both microbiological success and symptomatic clinical]success at LFU in the extended microITT population.

Microbiological Success: Demonstration that the bacterial pathogen found at study entry (≥10^5 CFU/mL) is eradicated to <10^3 CFU/mL at LFU in the microITT population.

Clinical Success: "Symptomatic resolution or return to pre-morbid baseline of all UTI-core symptoms patient is alive, and patient has not received additional antibacterial therapy for cUTI) at LFU in the microITT population.

End point type	Secondary

End point timeframe:

Late follow up (Days 28 to 35).

End point values	microITT Analysis Population: Cefepime-taniborbactam	microITT analysis population: Meropenem		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	293	143		
Units: participants				
Composite Success	187	74		
Microbiological Success	207	90		
Symptomatic Clinical Success	238	102		

Statistical analyses

Statistical analysis title	Composite Success at Late Follow Up
Statistical analysis description:	
95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.	
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	21.9

Statistical analysis title	Microbiological Success at Late Follow Up
Statistical analysis description:	
95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.	
Comparison groups	microITT analysis population: Meropenem v microITT Analysis Population: Cefepime-taniborbactam
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	17.3

Statistical analysis title	Symptomatic Clinical Success at Late Follow Up
Statistical analysis description: 95% confidence interval of between-treatment differences were based on Miettinen and Nurminen method.	
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response Rate Difference
Point estimate	9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	18.8

Secondary: Microbiological and Symptomatic Clinical Success at TOC	
End point title	Microbiological and Symptomatic Clinical Success at TOC
End point description: Microbiological Success: Demonstration that the bacterial pathogen found at study entry (≥10^5 CFU/mL) is eradicated to <10^3 CFU/mL at TOCin the microITT population. Symptomatic Clinical Success: Symptomatic resolution or return to pre-morbid baseline of all UTI-core symptoms patient is alive, and patient has not received additional antibacterial therapy for cUTI) at TOC in the microITT population.	
End point type	Secondary
End point timeframe: Tested at Test of Cure visit (Day 19 to 23).	

End point values	microITT Analysis Population: Cefepime-taniborbactam	microITT analysis population: Meropenem		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	293	143		
Units: participants				
Microbiological Success	229	95		
Symptomatic Clinical Success	251	116		

Statistical analyses

Statistical analysis title	Microbiological Success
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0085 [2]
Method	Miettinen and Nurminen
Parameter estimate	Response rate difference
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	21

Notes:

[2] - p-value for superiority test presented whenever lower confidence interval is greater than 0.

Statistical analysis title	Symptomatic Clinical Success
Comparison groups	microITT Analysis Population: Cefepime-taniborbactam v microITT analysis population: Meropenem
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Response rate difference
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	12.6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessed from screening to late follow-up visit (up to Day 35)

Adverse event reporting additional description:

Adverse events are presented for the safety analysis population, which consisted of all patients who received any dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Cefepime-taniborbactam

Reporting group description: -

Reporting group title	Meropenem

Reporting group description: -

Serious adverse events	Cefepime-taniborbactam	Meropenem	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 440 (2.05%)	4 / 217 (1.84%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (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			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			

Angioedema			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (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			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 440 (0.00%)	2 / 217 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cefepime-taniborbactam	Meropenem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	155 / 440 (35.23%)	63 / 217 (29.03%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	

Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 440 (2.05%)	2 / 217 (0.92%)	
occurrences (all)	9	3	
Phlebitis			
subjects affected / exposed	6 / 440 (1.36%)	1 / 217 (0.46%)	
occurrences (all)	6	1	
Hot flush			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Subclavian artery stenosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 440 (1.14%)	3 / 217 (1.38%)	
occurrences (all)	5	3	
Chills			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Face oedema			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Generalised oedema			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Infusion site swelling			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Injection site inflammation			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Injection site reaction			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hepatic cyst			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pruritus			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	5 / 440 (1.14%)	2 / 217 (0.92%)	
occurrences (all)	5	2	
Dyspnoea			
subjects affected / exposed	4 / 440 (0.91%)	0 / 217 (0.00%)	
occurrences (all)	4	0	
Pleural effusion			
subjects affected / exposed	3 / 440 (0.68%)	0 / 217 (0.00%)	
occurrences (all)	3	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Catarrh			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 440 (0.68%)	2 / 217 (0.92%)	
occurrences (all)	3	2	
Agitation			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Delirium			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Confusional state			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Disorientation			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Mental status changes			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Panic attack			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Restlessness			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Nightmare			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 440 (0.91%)	5 / 217 (2.30%)	
occurrences (all)	4	5	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 440 (0.45%)	2 / 217 (0.92%)	
occurrences (all)	2	2	
Human chorionic gonadotropin increased			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Blood phosphorus decreased			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Transaminases increased			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Blood creatine increased			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram change			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Fibrin D dimer increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Troponin increased			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Weight decreased			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Procedural dizziness			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Angina unstable			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Arrhythmia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Bundle branch block right			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Cardiomegaly			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Angina pectoris			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Atrioventricular block first degree			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	27 / 440 (6.14%)	8 / 217 (3.69%)	
occurrences (all)	27	8	
Dizziness			
subjects affected / exposed	7 / 440 (1.59%)	1 / 217 (0.46%)	
occurrences (all)	7	2	
Akathisia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Diabetic neuropathy			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Psychomotor hyperactivity			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	

Syncope			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Thoracic radiculopathy			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 440 (1.36%)	3 / 217 (1.38%)	
occurrences (all)	6	3	
Thrombocytopenia			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Granulocytosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Splenomegaly			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Thrombocytosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Eye disorders			

Photopsia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 440 (4.09%)	5 / 217 (2.30%)	
occurrences (all)	21	5	
Constipation			
subjects affected / exposed	14 / 440 (3.18%)	3 / 217 (1.38%)	
occurrences (all)	14	3	
Nausea			
subjects affected / exposed	9 / 440 (2.05%)	2 / 217 (0.92%)	
occurrences (all)	9	3	
Abdominal distension			
subjects affected / exposed	7 / 440 (1.59%)	3 / 217 (1.38%)	
occurrences (all)	7	3	
Vomiting			
subjects affected / exposed	6 / 440 (1.36%)	1 / 217 (0.46%)	
occurrences (all)	7	1	
Dyspepsia			
subjects affected / exposed	3 / 440 (0.68%)	1 / 217 (0.46%)	
occurrences (all)	3	1	
Abdominal pain upper			
subjects affected / exposed	2 / 440 (0.45%)	2 / 217 (0.92%)	
occurrences (all)	4	2	
Gastritis			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Stomatitis			

subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Colitis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Aphthous ulcer			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Diaphragmatic hernia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Enlarged uvula			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Glossitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Pancreatic steatosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Abdominal discomfort			

subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Diverticulum intestinal			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Eructation			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Rectal prolapse			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Regurgitation			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Swollen tongue			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	

Biliary dyskinesia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Cholecystitis acute			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Cholestasis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hepatic lesion			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Portal vein thrombosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 440 (0.91%)	0 / 217 (0.00%)	
occurrences (all)	4	0	
Rash			
subjects affected / exposed	3 / 440 (0.68%)	0 / 217 (0.00%)	
occurrences (all)	3	0	
Dermatitis allergic			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Urticaria			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Hair growth abnormal			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	3 / 440 (0.68%)	2 / 217 (0.92%)	
occurrences (all)	3	2	
Ureteric stenosis			

subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Acute kidney injury			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Bladder diverticulum			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Chronic kidney disease			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Diabetic nephropathy			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hydronephrosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Nephritis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Nephrosclerosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Perinephritis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Renal colic			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Urinary tract obstruction			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	3 / 440 (0.68%)	1 / 217 (0.46%)	
occurrences (all)	3	1	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Neck pain			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Arthralgia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Bone pain			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Bursitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Soft tissue swelling			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 440 (0.00%)	2 / 217 (0.92%)	
occurrences (all)	0	2	
Infections and infestations			
Vulvovaginal candidiasis			
subjects affected / exposed	3 / 440 (0.68%)	3 / 217 (1.38%)	
occurrences (all)	3	3	
Upper respiratory tract infection			
subjects affected / exposed	4 / 440 (0.91%)	2 / 217 (0.92%)	
occurrences (all)	6	2	
COVID-19			

subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	2 / 440 (0.45%)	1 / 217 (0.46%)	
occurrences (all)	2	1	
Clostridium difficile colitis			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Renal abscess			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis acute			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Clostridium difficile infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Device related bacteraemia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Myringitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			

subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Tinea pedis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Bacteraemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Mastitis fungal			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Procedural nausea			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 440 (0.45%)	2 / 217 (0.92%)	
occurrences (all)	2	2	

Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	7 / 440 (1.59%)	1 / 217 (0.46%)	
occurrences (all)	9	1	
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 440 (0.45%)	0 / 217 (0.00%)	
occurrences (all)	2	0	
Hypoproteinaemia			
subjects affected / exposed	1 / 440 (0.23%)	1 / 217 (0.46%)	
occurrences (all)	1	1	
Dehydration			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hypernatraemia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Lactose intolerance			
subjects affected / exposed	1 / 440 (0.23%)	0 / 217 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 217 (0.46%)	
occurrences (all)	0	1	
Hypoalbuminaemia			

subjects affected / exposed occurrences (all)	0 / 440 (0.00%) 0	1 / 217 (0.46%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2019	• Made clarifications regarding the assessments and procedures required at end of treatment (EOT) when EOT occurred on Study Day 1 • Updated the definitions used for the study endpoints in response to regulatory feedback from the EMA, including a definition of clinical failure that included use of additional antibiotics for the treatment of cUTI that occurred after EOT. • Corrected an error in the collection window at Study Day 3.
10 December 2019	• Changed unit in Inclusion #4 from cells/µL to cells per high power field • Clarified the primary endpoint and updated the secondary endpoints • Clarified definitions of microbiologically evaluable-End of Treatment, microbiologically evaluable-Test of Cure, and microbiologically evaluable-Late Follow-up populations • Clarified the treatment duration for patients without bacteremia • Added aspartate aminotransferase or alanine aminotransferase ≥10 × upper limit of normal as a potential reason for study drug discontinuation as a result of feedback from the Czech Republic regulatory agency • Revised the definition of success with treatment for asymptomatic bacteremia Added that the race variable African American should only be used for Americans of African descent • Added laboratory abnormalities should be reported as AEs if the result is considered to be clinically significant by the investigator • Added all pregnancies of female clinical study patients or partners of male study patients should be reported to sponsor. Added if written consent was obtained, monitoring of the pregnant patient or partner was to occur • Removed the contract research organization from signature page and replaced with sponsor medical representative.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported