# 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<br>Units: Subjects | | | |
| <65 years | 275 | 137 | 412 |
| 65 to 75 years | 111 | 56 | 167 |
| >75 years | 55 | 27 | 82 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 56.2 | 55.8 | |
| standard deviation | ± 17.43 | ± 18.15 | - |
| Gender categorical<br>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<br>Units: Subjects | | | |
| <65 years | 180 | 90 | |
| 65 to 75 years | 72 | 35 | |
| >75 years | 41 | 18 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 56.5 | 55.8 | |
| standard deviation | ± 17.64 | ± 17.93 | |
| Gender categorical<br>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:<br>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:<br>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.<br><br>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:<br>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<br>occurrences (all) | 0 / 440 (0.00%)<br>0 | 1 / 217 (0.46%)<br>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<br>• 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.<br>• 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<br>• Clarified the primary endpoint and updated the secondary endpoints<br>• Clarified definitions of microbiologically evaluable-End of Treatment, microbiologically evaluable-Test of Cure, and microbiologically evaluable-Late Follow-up populations<br>• Clarified the treatment duration for patients without bacteremia<br>• 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<br>• 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<br>• Added laboratory abnormalities should be reported as AEs if the result is considered to be clinically significant by the investigator<br>• 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<br>• 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