

## Supplemental Digital Content 1

### Inclusion Criteria

The following criteria were required to be met for study inclusion:

1. Patient must have been  $\geq 3$  calendar months to  $< 18$  years of age. Patients  $\geq 3$  calendar months to  $< 1$  year must have been born at term (defined as gestational age  $\geq 37$  weeks).
2. Written informed consent from parent(s) or other legally acceptable representative(s), and informed assent from patient (if age appropriate according to local regulations).
3. If female and has reached menarche, or has reached Tanner stage 3 development, (even if not having reached menarche) the patient was authorized to participate in this clinical study if the following criteria were met:
  - Patient reported sexual abstinence for the prior 3 months or reported the use of at least 1 of the acceptable methods of contraception, including an intrauterine device (with copper banded coil), levonorgestrel intrauterine system or regular medroxyprogesterone injections, or patient agreed to initiate sexual abstinence from the time of screening until 7 days after end of treatment (EOT) with study drug; and
  - Patient was advised to avoid conception from the time of screening until 7 days after receipt of study drug and agreed not to attempt pregnancy from the time of screening until 7 days after EOT with study drug; and

- Patient was provided guidelines regarding continuation of abstinence, initiation of abstinence or about allowed contraception; and
  - Patient had a negative serum human chorionic gonadotropin test just prior to study entry. As serum tests may miss an early pregnancy, relevant menstrual history and sexual history, including methods of contraception, should have been considered.
4. Patient had a clinically suspected and/or bacteriologically documented complicated urinary tract infection (cUTI) or acute pyelonephritis judged by the investigator to be serious and required the patient to be hospitalized for treatment with intravenous (IV) therapy.
5. Patient had pyuria:
- a. Cohorts 1 to 3: determined by a midstream clean catch or clean urethral catheterization urine specimen with  $\geq 10$  white blood cells (WBCs) per high-power field on standard examination of urine sediment or  $\geq 10$  WBCs/mm<sup>3</sup> in unspun urine.
  - b. Cohorts 4a and 4b: determined by a midstream clean catch or clean urethral catheterization urine specimen, or urine specimen obtained using urine collection pads (or supra-pubic collection if standard procedure in the assigned sites)  $\geq 5$  WBCs per high-power field on standard examination of urine sediment or  $\geq 5$  WBCs/mm<sup>3</sup> in unspun urine.
6. Patient had a positive urine culture: 1 midstream clean catch or clean urethral catheterization urine specimen taken within 48 hours of randomization

containing  $\geq 10^5$  colony-forming units (CFU)/mL of a recognized uropathogen known to be susceptible to IV study therapy.

7. Demonstrated either acute pyelonephritis or cUTI, as defined by the following criteria:

- Qualifying criteria: patients must have had at least 1 of the following signs/symptoms (signs/symptoms must have onset or have worsened within 7 days of enrolment) in addition to pyuria:
  - Dysuria (including perceived dysuria as referred by parent/caregiver)
  - Urgency
  - Frequency
  - Abdominal pain
  - Fever – defined as oral temperature  $>38.5^{\circ}\text{C}$  (or equivalent by other methods) with or without patient symptoms of rigor, chills or warmth
  - Nausea
  - Vomiting
  - Irritability
  - Loss of appetite
  - Flank pain

Or patients considered to have complicated UTI as indicated by 2 of the previous qualifying signs/symptoms, plus at least 1 complicating factor from the following:

- Recurrent UTI (2 or more within 12 months period)

- Obstructive uropathy that is scheduled to be surgically relieved during IV study therapy and before EOT
- Functional or anatomical abnormality of the urogenital tract, including anatomic malformations or neurogenic bladder
- Vesicoureteral reflux
- Use of intermittent bladder catheterization or presence of an indwelling bladder catheter for >48 hours before diagnosis of cUTI
- Urogenital procedure (eg, cystoscopy or urogenital surgery) within 7 days before study entry

### **Exclusion Criteria**

Patients were ineligible to participate in this study if any of the following criteria were met:

1. Involvement in the planning and/or conduct of the study.
2. Previous enrollment or randomization in this study, another ceftazidime-avibactam clinical trial or an interventional trial  $\leq 30$  days before IV administration of study drug.
3. Patients with a history of hypersensitivity to carbapenems, cephalosporins, penicillins or other  $\beta$ -lactam antibiotics.
4. Concurrent infection requiring systemic antibiotics in addition to the IV study drug therapy at the time of randomization.
5. Receipt of >24 hours of any systemic antibiotics after culture and before study drug therapy.

6. Receipt of systemic antibiotics within 24 hours before obtaining the study-qualifying pre-treatment baseline urine sample and before study drug therapy.
7. The child was suspected or documented to have an infection caused by organisms resistant to the prophylactic antibiotics.
8. A permanent indwelling bladder catheter or instrumentation including nephrostomy or current urinary catheter that would not be removed or anticipation of urinary catheter placement that would not be removed during the course of IV study drug therapy administration.
9. Patient had suspected or known complete obstruction of any portion of the urinary tract, perinephric abscess or ileal loops.
10. Patient had trauma to the pelvis or urinary tract.
11. Patient had undergone renal transplantation.
12. Patient had a condition or history of any illness that, in the opinion of the investigator, would have made the patient unsuitable for the study (eg, may have confounded the results of the study or posed additional risk in administering the study therapy to the patient).
13. Patient was considered unlikely to survive the 6 to 8-week study period or had a rapidly progressive illness, including septic shock, that was associated with a high risk of mortality.
14. At the time of randomization, patient was known to have a cUTI caused by pathogens resistant to the antimicrobials that were planned to be used in the study.
15. Presence of any of the following clinically significant laboratory abnormalities:
  - a. Haematocrit <25% or haemoglobin <8 g/dL (<80 g/L, <4.9 mmol/L).

b. Serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3 times the age-specific upper limit of normal (ULN), or total bilirubin >2 times ULN (except known Gilbert's disease).

i. For a) and b): unless if these values were acute and directly related to the infectious process being treated.

16. Creatinine Clearance (CrCL) <30 mL/min/1.73 m<sup>2</sup>.

17. History of seizures, excluding well-documented febrile seizures of childhood.

18. If female, currently pregnant or breast feeding.