

Supplemental Digital Content 1

Inclusion criteria

The following were regarded as criteria for inclusion in the study:

1. Must have been ≥ 3 calendar months to < 18 years of age. Patients age ≥ 3 calendar months to < 1 year must have been born at term (defined as gestational age ≥ 37 weeks).
2. Written informed consent obtained from parent(s) or other legally acceptable representative(s), and informed assent obtained from patient (if age appropriate according to local regulations).
3. For females who had reached menarche, or had 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:

At screening:

- i) a) Patient reported sexual abstinence for the prior 3 months or reported use of at least 1 of the acceptable methods of contraception, including an intrauterine device (with copper banded coil), levonorgestrel intrauterine system (eg, Mirena[®]), or regular medroxyprogesterone injections (Depo-Provera[®]); or (b) patient agreed to initiate sexual abstinence from the time of screening until 7 days after end-of-treatment (EOT) with study drug; and

- ii) 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
 - iii) Patient was provided with guidelines regarding continuation of abstinence, initiation of abstinence, or about allowed contraception; and
 - iv) Patient had a negative serum β -human chorionic gonadotropin test just prior to study entry. Since serum tests may miss an early pregnancy, relevant menstrual history and sexual history, including methods of contraception, were to be considered. Note: if the result of the serum β -human chorionic gonadotropin test could not be obtained prior to dosing of investigational product, a patient could have been enrolled on the basis of a negative urine pregnancy test, though a serum β -human chorionic gonadotropin test result must still have been obtained.
4. Must, based on the judgment of the investigator, have required hospitalization initially and antibacterial therapy for 7–15 days in addition to surgical intervention for the treatment of the current cIAI.
5. Required surgical intervention (eg, laparotomy, laparoscopic surgery or percutaneous drainage) to manage the cIAI.
6. Must have had clinical evidence of cIAI as follows:
- i) Pre-operative enrollment inclusion:
 - a. Required surgical intervention that was expected to be completed within 24 hours of enrollment
 - Laparotomy, laparoscopy, or percutaneous drainage.

- b. Evidence of a systemic inflammatory response (at least 1):
 - Fever (defined as oral temperature $>38.5^{\circ}\text{C}$, or equivalent to method used) or hypothermia (with a core body or rectal temperature $<35^{\circ}\text{C}$, or equivalent to method used);
 - Elevated white blood cells ($>15,000\text{ cells/mm}^3$);
 - C-reactive protein levels ($>10\text{ mg/L}$).
- c. Physical Findings consistent with intra-abdominal infection, such as:
 - Abdominal pain and/or tenderness;
 - Localized or diffuse abdominal wall rigidity;
 - Abdominal mass.
- d. Intention to send specimens from the surgical intervention for culture.
- e. (Optional) Supportive radiologic findings of intra-abdominal infection, such as perforated intraperitoneal abscess detected on:
 - Computed tomography scan or
 - Magnetic resonance imaging or
 - Ultrasound.

- ii) Intra-operative/postoperative enrollment inclusion (in cases of postoperative enrollment, must be within 24 hours after the time of incision):

Visual confirmation of intra-abdominal infection associated with peritonitis at laparotomy, laparoscopy, or percutaneous drainage (to be confirmed pending feasibility); must have 1 of these diagnoses:

- Appendiceal perforation or peri-appendiceal abscess;
- Cholecystitis with gangrenous rupture or perforation or progression of the infection beyond the gallbladder wall;
- Acute gastric or duodenal perforations, only if operated on >24 hours after singular perforation occurs;
- Traumatic perforation of the intestines, only if operated on >12 hours after perforation occurs;
- Secondary peritonitis (but not spontaneous bacterial peritonitis associated with cirrhosis and chronic ascites).

Exclusion criteria

The following were regarded as criteria for exclusion from the study:

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 ≤30 days before intravenous administration of study drug.
3. Patients with a history of hypersensitivity to β -lactam antibiotics, metronidazole or nitroimidazole derivatives.
4. Concurrent infection at the time of randomization that may interfere with evaluation of response.
5. Receipt of additional effective concomitant systemic antibacterial drugs.
6. Receipt of non-study systemic antibacterial drug used for the treatment of cIAI in the 72 hours prior to intravenous study drug administration for >24 hours, except if proven pathogen resistance to the administered antibacterial drug and/or worsening of the clinical condition. More than 2 consecutive

doses were not permitted if the individual doses were expected to give >12 hours of cover. Only 1 dose of post-operative non-study drug therapy was permitted for patients enrolled post-surgical procedure.

7. Patient unlikely to survive the 6–8-week study period.
8. Patient unlikely to respond to 7–15 days of treatment with antibiotics.
9. Receipt of hemodialysis or peritoneal dialysis.
10. Diagnosis of uncomplicated or gangrenous appendicitis without rupture, primary peritonitis, peritonitis associated with cirrhosis or chronic ascites, or peritoneal soiling prior to established infection.
11. Patient known to have a complicated intra-abdominal infection caused by pathogens resistant to study therapy at the time of randomization.
12. Clinically significant laboratory abnormalities.
13. Patients with creatinine clearance (CrCL) <30 mL/min/1.73 m².
14. History of seizures, excluding well-documented febrile seizures of childhood.
15. Any patient considered by the investigator as unsuitable for study drug administration.
16. Female patient, currently pregnant or breast feeding.