Ceftazidime-Avibactam and Comparator Agents Tested Against Urinary Tract Isolates from a Global Surveillance Program (2011)

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Abstracted Material

Background: Ongoing Phase III clinical trials for ceftazidime-avibactam (CAZ-AVI) provide evidence of activity against extended-spectrum β-lactamase (ESBL) and carbapenem-resistant agents against a contemporary collection of UTI isolates from the USA, Europe and Mediterranean region (EMR), Latin America (LATAM), and the Asia-Pacific and South Africa (APAC) regions.

Methods: Clinical isolates (one per patient) were collected from hospitalized patients in a UTI during 2011. A total of 1,797 isolates were collected from 159 medical centers (no. of medical centers [no. of isolates]: USA: 48 [610], EMR: 16 [183], LATAM: 30 [138], APAC: 30). Isolates were processed at the medical centers and forwarded to a central laboratory (JM Laboratories, North Liberty, Iowa, USA) for confirmatory identification and susceptibility testing (SST) using CLSI methods. CAZ was tested at a fixed concentration of 4 µg/mL.

Results: CAZ-AVI was highly active against Gram-negative (GN) including Enterobacteriaceae (ENT) and P. aeruginosa (PA). In the USA, EMR, LATAM and APAC there were 0.5/100, MIC 0.06/500 µg/mL CAZ-AVI was 1 µg/mL. In the USA, MIC values were 0.06/250 µg/mL. 94.9% of values in the EMR were 0.5/40 µg/mL. ESBL breakpoints for CAZ were 1 µg/mL in all regions. 25.0/800 µg/mL in APAC. 93.0/1000 (49.1/180) of ENT MIC values were 0.5/40 µg/mL. A total of 0.1% (2/1801) of the USA, 23.5% (28/120) in the EMR, 61.7% (62/98) in LATAM, and 75.0% (72/96) in APAC showed an ESBL phenotype. The MIC values for CAZ in the USA and EMR were 0.06 and 0.12 µg/mL, respectively, while CAZ was the MIC values were 0.06 and 0.32 µg/mL. A total of 1.0/62% of K. pneumoniae isolates in the USA, were non-susceptible (MIC 32 µg/mL). K. oxytoca and 50.0/250 µg/mL in LATAM. The MIC values of 50.0/250 µg/mL in APAC were 0.12 and 0.25 µg/mL, respectively. For CAZ alone the MIC values were 0.12 and 0.25 µg/mL.

Conclusions: CAZ-AVI demonstrated in vitro activity against GN bacteria and PA, including activity against multidrug-resistant organisms.

Introduction

Urinary tract infections are common in both the community and hospital settings. Increasingly resistant and more may occur in complicated urinary tract infections (cUTI), thus making the selection of an appropriate agent for therapy essential. While variation exists in the choice of antimicrobial agents and duration of treatment, the differences occur due to concerns about bacterial resistance among drug classes, drug availability and cost, and expected efficacy and a desire to limit the effect of the antimicrobial on normal bacterial flora.

Ceftazidime-avibactam is a combination agent consisting of the β-lactam bactericidal component ceftazidime and the β-lactamase inhibitor avibactam. Ceftazidime-avibactam administered at 600 mg every 12 hours 8 hours was shown to have efficacy and safety similar to imipenem-cilastatin administered at 600 mg every 6 hours in a Phase II study of UTI (Nctoz et al 2017). A favorable microbiologic outcome of 70.4% and clinical outcome was shown for ceftazidime-avibactam compared to 71.4% for imipenem-cilastatin. In the trial, 18 patients recovered from amongst these patients.

In an effort to evaluate the activity of ceftazidime-avibactam against uropathogens on a global scale, the present study evaluated the activity of ceftazidime-avibactam and comparator agents against a contemporary collection of UTI isolates from the USA, Europe and Mediterranean region (EMR), Latin America (LATAM), and the Asia-Pacific and South Africa (APAC) regions.

Materials and Methods

Organism Collection: Clinical isolates were identified as UTI pathogens based on pathogens both complicated and uncomplicated infections (UTI), as well as from the infections cases that had been treated by the laboratory participant. Isolates were collected from 159 medical centers (no. of medical centers [no. of isolates]: USA: 48 [610], EMR: 16 [183], LATAM: 30 [138], APAC: 30). Isolates were processed at the medical centers and forwarded to a central laboratory (JM Laboratories, North Liberty, Iowa, USA) for confirmatory identification and susceptibility testing (SST) using CLSI methods.

Susceptibility Testing: Isolates were susceptibility tested against ceftazidime-avibactam and comparators by CLSI reference broth microdilution methods. CLSI interpretive criteria were applied per M7-S23.

Results: CAZ-AVI was highly active against ENT bacteria (Table 1) and K. oxytoca and 50.0/250 µg/mL in LATAM. The MIC values of 50.0/250 µg/mL in APAC were 0.12 and 0.25 µg/mL, respectively. For CAZ alone the MIC values were 0.12 and 0.25 µg/mL.

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