Ceftazidime-Avibactam Activity Tested Against Select Gram-Negative Organisms from a Global Surveillance Programme (2011) in Relation to the Ceftazidime Epidemiological Cut-off Value

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Abstract

Objectives: The effect of avibactam (AVI) on the activity of ceftazidime (CAZ) as measured by the CAZ-AVI MIC distribution of select Gram-negative (GN) clinical isolates from the SENTRY Antimicrobial Surveillance Program (SAP) was evaluated as compared to European Committee for Antimicrobial Susceptibility Testing (EUCAST) MIC epidemiological cut-off values (ECOFF) for CAZ-AVI and CAZ. The focus was on novel β-lactamase inhibitors (BLIs) targeting CAZ.

Methods: The activity of CAZ-AVI and CAZ was measured against a global collection of GN bacteria including bloodstream, respiratory, skin and soft tissue, urinary and others. The CAZ-AVI and CAZ were tested in a CLSI broth microdilution method in four regions: EMR, LATAM, APAC, and USA. For each region, a total of 1822 isolates were selected to cover the global surveillance programme, and 670 isolates were excluded from the analysis.

Results: For Enterobacteriaceae, CAZ-AVI MICs ranged from 0.06–0.12/0.25–1 mg/L, for each region and in each region, MICs ranged from 0.25–0.5/0.5–1 mg/L. The lowest levels of CAZ-AVI activity were observed for Proteus mirabilis, Stenotrophomonas maltophilia, and Acinetobacter baumannii. The MIC50/EC50 values for CAZ-AVI were 0.12/0.25 mg/L. Within each region, the MIC distribution against enterobacteriaceae harboring β-lactamases such as CTX-M-15 and CTX-M-9 was similar to those harboring VIM-2.

Conclusions: The results from this study demonstrate that CAZ-AVI has high activity against clinical isolates from the global surveillance programme and is not affected by the presence of β-lactamase inhibitors such as CTX-M-15 and CTX-M-9.

Introduction

The novel non-β-lactam β-lactamase inhibitor avibactam provides a broad spectrum inhibition profile against both class A and class C enzymes, including extended spectrum β-lactamases and KPC-negative strains, as well as activity against some class D enzymes. As an β-lactamase inhibitor, avibactam has very limited intrinsic antibacterial activity. The activity profile of the ceftazidime-avibactam combination determines the antibacterial activity of ceftazidime. Ceftazidime-avibactam has been shown to exhibit in vitro activity against negative bacteria including Enterobacteriaceae strains producing class A and C β-lactamases and Pseudomonas aeruginosa. The activity profile of the ceftazidime-avibactam combination has been investigated in the current study for further evaluation of the MIC distribution for the global collection of Enterobacteriaceae, including bloodstream, respiratory, skin and soft tissue, urinary and others. The study was conducted in four regions: EMR, LATAM, APAC, and USA. For each region, a total of 1822 isolates were selected to cover the global surveillance programme, and 670 isolates were excluded from the analysis.

Materials and Methods

Clinically relevant isolates were collected at medical centres in Europe and the Mediterranean region, Latin America (LATAM), Asia-Pacific (APAC), and USA-Latin America (USA) regions. The isolates included bloodstream, respiratory, skin and soft tissue, urinary, and others. Susceptibility testing was performed using CLSI guidelines, and the MIC distribution was determined according to CLSI and Clinical Laboratory Standards Institute (CLSI) guidelines in colan-colonized Mueller-Hinton broth in validated broth microdilution panels. The CLSI breakpoints for CAZ and CAZ-AVI were used. The MIC distributions were analyzed using various statistical methods.

Results

For Enterobacteriaceae, the CAZ-AVI MIC distribution was broad with MIC values ranging from 0.06–0.12/0.25–1 mg/L. The lowest levels of CAZ-AVI activity were observed for Proteus mirabilis, Stenotrophomonas maltophilia, and Acinetobacter baumannii. The MIC50/EC50 values for CAZ-AVI were 0.12/0.25 mg/L. Within each region, the MIC distribution against enterobacteriaceae harboring β-lactamases such as CTX-M-15 and CTX-M-9 was similar to those harboring VIM-2.

Conclusions

The results from this study demonstrate that CAZ-AVI has high activity against clinical isolates from the global surveillance programme and is not affected by the presence of β-lactamase inhibitors such as CTX-M-15 and CTX-M-9.

References


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