Introduction

Antimicrobial Activity of Ceftazidime-Avibactam and Comparator Agents Tested against Enterobacteriaceae and Pseudomonas aeruginosa from United States Medical Centers Stratified by Infection Type (2015–2016)

INTRODUCTION

Antimicrobial resistance is a significant public health concern in the United States and worldwide. The emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) Enterobacteriaceae has become a major clinical challenge. This study aimed to evaluate the in vitro activity of ceftazidime-avibactam (CAZ-AVI) compared to key comparator agents against Enterobacteriaceae and Pseudomonas aeruginosa isolates from U.S. medical centers.

Materials and Methods

Enterobacteriaceae MDR, XDR, and PDR Enterobacteriaceae isolates were collected from 37 states from all 9 U.S. census divisions in 2015–2016 as part of the INFORM program. These isolates were collected from patients with bloodstream (BSI; 3,434 isolates; 14.7%), pneumonia (6,439 isolates; 28.0%), and/or urinary tract infection (UTI; 3,434 isolates; 14.7%). Only isolates determined to be significant by local criteria as the reported probable cause of infection were included in the program. These isolates were collected from 85 medical centers and/or drug representatives used in the analysis.

Susceptibility testing

Growth of organisms was tested accordingly to CLSI, and ceftazidime-avibactam was tested with antibiotics at fixed concentrations of 1 mg/mL. The inhibitory concentrations (MIC) were susceptible to these antibiotics, and the EUCAST breakpoints were applied for ceftazidime-avibactam (susceptible at ≤8 μg/mL and resistant at ≥16 μg/mL when testing CLSI susceptibility interpretive criteria were applied for comparator agents, and the US FDA breakpoint criteria – PDR = NS to all antimicrobial classes, MDR = nonsusceptible (NS; CLSI breakpoints) to at least 3 antimicrobial classes).

Results

Ceftazidime-avibactam was active against 99.9% of MDR Enterobacteriaceae and 97.6% of XDR Enterobacteriaceae (Figure 1). Susceptibility rates were generally lower among Enterobacteriaceae isolates from SSSI compared to other infection types for β-lactams such as ceftazidime (82.3% vs. 87.1%–90.8%), piperacillin-tazobactam (87.5% vs. 91.5%–94.0%), and gentamicin (80.0% vs. 84.0%–86.0%). The best overall coverage against Enterobacteriaceae was provided by CAZ-AVI, whereas meropenem was very active against P. aeruginosa (99.9% and 97.6%, respectively); whereas meropenem was very active against P. aeruginosa and K. pneumoniae, whereas imipenem was very active against E. coli and K. pneumoniae. The occurrence of MDR, XDR, and CRE phenotypes were markedly higher among isolates from patients with pneumonia compared to other infection types (Figure 2).

Conclusion

Ceftazidime-avibactam represents a potential valuable option for empiric antimicrobial therapy in US hospitals with high prevalence rates of MDR Enterobacteriaceae and P. aeruginosa isolates.

Acknowledgements

All participants of the INFORM Network for Optimal Resistance Monitoring (INFORM) program for providing bacterial isolates.

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The frequency of P. aeruginosa isolates with MDR and XDR phenotypes, as well as nonsusceptible to ceftazidime, meropenem, and piperacillin-tazobactam, was also higher among isolates from patients with pneumonia compared to other infection types. The best overall coverage against Enterobacteriaceae and P. aeruginosa isolates was provided by CAZ-AVI, whereas meropenem was very active against P. aeruginosa and K. pneumoniae, whereas imipenem was very active against E. coli and K. pneumoniae. (Figure 2)

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