Antimicrobial Spectrum and Potency of Ceftaroline-Avibactam when Tested against Bacterial Isolates from Urinary Tract Infections in the United States

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HS SADER, M CASTANHEIRA, RN JONES
JMI Laboratories, North Liberty, Iowa, USA

Abstract

Objective: To evaluate the activity of ceftaroline combined with avibactam (at fixed 4 mg/L) against isolates from complicated urinary tract infections (cUTI) collected in USA medical centers. The MIC activity of ceftaroline-avibactam compared to other β-lactam/β-lactamase inhibitor combinations (piperacillin/tazobactam, imipenem/cilastatin, and meropenem) exhibited low ceftaroline MIC values (≤0.5 mg/L).

Methods: Ceftaroline-avibactam and comparators were tested for susceptibility by CLSI broth microdilution methods against 1131 isolates, including Enterobacteriaceae (46.8% ESBL-phenotype), Streptococcus spp. (103), and Staphylococcus aureus (78), and in 2009-2010 from 65 medical centers located in all nine USA Census Regions.

Results: Overall, 98.4% of strains were inhibited at ≤0.25 mg/L of ceftaroline-avibactam and all 18 isolates with ceftaroline-avibactam MIC at ≤2 mg/L were E. faecalis. E. coli and Klebsiella spp. were very susceptible to ceftaroline-avibactam with MICs of ≤0.03/0.06 and 0.06/0.12 mg/L, respectively. Ceftazidime and ciprofloxacin were active against 92.0% and 73.9% of E. coli and 92.3% and 94.2% of Klebsiella spp., respectively. 1.5% of Klebsiella spp. were resistant to meropenem (Table 1).

Conclusions: Ceftaroline combined with avibactam represents a potential therapeutic option for the treatment of multidrug-resistant organisms causing UTIs.

References


Materials and Methods

Introduction

Urinary tract infection (UTI) is one of the commonest nosocomial infections and a main source of bacteremia in hospitalized patients. Ceftaroline, the active component of ceftaroline fosamil, is a broad-spectrum cephalosporin with potent activity against Gram-positive organisms (including methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus epidermidis (MRSE)). No single agent has limited activity against organisms that produce extended-spectrum β-lactamase (ESBL). Ceftriaxone, deprosper AmpC and carbapenemases.

Avibactam (also known as NXL014) is a non-β-lactam inhibitor of class D β-lactamases that displays a broad-spectrum inhibition profile against both class A and class C β-lactamases. It is a variable activity of class D β-lactamases. Avibactam, however, is not inhibited from hydrolysis by a variety of strains producing enzymes, including AmpC, AmpC and KPC types. In this study, we report the activity of the inhibitory combination with avibactam (fixed 4 mg/L) against isolates from complicated UTI (cUTI), including ESBL and AmpC-producing recovered in USA medical centers in 2009 and 2010.

Table 1. Summary of ceftaroline activity against organisms collected from patients with urinary tract infections in USA medical centers (2009 - 2010).

Table 2. Antimicrobial activity of ceftaroline-avibactam and comparator agents tested against bacterial isolates from urinary tract infections.

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Antimicrobial susceptibility testing:

All isolates were tested for antimicrobial susceptibility by the broth microdilution method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI) (M07-A9). Interpretive criteria for ceftaroline-avibactam were established by CLSI, with ceftaroline-avibactam activity against a large collection of Enterobacteriaceae and Gram-positive organisms isolated in USA medical centers from patients with cUTI by EUCAST.

For Enterobacteriaceae strains resistant to broad-spectrum cephalosporins (ceftaxime and ceftazidime), β-lactam/β-lactamase inhibitor combinations (piperacillin/tazobactam and meropenem) exhibited low ceftaroline MIC values (≤0.5 mg/L). Ceftaroline combined with avibactam represents a potential therapeutic option for the treatment of multidrug-resistant organisms causing UTIs.