Activity of Ceftazidime-Avibactam Tested Against Contemporary (2012) Pathogens from Urinary Tract and Intraabdominal Infections from Patients in the USA

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Abstract

Background: The investigational antimicrobial combination of ceftazidime-avibactam and the novel β-lactamase inhibitor avibactam (AVI) is undergoing Phase III clinical development. In this report, we present the results of testing CAZ-AVI and meropenem (MER) against clinical isolates from patients with urinary tract (UTI) or intraabdominal (IAI) infections.

Methods: UTI and IAI isolates (one per patient episode) were collected during 2012 at 73 USA medical centers. Isolates were processed at the medical centers and forwarded to a central laboratory for confirmatory identification and susceptibility (S) testing using CLSI methods. Results: CAZ-AVI demonstrated potent activity against Enterobacteriaceae (ENT) isolated from both UTI and IAI (MIC, ≤0.12/0.06 µg/mL for both). The most active agent against ENT for both UTI and IAI was colistin (MIC, ≤0.5/0.5 µg/mL), followed by ceftazidime (MIC, ≤0.5/0.5 µg/mL). CAZ-AVI and MER both had excellent activity against Enterobacter cloacae spp. from UTI and IAI isolates from IAI, the MIC50 and MIC90 were 0.5 and 1 µg/mL, respectively. The investigational antimicrobial combination of ceftazidime-avibactam and comparator agents against a contemporary collection of isolates from patients with UTI and IAI in the USA (2012).

Introduction

Antibiotics is an investigational non β-lactam B-lactamase inhibitor that has been linked to a small-incretin pump inhibition profile against both class A and class C β-lactamases, including extended spectrum β-lactamase (ESBL) and metallo-β-lactamases, as well as activity against some class D β-lactamases. Avibactam alone has very low intrinsic antibacterial activity. When combined with ceftazidime, the combination has shown potent in vitro activity against many CRE and non-S PSA isolates including resistant Enterobacteriaceae (ENT) isolated from both UTI and IAI.

Results

<table>
<thead>
<tr>
<th>Organism/antimicrobial</th>
<th>MIC (µg/mL)</th>
<th>%S / %I / %R</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli UTI</td>
<td>0.12/2</td>
<td>91.8 / 0.9 / 7.1</td>
</tr>
<tr>
<td>E. coli IAI</td>
<td>0.5/32</td>
<td>66.7 / 3.3 / 30.0</td>
</tr>
<tr>
<td>P. aeruginosa UTI</td>
<td>2/32</td>
<td>84.0 / 1.8 / 14.2</td>
</tr>
<tr>
<td>P. aeruginosa IAI</td>
<td>4/32</td>
<td>81.7 / 2.2 / 16.1</td>
</tr>
</tbody>
</table>

Conclusions: CAZ-AVI demonstrated potent activity against contemporary Gram-negative pathogens including multidrug-resistant isolates from patients with UTI and IAI in USA hospitals.

Acknowledgment

This study was supported by Astellas USA, Inc. The efficacy and safety of ceftazidime-avibactam were demonstrated in a randomized study. The present study is an informational supplement.

References