Activity of Ceftazidime-Avibactam and Comparators Against Carbapenemase-Producing Enterobacteriaceae Isolated in Sampled Countries of the European Union: 2013 INFORM Surveillance Program

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Abstract

Two of these three strains were resistant to all drugs, and one was resistant to all drugs except colistin. Overall, 84.7% of two isolates contained a MBL and a KPC, and one isolate contained an MBL and an OXA-48 (not included in the Table).

Introduction

Carbapenem-resistant Enterobacteriaceae (CRE) are becoming a global threat. Resistance in these organisms is mainly driven by production of carbapenemases, which are being disseminated among these species worldwide (carbapenemase-producing Enterobacteriaceae, or CPE).

Carbapenemase-avibactam, a combination of ceftazidime with the novel non-β-lactam β-lactamase-inhibitor avibactam, has promising activity against Enterobacteriaceae, including those that are resistant to carbapenems.

Here we assessed the in vitro activity of ceftazidime-avibactam and comparator agents against molecularly characterised CRE isolated from member states of the European Union in the 2013 INFORM surveillance program.

Materials & Methods

MICs were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [1]. MIC interpretive criteria followed EUCAST guidelines [2].

An isolate of Enterobacteriaceae was defined as CRE if it was not susceptible to meropenem, using EUCAST interpretive criteria [2]. The presence of genes encoding β-lactamases (OXA-48, KPC, and MBLs) was assessed via multiplex PCR, followed by sequencing.

No breakpoints have been defined for ceftazidime-avibactam and a reference value of MIC ≤5 μg/mL (based upon PK/PD target attainment) was used for comparative purposes.

Results

Table 1. In vitro Activity of Ceftazidime-Avibactam and Comparator Agents Tested Against Enterobacteriaceae

<table>
<thead>
<tr>
<th>Group</th>
<th>β-Lactamase Type</th>
<th>MIC (μg/mL)</th>
<th>% Susceptible</th>
<th>% Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Enterobacteriaceae</td>
<td>MBL only</td>
<td>≤0.5</td>
<td>96.9</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>MBL, KPC, OXA-48</td>
<td>≤0.5</td>
<td>95.5</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>MBL, KPC</td>
<td>≤0.5</td>
<td>95.5</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>MBL, OXA-48</td>
<td>≤0.5</td>
<td>95.5</td>
<td>4.5</td>
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<tr>
<td></td>
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<td>≤0.5</td>
<td>95.5</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Ceftazidime-avibactam was active against CRE in vitro, with 99% of isolates susceptible to avibactam.

Figure 1a and b. Country Distribution of CRE Isolates Collected From European Union

Figure 2a and b. Species Distribution of CRE Isolates Collected From European Union

Conclusions

• Carbapenem-avibactam was active in vitro against Enterobacteriaceae isolated from member states of the European Union in the 2013 INFORM surveillance program.

• Carbapenem-avibactam was active in vitro against CRE, with the exception of isolates that carried genes encoding MBL enzymes.

• Carbapenem-avibactam was active against CRE mediated by KPC- or OXA-48.

• Carbapenem-avibactam was active against CRE where carbapenem resistance was not mediated by known carbapenemases.

• Carbapenem-avibactam is a potentially valuable therapeutic option for the treatment of infections of infections caused by non-MBL-carrying CRE.

References and Acknowledgments


http://www.eucast.org/clinical_breakpoints/

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