Activity of ceftazidime-avibactam against carbapenem non-susceptible Enterobacteriaceae isolated from respiratory infections as part of the INFORM global surveillance program, 2014–2015

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Abstract

Ceftazidime-avibactam was not active against MBL-positive isolates (<6% susceptible), as expected. As GES, n=1). Ceftazidime-avibactam showed potent activity against carbapenemase-positive MBL-negative isolates, including 98.9% (MIC ≤8 mg/L) of CRE carrying KPC, OXA-48-like β-lactamases developed to treat infections caused by CRE that possess serine carbapenemases or non-carbapenemase-mediated mechanisms. We evaluated the activity of ceftazidime-avibactam in vitro against 220 CRE isolates from patients with RTI collected from patients with RTI (n=220). The in vivo activity of ceftazidime-avibactam was greater than that of comparator agents (cefepim, levofloxacin, tigecycline, and meropenem) against MBL-negative CRE (Figure 2E). Ceftazidime-avibactam was active in vitro against 48.9% (MIC ≤8 mg/L) of CRE carrying KPC, OXA-48-like β-lactamases developed to treat infections caused by CRE that possess serine carbapenemases or non-carbapenemase-mediated mechanisms. The activity of ceftazidime-avibactam was comparable to that of colistin in AP and exceeded it in all other regions (Table 1). Ceftazidime-avibactam provides a new treatment option for respiratory infections caused by CRE that possess serine carbapenemases or non-carbapenemase-mediated resistance mechanisms varied among regions.

Table 1. In vitro activity of ceftazidime-avibactam and comparator agents against CRE collected globally from patients with RTI.

<table>
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<tr>
<th>Agent</th>
<th>MIC Distribution (%)</th>
<th>0.03</th>
<th>0.12</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>16</th>
<th>32</th>
<th>64</th>
<th>128</th>
<th>&gt;128</th>
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<td>Ceftazidime</td>
<td></td>
<td>≤0.015</td>
<td>0.06</td>
<td>0.12</td>
<td>&gt;128</td>
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Results


Conclusions

• Ceftazidime-avibactam provides a new treatment option for respiratory infections caused by CRE that possess serine carbapenemases or non-carbapenemase-mediated resistance mechanisms varied among regions.
• Regional differences in the incidence of MBL-mediated resistance are important to consider when assessing the value of ceftazidime-avibactam.

Materials & Methods

1. CRE isolates were collected from 417 medical centers in 27 countries. Infection sources included sputum (n=241), respiratory secretion (n=125), bronchoalveolar lavage (n=10), skin (n=2), joint (n=2), bile (n=1), and other (n=2).

2. CRE were atypical isolates with resistance to carbapenem (MIC >8 mg/L) and were screened for the presence of β-lactamase genes encoding carbapenemases (CPE, OXA-48-like, OXA-163, OXA-164, OXA-232, NDM-1), metallo-β-lactamases (MBL, IMP-1, VIM-1, SIM-1), extended-spectrum β-lactamases (ESβ-lactamases), ketolactamases, cephalosporinases, beta-lactam/beta-lactamase (BL/BLase) in vitro

3. ISs were performed by PCR followed by sequencing as described previously.

Figure 2A. Ceftazidime-avibactam MIC distributions against CRE isolates collected globally from patients with RTI (n=220).

Figure 2B. Ceftazidime-avibactam MIC distributions against carbapenemase-negative CRE isolates collected from patients with RTI (n=220).

Figure 2C. Ceftazidime-avibactam MIC distributions against MBL-negative CRE isolates collected from patients with RTI (n=220).

Figure 2D. Ceftazidime-avibactam MIC distributions against OXA-48-like CRE isolates collected from patients with RTI (n=220).

Figure 2E. Ceftazidime-avibactam MIC distributions against MBL-positive CRE isolates collected from patients with RTI (n=220).

Table 1. In vitro activity of ceftazidime-avibactam and comparator agents against CRE collected globally from patients with RTI.