Antimicrobial Activity of Aztreonam-Avibactam and Comparator Agents Tested against Contemporary (2016) Clinical Enterobacteriaceae Isolates

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INTRODUCTION

• Infection due to carbapenem-resistant Enterobacteriaceae (CRE) has become a major public health concern. The ability to evaluate the in vitro activity of novel agents against contemporary (2016) CRE isolates is necessary for guiding the selection of appropriate therapy.

• Aztreonam-avibactam (AZT-AB) is a novel β-lactamase inhibitor/β-lactam combination being studied as a potential therapeutic agent for CRE infections due to its potential activity against metallo-β-lactamases (MBLs).

MATERIALS AND METHODS

• Isolates were collected from 250 US hospitals (106 CRE) and healthcare settings (144 non-CRE) during 2016.

• CRE isolates were identified as carbapenemase producing resistant Enterobacteriaceae (CRE) and were collected from the United States.

• CLSI MDR breakpoints (≤2 μg/mL for susceptible and ≥4 for resistant) were applied to determine the disc susceptibility profile.

• CRE isolates were collected from 250 US hospitals (106 CRE) and healthcare settings (144 non-CRE) during 2016.

RESULTS

• Among MDR isolates (n = 106), aztreonam-avibactam was very active (MIC ≤0.03 μg/mL) against Enterobacter aerogenes (96.8%), Klebsiella pneumoniae (87.5%), and Enterobacter cloacae (82.4%).

• Aztreonam-avibactam was compared to selected carbapenem, ß-lactamase inhibitor, and ß-lactamase inhibitor/ß-lactam agents.

• Breakpoints from US FDA Package Insert were applied to carbapenem agents.

• Carbapenemase-negative CRE isolates were generally susceptible (≥90%) to the carbapenem agents tested.

• Carbapenemase-producing CRE isolates were generally susceptible (≥90%) to the carbapenem agents tested.

• Aztreonam-avibactam was very active (MIC ≤0.03 μg/mL) against MDR CRE isolates from the United States.

• Aztreonam-avibactam was compared to selected carbapenem, ß-lactamase inhibitor, and ß-lactamase inhibitor/ß-lactam agents.

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• Aztreonam-avibactam was very active (MIC ≤0.03 μg/mL) against MDR CRE isolates from the United States.

Table 1: Antimicrobial activity of aztreonam and avibactam against CRE isolates from United States hospitals (2016)

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>MIC50 (µg/mL)</th>
<th>MIC90 (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam-avibactam</td>
<td>&lt;0.03</td>
<td>&lt;0.06</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0.03</td>
<td>0.06</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>&gt;32</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&gt;8</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Timentin</td>
<td>&gt;2</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Colistin</td>
<td>&gt;32</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>&gt;0.5</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Aztreonam</td>
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<td>&gt;2</td>
</tr>
<tr>
<td>Amikacin</td>
<td>&gt;8</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>

Table 2: Activity of aztreonam and avibactam against CRE isolates from United States hospitals (2016)

- Carbapenemase-negative CRE isolates were generally susceptible (≥90%) to the carbapenem agents tested.
- Carbapenemase-producing CRE isolates were generally susceptible (≥90%) to the carbapenem agents tested.
- Aztreonam-avibactam was very active (MIC ≤0.03 µg/mL) against MDR CRE isolates from the United States.

Table 3: Carbenapenem results by organism for 120 carbapenem-resistant Enterobacteriaceae (CRE) isolates collected during 2016 in the United States

Table 4: Carbapenem results by organism for 250 carbapenem-resistant Enterobacteriaceae (CRE) isolates collected during 2016 worldwide (ex-US)

CONCLUSIONS

• Aztreonam-avibactam is a promising agent with activity against a large collection of contemporary (2016) CRE isolates, including MDR, XDR, and pan-drug resistant Enterobacteriaceae.

• Aztreonam-avibactam is an attractive option for the treatment of CRE infections, especially in regions with high rates of MDR CRE isolates.

ACKNOWLEDGEMENTS

• The authors would like to thank all the hospitals involved in the design and execution to provide these results, and JMI Laboratories for supporting the research.

REFERENCES


Figure 1: Antimicrobial activity of aztreonam-avibactam tested against carbapenem-resistant Enterobacteriaceae (CRE) isolates.

Figure 2: Activity of aztreonam and avibactam against CRE isolates from United States hospitals (2016).