Activity of Eravacycline against Carbapenemase-producing Enterobacteriaceae and Acinetobacter baumannii

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Background: Eravacycline is a fluorocycline antibiotic, now in Phase 3, which largely evades acquired efflux and ribosomal types of tetracycline resistance. We evaluated its MICs vs. carbapenem- and tigecycline-resistant Enterobacteriaceae and Acinetobacter isolates, mostly with resistance to beta-lactams, quinolones, aminoglycosides and classical tetracyclines. Methods: Organisms (n=370) were recent submissions to the UK reference laboratory; carbapenemase genes were sought by PCR, with MICs determined by CLSI broth dilution. Results: Eravacycline MIC₉₀ for Enterobacteriaceae with KPC, NDM, OXA or VIM carbapenemases, excluding (i) Proteae and (ii) isolates specifically chosen for tigecycline resistance, were 1-2 mg/L vs. 1-4 mg/L tigecycline. Corresponding MIC₉₀s for carbapenem-susceptible control strains were 0.5 and 1 mg/L, respectively. This differential between MIC₉₀s for carbapenemase producers vs. control strains partly reflected a greater proportion of E. coli among the latter but the trend persisted when Klebsiella spp. alone were considered. Eravacycline MIC₉₀s for A. baumannii with OXA carbapenemase were 1 mg/L vs. 2-4 mg/L tigecycline; corresponding MIC₉₀s for carbapenem-susceptible controls were 0.5 mg/L eravacycline and 2 mg/L tigecycline. A frequent 2-fold MIC advantage of eravacycline over tigecycline for Enterobacteriaceae (2-4-fold for Acinetobacter spp.) persisted across the full ranges of MICs (Table).

<table>
<thead>
<tr>
<th>Tigecycline MIC, mg/L</th>
<th>Eravacycline MIC : tigecycline MIC ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae, excluding Proteae</td>
<td>0.12</td>
</tr>
<tr>
<td>&lt;=1</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>&gt;=4</td>
<td>24</td>
</tr>
<tr>
<td>A. baumannii</td>
<td></td>
</tr>
<tr>
<td>&lt;=1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>&gt;=4</td>
<td>9</td>
</tr>
</tbody>
</table>

Conclusions: Eravacycline was widely active vs. carbapenemase-producing Enterobacteriaceae and Acinetobacter. MICs rarely exceeded 1-2 mg/L and mostly were 2-fold lower than for tigecycline,
including for tigecycline-resistant strains. Nevertheless, eravacycline (and tigecycline) MICs often were slightly higher for carbapenemase producers than for carbapenem-susceptible isolates.

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