Activity of meropenem-vaborbactam and single-agent comparators against Enterobacteriales isolates, including KPC-producing isolates, from European patients hospitalized with pneumonia including ventilator-associated pneumonia (2014–2019)

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Introduction
- Carbapenem-resistant Enterobacteriales (CRE) isolates are a growing global antimicrobial resistance threat and are endemic in many hospitals in various countries.
- CRE, including VAP isolates, are often multiply resistant and have limited treatment options.
- Carbapenemase-producing isolates are defined by a combination of their carbapenem resistance and the presence of at least one carbapenemase.
- Carbapenemase enzymes are often used as treatments for infections caused by CRE strains.

Figure 1 Five most common Enterobacteriales species isolated from pneumonia

Materials and Methods
- 6,846 Enterobacteriales PH isolates collected in 40 European hospitals across 20 countries were susceptibility tested using reference broth microdilution methods (CLSI 2018).
- 1,454 isolates were also screened for the extended-spectrum beta-lactamase (ESBL) phenotype (CLSI 2020), isolates that were ESBL-positive and/or isolates with high levels of resistance were tested for carbapenemase activity.
- Carbapenemase activity was determined by using the Kirby–Bauer method and interpreted according to CLSI guidelines.
- Enterobacterales isolates were screened for ESBL, OXA-48-like, and VIM or NDM enzymes, and Enterobacterales isolates that were ESBL-positive were tested for carbapenemase activity.

Table 1 Susceptibility of meropenem-vaborbactam and comparators against Enterobacteriales isolates from patients hospitalized with pneumonia

<table>
<thead>
<tr>
<th>Organisms/organism groups</th>
<th>Meropenem-vaborbactam</th>
<th>Meropenem</th>
<th>Amikacin</th>
<th>Gentamicin</th>
<th>Levofloxacin</th>
<th>Colistin</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRE (81)</td>
<td>100.0/100.0</td>
<td>0.0/0.0</td>
<td>56.0/48.0</td>
<td>41.3/38.9</td>
<td>7.7/7.7</td>
<td>-/81.3</td>
</tr>
<tr>
<td>ESBL-phenotype (455)</td>
<td>84.2/86.8</td>
<td>69.9/73.8</td>
<td>75.6/67.3</td>
<td>46.2/44.6</td>
<td>20.7/20.7</td>
<td>-/86.5</td>
</tr>
<tr>
<td>ESBL non-CR (324)</td>
<td>100.0/100.0</td>
<td>96.6/100.0</td>
<td>89.2/82.4</td>
<td>49.1/47.8</td>
<td>27.5/27.5</td>
<td>-/90.4</td>
</tr>
<tr>
<td>CRE (144)</td>
<td>45.8/56.2</td>
<td>4.9/11.1</td>
<td>45.8/34.7</td>
<td>41.7/38.9</td>
<td>7.7/7.7</td>
<td>-/77.1</td>
</tr>
</tbody>
</table>

Conclusions
- The highest susceptibility (≥79.5%) of tested agents against pathogens isolated from patients hospitalized with pneumonia, including VAP.
- CRE-isolated VAP isolates had similar susceptibilities for meropenem and vaborbactam, with a lower susceptibility for colistin.
- The overall rate of CRE isolates was 5.2%, and the type of carbapenemase was associated with some MIC ranges.
- For VABP, meropenem-vaborbactam and colistin producing isolates in Eastern European countries.
- Carbapenem resistance was very high against Enterobacteriales isolates producing VAP isolates (100%) of all isolates.
- These data suggest meropenem-vaborbactam is a useful treatment option for both ICU and non-ICU patients hospitalized with pneumonia, including VAP isolates from CRE-resistant Enterobacterales isolates in Europe with high levels of resistance.

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References

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Table 2 Activity of meropenem and meropenem-vaborbactam against KPC-producing isolates

<table>
<thead>
<tr>
<th>Organism</th>
<th>Meropenem</th>
<th>Meropenem-vaborbactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. pneumoniae</td>
<td>≤0.5</td>
<td>≤0.12</td>
</tr>
<tr>
<td>E. coli</td>
<td>≤0.5</td>
<td>≤0.12</td>
</tr>
</tbody>
</table>

Figure 2 Meropenem-vaborbactam MICs (mg/L) distribution of Enterobacteriales isolates from PHP® for ICU non-CRE patients and patients for which ICU status was not available

Figure 3 Activity of meropenem and meropenem-vaborbactam against KPC-producing isolates

Figure 4 European countries with KPC, metals-2-lactamases or ≤0.48-log carbapenemases

*PHP, patients hospitalized with pneumonia; ICU, intensive care unit; ICU-VAP, ICU patients with ventilator-associated pneumonia; non-ICU, in hospital - CR carbapenem resistant, b No CLSI susceptible category for colistin.