Activity of Meropenem-Vaborbactam and Comparators Against Globally Disseminated Klebsiella pneumoniae

Sequence Type 258

Dee Shortridge, Lalitgauri Deshpande, Tim Doyle, Jennifer Streit, Mariana Carsteanu

JMI Laboratories, North Liberty, IA, USA

Introduction

- Meropenem-vaborbactam (MVB) is a combination of a carbapenem and a β-lactamase inhibitor active against β-lactamases, including some carbapenemases (Carsteanu, Nickel et al. 2017).
- MVB recently was approved in the US and Europe for the treatment of carbapenem-resistant (CR) K. pneumoniae. It is approved in Europe for treatment of carbapenem-resistant infections, hospital-acquired bacterial pneumonia, ventilator-associated pneumonia, and K. pneumoniae (Klebsiella Therapeutics 2019).
- Carbapenemases producing Enterobacteriaceae, particularly K. pneumoniae, have spread worldwide and are considered endemic in many countries (Carsteanu, Nickel et al. 2017).
- Approximately 2,000–3,000 KPC-producing strains were identified in 2016 among all Enterobacteriaceae in the SENTRY Antimicrobial Surveillance Program (Carsteanu, Nickel et al. 2017).
- Multiple outbreaks have been associated with KPC, resulting in ST258 (Chen, Mathema et al. 2014).
- In this study, we examined the susceptibilities of 130 ST258 isolates collected as part of the SENTRY antimicrobial susceptibility program.

Materials and Methods

- As part of the SENTRY Antimicrobial Surveillance Program for carbapenemase-resistant MVB from 2016–2018, 130 K. pneumoniae were collected.
- Isolates were tested for susceptibility against meropenem-vaborbactam and comparator agents using the reference broth microdilution method as described by the Clinical and Laboratory Standards Institute (CLSI 2018).
- MVB was tested at a fixed final concentration of 0.1 mg/L.
- Quality control (QC) was performed according to the CLSI M100 (2020) criteria.
- All QC MIC results were within acceptable ranges.
- Clinical and laboratory standards Institute (CLSI 2018).
- Carbapenem-resistant K. pneumoniae (CR-KPC) isolates were identified as resistant to ≥2 mg/L.
- CR-KPC isolates were submitted to whole genome sequencing on a MiSeq (Illumina, CA, USA) and assembled, searched for the presence of acquired carbapenemases using a curated library, and aligned the criteria of ≥94% sequencing identity and 40% minimum length coverage.
- The sequence type was determined by whole genome sequencing analysis.

Results

- The most common infection type from which K. pneumoniae was isolated was bloodstream infection (34, 25%). followed by pneumonia in hospitalized patients (26, 19%).
- 1,877 isolates were CR (13.0%).
- A subset of 130 CR-K. pneumoniae ST258 isolates were selected for further study. Susceptibilities of MVB and comparators for these isolates are shown in Table 1.
- The MIC distributions for the isolates and comparators are shown in Table 2.
- MVB inhibited 62.0% of the isolates and was the most active agent overall; only 23.1% of these isolates were meropenem susceptible.
- Of 130 isolates, 127 isolates were MDR and 83 isolates were XDR.
- Tigecycline was the most active comparator with 98.5% susceptibility.
- Ambicillin had 30.8% susceptibility.
- The geographic distribution of ST258 isolates is shown in Figure 1.
- The MIC distributions for the isolates and comparators are shown in Figure 2.
- Tigecycline was the most common carbapenemase; 73 isolates produced KPC (including 2 KPC-1 and 2 KPC-2). The 130 had 24 KPC-2 isolates, followed by BL, and Greece, which had 17 each.
- K. pneumoniae was produced by 25 isolates, 19 of which were from the US.
- The MIC distributions for the isolates and comparators are shown in Figure 2.

Conclusions

- Isolates from the internationally disseminated K. pneumoniae clone ST258 were found in 6 countries.
- ST258 was most frequently found in the US (45.3%).
- KPC was the most common carbapenemase among CR isolates.
- Only 7 non-KPC carbapenemase-producing isolates were found.
- The MIC distributions for the isolates and comparators are shown in Figure 2.
- KPC may be useful for the treatment of infections caused by MDR and XDR K. pneumoniae.

Table 1: Susceptibilities of meropenem-vaborbactam and comparators to K. pneumoniae ST258 isolates by country

<table>
<thead>
<tr>
<th>Country</th>
<th>MVB</th>
<th>Colistin</th>
<th>Piperacillin-tazobactam</th>
<th>Imipenem</th>
<th>Tigecycline</th>
<th>Meropenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>98</td>
<td>97</td>
<td>68</td>
<td>68</td>
<td>85</td>
<td>71</td>
</tr>
<tr>
<td>Europe</td>
<td>89</td>
<td>61</td>
<td>42</td>
<td>50</td>
<td>74</td>
<td>70</td>
</tr>
<tr>
<td>Latin America</td>
<td>75</td>
<td>63</td>
<td>37</td>
<td>50</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Asia</td>
<td>57</td>
<td>63</td>
<td>37</td>
<td>50</td>
<td>75</td>
<td>70</td>
</tr>
</tbody>
</table>

Table 2: MIC distributions of meropenem-vaborbactam and comparators for 130 K. pneumoniae ST258 isolates

<table>
<thead>
<tr>
<th>Drug</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>≥256</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meropenem</td>
<td>32.7</td>
<td>21.5</td>
<td>3.8</td>
<td>0.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaborbactam</td>
<td>65.4</td>
<td>14.5</td>
<td>0.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVB</td>
<td>90.8</td>
<td>2.3</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Acknowledgements

This study was supported by Klebsiella Therapeutics, Inc.

References


JMI (2020). "JMI Laboratories, North Liberty, IA, USA.”

Klebsiella Therapeutics (2019). "Meropenem-Vaborbactam Tested against Contemporary Gram-Negative Bacteria: Multidrug-Resistant Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter baumannii.”


Microbiol Therapeutics (2019). "Meropenem-Vaborbactam Tested against Contemporary Gram-Negative Bacteria: Multidrug-Resistant Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter baumannii.”


Contact

Dee Shortridge, PhD
JMI Laboratories
2502 S. Center Street, Suite 4
North Liberty, Iowa 52317
Phone: (319) 263-5770
Fax: (319) 663-3777
Email: dee-shortridge@jmilabs.com