Introduction

PLG0206 is an investigational, engineered cationic antimicrobial peptide designed to overcome the shortcomings of other natural AMPs, such as toxicity and limited activity (1,2). PLG0206 has recently been shown to be well tolerated and safe in a phase 1 study (3).

The current study evaluated the activity of PLG0206 and comparator antimicrobials against Enterobacterales isolates collected from various worldwide locations in 2019.

Materials and Methods

- Isolates tested included Citrobacter spp. (151), Enterobacter cloacae (152), Escherichia coli (300), Klebsiella pneumoniae (300), Morganella morganii (43), Proteus spp. (152), Providencia spp. (61) and Serratia marcescens (45).
- The isolates were collected in 2019, with approximately one-third from Europe and the remainder from other regions (Figure 1). The isolates originated from a variety of infection types (Figure 2).
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (4) in cation-resistant Mueller Hinton broth (CA-MHB), except for PLG0206 which was tested in MOPS RPMI-1640 medium supplemented with 0.004% Tween-80 due to precipitation of PLG0206 observed in CAMHB.
- The susceptibility of comparator antimicrobials was determined using the 2022 CLSI breakpoints (5). Multi-drug-resistance (MDR) was defined as resistance to 3 or more of the antimicrobials tested by class of antimicrobial including aminoglycosides (amikacin, gentamicin or tobramycin), cephalosporins (cefepime, cefoxitin or ceftazidime), fluoroquinolones (levofloxacin or ciprofloxacin) and tetracyclines (doxycycline or tetracycline [non-susceptible]) or by individual antimicrobial for aztreonam, colistin, ceftazidime/avibactam, meropenem, and meropenem/vaborbactam.

Results

Table 2: Summary activity of PLG0206 and comparators against Citrobacter spp.

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC (μg/mL)</th>
<th>%S</th>
<th>%I</th>
<th>%R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrobacter spp.</td>
<td>0.25</td>
<td>90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>E. coli</td>
<td>0.25</td>
<td>90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>E. cloacae</td>
<td>0.25</td>
<td>90</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions

- PLG0206 was active against Citrobacter spp., E. coli, E. cloacae, and K. pneumoniae, but inactive against Providencia spp., M. morganii, Proteus spp. and S. marcescens (Figure 3).
- PLG0206 activity compared well with the other test antimicrobials with MIC<sub>50</sub> values lower than most comparators (Tables 1 and 2).
- PLG0206 retained activity against MDR isolates of Citrobacter spp. (26), E. coli (62), E. cloacae (45), and K. pneumoniae (132) with virtually unchanged MIC<sub>50</sub> or MIC<sub>90</sub> (Table 3).

References

5. CLSI. 2023. Performance Standards for Antimicrobial Susceptibility Testing. 32nd ed. CLSI supplement M100. CLSI, Wayne, PA, USA.

Acknowledgments

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