Activity of Pexiganan When Tested Against Contemporary Gram-Negative, Gram-Negative Bacteria and Yeast Collected from North America, Europe and Japan

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Amended Abstract

Background: Pexiganan is a new carbapenem antibiotic. Methods CFP-50 in Phase 3 clinical trials as a topical cream for the treatment of infections caused by beta-lactamase-producing pathogens. This study was to evaluate the current in vitro activity of pexiganan against beta-lactamase-producing isolates from Europe, North America, and Japan.

Methods: A total of 0.26% Gram-positive (97) and 274 Gram-negative (77) and 153 Candida albicans isolates (94% from Europe, 5% from Japan, and 1% from North America) were used for determination of MICs and compared with CLSI and EUCAST reference broth dilution methods. Isolates were from human sources of infection including skin and soft tissue, bloodstream, respiratory, and others.

Results: Pexiganan was active against Staphylococcus aureus (MIC ≤0.25 µg/mL), Enterococcus faecalis (MIC ≤0.5 µg/mL), and Candida albicans (MIC ≤0.25 µg/mL). The MIC90 were non-susceptible to pexiganan (49.0 µg/mL) and linezolid (MIC ≤0.25 µg/mL).

Conclusions: Pexiganan was active against a broad range of microorganisms resistant to commercially available agents.

Introduction

Pexiganan is a new synthetic carbapenem antibiotic. This study in Phase 3 clinical trials as a topical cream for the treatment of infections caused by beta-lactamase-producing pathogens. This study was to evaluate the current in vitro activity of pexiganan against beta-lactamase-producing isolates from Europe, North America, and Japan collected within the last 5 years. A total of 259 isolates were selected for the study (Table 1). Activity of pexiganan was assessed using Clinical and Laboratory Standards Institute (CLSI) broth microdilution method. The MIC values were determined using CLSI and EUCAST methods. Quality control susceptibility testing was performed according to CLSI. Pexiganan and comparator agents were tested in 96-well, frozen, frozen-formulated broth microdilution methods provided by JMI Laboratories (Pleasanton, CA, USA). The MIC values were determined using CLSI and EUCAST methods.

Table 1. Antimicrobial activity of pexiganan tested against the main organisms and organism groups of isolates included in this study.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Clindamycin</th>
<th>Tetracycline</th>
<th>Amoxicillin/Clavulanic Acid</th>
<th>Pexiganan</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>95.5%</td>
<td>96.1%</td>
<td>95.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>E. coli</td>
<td>95.5%</td>
<td>95.5%</td>
<td>95.5%</td>
<td>95.5%</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>99.0%</td>
</tr>
<tr>
<td>C. albicans</td>
<td>100.0%</td>
<td>99.0%</td>
<td>100.0%</td>
<td>99.0%</td>
</tr>
</tbody>
</table>

Activity of pexiganan was assessed using CLSI broth microdilution methods. The MIC values were determined using CLSI and EUCAST methods.

Methods

- MIC values for bacteria were determined using Clinical and Laboratory Standards Institute (CLSI) broth microdilution method. MIC values for yeast were determined using CLSI and EUCAST methods.
- Quality control susceptibility testing was performed according to CLSI.
- Pexiganan and comparator agents were tested in 96-well, frozen, frozen-formulated broth microdilution methods provided by JMI Laboratories (Pleasanton, CA, USA).
- The MIC values were determined using CLSI and EUCAST methods.

Results

Table 2. Activity of pexiganan against colistin-resistant strains isolated from a non-fermentative Gram-negative bacilli (MIC, µg/mL).

<table>
<thead>
<tr>
<th>Organism</th>
<th>Clindamycin</th>
<th>Tetracycline</th>
<th>Amoxicillin/Clavulanic Acid</th>
<th>Pexiganan</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. freundii</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>C. koseri</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>C. maltophilia</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>C. atroseptica</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 3. Activity of pexiganan against colistin-resistant Enterobacteriaceae (MIC, µg/mL).

<table>
<thead>
<tr>
<th>Organism</th>
<th>Clindamycin</th>
<th>Tetracycline</th>
<th>Amoxicillin/Clavulanic Acid</th>
<th>Pexiganan</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>E. freundii</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>E. aerogenes</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>E. kawasaki</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Conclusions

- Pexiganan was active against a broad range of microorganisms resistant to commercially available agents.
- Pexiganan was non-susceptible to pexiganan (49.0 µg/mL) and linezolid (MIC ≤0.25 µg/mL).
- Pexiganan also showed good activity against 205 isolates of C. albicans (MIC range 4.0-128 µg/mL).
- Pexiganan was non-susceptible to pexiganan (49.0 µg/mL) and linezolid (MIC ≤0.25 µg/mL).

Acknowledgements

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References

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