Antimicrobial Activity of Dalbavancin Tested against Staphylococcus aureus with Decreased Susceptibility to Glycopeptides, Daptomycin, and/or Linezolid from United States Medical Centers

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INTRODUCTION

• Dalbavancin was approved in the United States (2014) and Europe (2015) to treat adults with acute bacteremia and skin and skin structure infections (ABSSSI) caused by susceptible Staphylococcus aureus

• Dalbavancin is a lipoglycopeptide derived from Streptococcus aureus (S. aureus, strain S259), S. epidermidis (S. epidermidis, strain 35515), and Streptococcus pyogenes (S. pyogenes, strain S259) that binds to the cell wall and inhibits the transpeptidase

• Dalbavancin allows for a convenient parenteral administration to treat ABSSSI, which can be a single 1,000 mg intravenous dose followed by weekly infusions for up to 6 weeks (total of 6 doses)

• Dalbavancin has broad spectrum activity against Gram-positive bacteria, including MRSA and linezolid-resistant strains

• Dalbavancin activity was assessed against a large collection of S. aureus clinical isolates with decreased susceptibility to at least three key antimicrobial agents used to treat S. aureus infections

MATERIALS AND METHODS

Bacterial isolates

The organism collection evaluated in the investigation included:

• Isolates with decreased susceptibility to vancomycin (MIC ≥16 μg/mL), 1,141 isolates

• Isolates nonsusceptible to daptomycin (MIC ≥2 μg/mL), 40 isolates

• Isolates with decreased susceptibility to telcofilm (MIC ≥1 μg/mL), 52 isolates

• Isolates with decreased susceptibility to teicoplanin (MIC ≥4 μg/mL), 143 isolates

• Isolates resistant to linezolid (MIC ≥8 μg/mL), 25 isolates

• Isolates selected from among 59,903 isolates collected from 139 US medical centers between 2002 and 2010 (Table 1; 2002–2010)

• Isolates were determined to be clinically significant based on local guidelines and were submitted to a central monitoring laboratory, JMI Laboratories, North Liberty, Iowa

• Isolates were initially identified by the participating laboratory, and bacterial identifications were confirmed by reference monitoring laboratory when necessary

Antimicrobial susceptibility testing

Isolates were tested for susceptibility by broth microdilution following guidelines in the CLSI M07–A10 document, and testing was performed using reference broth panels manufactured by JMI Laboratories.

Quality assurance was performed by concurrently testing CLSI-recommended QC reference strains (S. aureus ATCC 29212, E. faecalis ATCC 29212, and Staphylococcus pyogenes ATCC 49910), and all QC results were within published acceptable ranges

RESULTS

• Only 3 of 59,903 (0.01%) S. aureus isolates were determined to be daptomycin nonsusceptible (MIC ≥2 μg/mL) and breakpoint criteria for comparator agents were those from CLSI (M100-S27)

• Table 1: Summary of dalbavancin activity when tested against S. aureus isolates with decreased susceptibility to glycopeptides, daptomycin, and/or linezolid from United States medical centers

<table>
<thead>
<tr>
<th>Isolates</th>
<th>Vancomycin</th>
<th>Daptomycin</th>
<th>Linezolid</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIC (μg/mL)</td>
<td>≤0.25</td>
<td>≥1</td>
<td>≥8</td>
</tr>
<tr>
<td>≤0.25 to &gt;2</td>
<td>26.9</td>
<td>73.1</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;0.25 to ≤4</td>
<td>96.0</td>
<td>4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;4</td>
<td>0.0</td>
<td>100.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

• Table 2: Activity of dalbavancin and comparator antimicrobial agents tested against S. aureus isolates with decreased susceptibility to glycopeptides, daptomycin, and/or linezolid from United States medical centers

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</tr>
<tr>
<td>≤0.25 to &gt;2</td>
<td>26.6</td>
<td>73.4</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;0.25 to ≤4</td>
<td>100.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;4</td>
<td>0.0</td>
<td>100.0</td>
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CONCLUSIONS

Dalbavancin demonstrated potent in-vitro activity against S. aureus isolates displaying decreased susceptibility, including those resistant to vancomycin, daptomycin, and linezolid, and was consistently more potent than comparator agents

• Only 8 of 59,903 (0.01%) S. aureus isolates were determined to be linezolid-resistant (MIC ≥8 μg/mL): 25 isolates

• Of these 25 isolates, 5 (20.0%) were resistant to linezolid with MIC ≥8 μg/mL

• Over 95% of S. aureus isolates resistant to vancomycin, daptomycin, and/or linezolid were daptomycin nonsusceptible (MIC ≥2 μg/mL)

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REFERENCES


