In Vitro Activity of Telavancin and Other Antibiotics Against Methicillin Resistant Staphylococcus aureus (MRSA) Isolates from a Community Hospital in the Mid-Michigan Area

MaryAnn P. Tran, MD, Apoorv Kalra, MD, Gary E. Stein, PharmD, Amy Scharmen, BS
College of Human Medicine, Michigan State University, East Lansing, MI

ABSTRACT

Background: Although vancomycin (VAN) has been the standard of care for treatment of serious methicillin resistant Staphylococcus aureus (MRSA) infections, there is an increasing need for more potent and effective antibiotics. Telavancin (TLV) is one of such options and was recently reintroduced with a new treatment indication and susceptibility testing methodology. In this study, we evaluated the in vitro activity of TLV, VAN, daptomycin (DAP), linezolid (LZD), and ceftaroline (CPT) against recent clinical MRSA isolates.

Methods: In 2015, 103 unique clinical MRSA isolates (blood, sputum, skin) were collected. Minimum inhibitory concentrations (MICs) of TLV, VAN, DAP, LZD, and CPT were determined using the CLSI guidelines. Time-kill experiments were performed to simulate free drug concentrations seen in patients. TLV experiments were performed in CAMHB with 0.002% Polysorbate 80 and DAP experiments were performed in CAMHB with adjusted 50% DMSO concentration in the sample well. Pooled normal human serum was mixed 50% (v/v) with CPT to simulate clinical peak serum levels for VAN, DAP, LZD, and CPT. Cation Adjusted Mueller-Hinton Broth (CAMHB) was used for susceptibility testing according to the CLSI guidelines.

Results: VAN had low MICs (≤ 0.06 µg/mL) for all isolates by broth dilution and Etest (Tables 1 and 2). TLV had low MICs (≤ 0.06 µg/mL) for all isolates by broth dilution and Etest (Tables 1 and 2).

Clinical isolates of MRSA cultured from blood, sputum, and skin/soft tissue were collected for one month (July 2015).

Antimicrobials tested: TLV, DAP, VAN, LZD, and CPT

Cation Adjusted Mueller-Hinton Broth (CAMHB) was used for susceptibility testing according to the CLSI guidelines with broth dilution and CLSI Sensititre panels (TREK) (Thermo Scientific, OH) and Etest strips (bioMerieux, NC).

Time-kill experiments:

- Performed on 2 random blood MRSA isolates at 100% clinical peak levels for VAN, DAP, LZD, and CPT and 50% peak level for TLV in order to limit the DMSO concentration in the sample well.
- Pooled normal human serum was mixed 50% (v/v) with Cation Adjusted Mueller-Hinton broth (CAMHB) for the time-kill experiments to simulate free drug concentrations seen in patients.
- TLV experiments were performed in CAMHB with 0.002% Polysorbate 80 and DAP experiments were performed in CAMHB with adjusted 50% DMSO concentration in the sample well.
- Pooled normal human serum was mixed 50% (v/v) with CAMHB to simulate free drug concentrations.
- CAMHB with 0.002% Polysorbate 80 was used for TLV and CAMHB with adjusted 50% DMSO concentration in the sample well for DAP.

Table 1. Microbroth Dilution (TREK) Susceptibility Data

<table>
<thead>
<tr>
<th>MIC µg/mL</th>
<th>≤0.015</th>
<th>0.03</th>
<th>0.06</th>
<th>0.12</th>
<th>0.25</th>
<th>0.5</th>
<th>1.0</th>
<th>MIC₉₀</th>
<th>MIC₉₉</th>
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<td>7</td>
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<td></td>
<td></td>
<td></td>
<td>0.03</td>
<td>0.03</td>
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<tr>
<td>VAN</td>
<td>93</td>
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<td>0.5</td>
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<tr>
<td>DAP</td>
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<td>85</td>
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<td>2</td>
<td>0.12</td>
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<td>LZD*</td>
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* One isolate had an MIC > 4 for LZD.

Figure 1. Time-Kill Curves of Isolate #78

CONCLUSION

Each agent, except LZD, exhibited bactericidal activity.

No re-growth was seen by 24hrs for all agents.

TLV is the most potent drug against MRSA clinical isolates in this study and is rapidly bactericidal similar to daptomycin.

TLV may be considered as an alternative agent for MRSA infections, including concurrent bacteremia.

REFERENCES

1. In this study, TLV was the most potent agent against clinical isolates of MRSA and was observed to be rapidly bactericidal, exhibiting a rapid and prolonged decrease in bacterial colony counts in time-kill investigations.

2. Clinical isolates of MRSA cultured from blood, sputum, and skin/soft tissue were collected for one month (July 2015).

3. Antimicrobials tested: TLV, DAP, VAN, LZD, and CPT

4. Cation Adjusted Mueller-Hinton Broth (CAMHB) was used for susceptibility testing according to the CLSI guidelines.

5. Time-kill experiments:

- Performed on 2 random blood MRSA isolates at 100% clinical peak levels for VAN, DAP, LZD, and CPT and 50% peak level for TLV in order to limit the DMSO concentration in the sample well.
- Pooled normal human serum was mixed 50% (v/v) with Cation Adjusted Mueller-Hinton broth (CAMHB) for the time-kill experiments to simulate free drug concentrations seen in patients.
- TLV experiments were performed in CAMHB with 0.002% Polysorbate 80 and DAP experiments were performed in CAMHB with adjusted 50% DMSO concentration in the sample well.
- Pooled normal human serum was mixed 50% (v/v) with CAMHB to simulate free drug concentrations.
- CAMHB with 0.002% Polysorbate 80 was used for TLV and CAMHB with adjusted 50% DMSO concentration in the sample well for DAP.

6. VAN had low MICs (≤ 0.06 µg/mL) for all isolates by broth dilution and Etest (Tables 1 and 2).

7. TLV had low MICs (≤ 0.06 µg/mL) for all isolates by broth dilution and Etest (Tables 1 and 2).

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* One isolate had an MIC > 4 for LZD.

Figure 1. Time-Kill Curves of Isolate #78

Table 2. Etest Susceptibility Data

Table 3. Time-Kill Analysis

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