INTRODUCTION

- Bloodstream infections (BSIs), including those associated with central-line catheters, are serious life-threatening infections in the nosocomial setting, particularly in the intensive care unit. The clinical consequences of BSIs include increased mortality (20%-30%), significant morbidity, and increased length of hospital stay and costs.

- bloodstream infection (BSI) agents are a common pathogen responsible for serious infections worldwide, including BSIs, and the outcomes can be improved by appropriate diagnostic and therapeutic management.

- Tedizolid is currently approved to treat acute fasciitis skin and skin structure infection (AFOSS) in an ongoing Phase III clinical trial for this indication.

- This study evaluated tedizolid and comparator agent activities against gram-positive and gram-negative isolates causing BSIs in hospitalized patients in Europe and adjacent countries.

MATERIALS AND METHODS

Organism collection

A total of 25,695 Gram-positive bloodstream isolates from 23 European countries were collected and submitted to a monitoring laboratory as part of the Surveillance of Tedizolid Activity and Resistance (STAR) program.

- Isolates were initially identified by the participating laboratory and submitted to a central monitoring facility. Laboratories, North Liberty, Iowa, USA, where susceptibility testing was performed, and the participating laboratories were blinded to the test results. Isolates were then characterized by matrix-assisted laser desorption ionization time of flight (MALDI-TOF) analysis.

- All positive blood cultures were selected from patients with documented BSIs, particularly in the intensive care unit.

- All isolates were identified by MALDI-TOF (MALDI Biotyper, Bruker, Votersville, Germany) and confirmed by routine lab procedures. The identity was accepted if it had an identification score of 2.0 or greater.

- Breakpoint criteria for tedizolid and comparator agents were those from EUCAST (2016) and CLSI M100-S27 (2016).

- A total of 25.6% of S. aureus were methicillin-resistant (MRSA), while an additional 7.4% were resistant to oxacillin (OXACillin) or oxacillin and clindamycin (OXACillin/CLIND). Other gram-positive organisms were less prevalent (S. pneumoniae 25%, S. agalactiae 22%, S. pyogenes 12%, S. mitis/oralis 10%, S. dysgalactiae 10%, and S. anginosus 7%).

- All results were within published acceptable regions.

RESULTS

- Tedizolid compared 82% of all Gram-positive clinical isolates causing BSIs included in this study (Table 1).

- S. aureus, S. pyogenes, and other streptococci (GAS) comprised 44.2% and 16.6%, respectively.

- S. pneumoniae (27% of the total) consisted of the majority of GAS.

Table 1. Antimicrobial activity of tedizolid tested against the main gram-positive organisms and organism groups of isolates causing BSIs in 2016-2017.

<table>
<thead>
<tr>
<th>Organism/organism group (no. of isolates)</th>
<th>MIC50 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Range (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus (9,977)</td>
<td>0.34</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>S. pyogenes (2,827)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>GAS (3,519)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>S. pneumoniae (4,012)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-0.5</td>
</tr>
<tr>
<td>S. dysgalactiae (1,158)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>S. anginosus (1,565)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>S. mitis/oralis (840)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>S. pseudintermedius (132)</td>
<td>0.50</td>
<td>0.25</td>
<td>0.03-1</td>
</tr>
<tr>
<td>Enterococcus faecalis (514)</td>
<td>1.00</td>
<td>0.50</td>
<td>0.12-8</td>
</tr>
<tr>
<td>Enterococcus faecium (512)</td>
<td>2.00</td>
<td>1.00</td>
<td>0.12-16</td>
</tr>
<tr>
<td>Penicillin-susceptible S. pneumoniae (1,120)</td>
<td>0.12</td>
<td>0.06</td>
<td>≤0.06</td>
</tr>
</tbody>
</table>

- A total of 22.7% and 11.2% of viridans group streptococci were nonsusceptible to penicillin and/or ceftriaxone, respectively.

- A total of 25.6% of S. aureus were methicillin-resistant (MRSA), while an additional 7.4% were resistant to oxacillin (OXACillin) or oxacillin and clindamycin (OXACillin/CLIND).

- Other gram-positive organisms were less prevalent (S. pneumoniae 25%, S. agalactiae 22%, S. pyogenes 12%, S. mitis/oralis 10%, S. dysgalactiae 10%, and S. anginosus 7%).

- All results were within published acceptable regions.

CONCLUSIONS

- Tedizolid is active against the majority of S. aureus and other Gram-positive organisms causing BSIs.

- A total of 25.6% of S. aureus were methicillin-resistant (MRSA), while an additional 7.4% were resistant to oxacillin (OXACillin) or oxacillin and clindamycin (OXACillin/CLIND).

- Other gram-positive organisms were less prevalent (S. pneumoniae 25%, S. agalactiae 22%, S. pyogenes 12%, S. mitis/oralis 10%, S. dysgalactiae 10%, and S. anginosus 7%).

- All results were within published acceptable regions.

ACKNOWLEDGMENTS

- Tedizolid may be an additional option for treating infections caused by VRE, where options are limited.

- These data warrant the clinical development of tedizolid for treating BSIs in patients hospitalized in Europe and adjacent countries.

REFERENCES
