Tigecycline demonstrated potent in vitro activity against S. pneumoniae: A Global Study

REVISED ABSTRACT

Objectives: S. pneumoniae (SPN) continues to be recognized as a significant respiratory and bacteremia pathogen. Resistance to both oral and parenteral antibiotics used to treat SPN infection is evolving and newer antibiotics are needed with anti-SPN activity. This report documents the activity of tigecycline and comparators against 6476 SPN collected globally since 2004. Methods: Between 2004-2008, 387 hospital sites in 48 countries collected 6476 SPN deemed clinically significant from a variety of sources. MICs were determined at each site using supplied broth microdilution panels and MIC results interpreted by CLSI standards at each site. Results: The % inhibition at each MIC are shown below:

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC (mg/mL)</th>
<th>% Inhibited at MIC</th>
<th>0.06</th>
<th>0.12</th>
<th>0.25</th>
<th>&gt;0.5</th>
<th>&gt;1.0</th>
<th>&gt;8.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tigecycline</td>
<td>NA</td>
<td>100</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Amox/Clav</td>
<td>NA</td>
<td>100</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.5</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Penicillin</td>
<td>2</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
<td>&gt;95</td>
</tr>
</tbody>
</table>

Conclusions: Tigecycline demonstrated excellent in vitro activity against SPN with 100% of isolates inhibited at ≤0.5 mcg/ml. Overall, 61.5% of SPN were susceptible to penicillin, while 22% were resistant to levofloxacin. Continued surveillance of resistance in SPN to new and established antimicrobials is warranted.

BACKGROUND

Tigecycline is a broad-spectrum antimicrobial agent and first-in-class of the semisynthetic glycy cyclines to be approved for human use [1]. This synthetic analogue of the minocycline molecule exhibit significant antibacterial activity that is both bactericidal and, in certain instances, bacteriostatic with killing activity that is as much as fourfold better than vancomycin and daptomycin [2, 3]. The development of tigecycline is important in that tigecycline and other glycy cyclines are active against Gram-negative bacterial strains carrying either one or both of the two major forms of tetracycline resistance: efflux and ribosomal protection. Certain substituents at the 8-position of the tetracycline molecule restored activity against bacteria harboring genes encoding either or both efflux and ribosomal protection. A single chemical modification of tigecycline overcomes the two major forms of resistance while maintaining activity against susceptible gram-positive, gram-negative, aminoglycosides and anaerobic bacteria. Furthermore, resistance to tigecycline is difficult to produce even in the laboratory.

METHODS

All isolates were derived from blood, respiratory tract, body fluids and other defined sources. Only one isolate per patient was accepted into the study. Clinical isolates were collected and tested between January 2004 and April 2008 from 387 study centers in 48 countries globally. Isolates were identified to the species level and tested at each site by the participating laboratory.

Organism collection, transport, confirmation of organism identification, as well as, development and management of a centralized database was coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.

A larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program was designed to document the in vitro activity of Tigecycline against significant numbers of S. pneumoniae collected from 387 laboratories in 48 countries. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program.

QUALITY CONTROLS

MICs were determined at each site using supplied broth microdilution panels and MIC results interpreted by CLSI standards at each site. All isolates were collected and tested between January 2004 and April 2008 from 387 study centers in 48 countries globally. Isolates were identified to the species level and tested at each site by the participating laboratory.

REFERENCES

1. CLSI, **Tigecycline in the MIC break point panels for the minimum inhibitory concentration test methods**, M07-A8, Approved standard, 2010, Clinical Laboratory Standards Institute, Wayne, PA, USA.
2. CLSI, **Performance standards for antimicrobial susceptibility testing; sixteenth information supplement**, CLSI document M100-S16, Approved standard, 2010, Clinical Laboratory Standards Institute, Wayne, PA, USA.
4. Global Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) program, Isolates from the Global Tigecycline Evaluation and Surveillance Trial (TEST Program; 2004) and comparators against 6476 SPN collected globally since 2004. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program.
5. Global Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) program, Clinical Isolates from the United States Tigecycline Evaluation and Surveillance Trial (TEST Program; 2004) and comparators against 6476 SPN collected globally since 2004. This study is part of the larger ongoing global Tigecycline Evaluation and Surveillance Trials (T.E.S.T.) program.
7. International Health Management Associates, Inc. located in Schaumburg, IL, USA.
12. Wyeth Pharmaceuticals.

CONCLUSIONS

Tigecycline demonstrated potent in vitro activity against S. pneumoniae in this surveillance study of clinical isolates from 48 countries.

Tigecycline MIC50 and MIC90 values of 0.03 and 0.25 mcg/mL, respectively, against S. pneumoniae remained constant against all isolates and was unaffected by the penicillin-resistant phenotype.

The in vitro activity of tigecycline in this study suggests that tigecycline is highly active against all study strains of S. pneumoniae and may be an effective treatment option for this clinical pathogen.