Antimicrobial Susceptibilities of a Worldwide Collection of *Stenotrophomonas maltophilia* Isolates Tested against Tigecycline and Agents Commonly Used for *S. maltophilia* Infections

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Antimicrobial susceptibilities were determined for 1,586 isolates of *Stenotrophomonas maltophilia* from globally diverse medical centers using the Clinical Laboratory Standards Institute broth microdilution method. The combination trimethoprim-sulfamethoxazole (96.0% of isolates susceptible at ≤2 μg/ml trimethoprim and 38 μg/ml sulfamethoxazole) and tigecycline (95.5% of isolates susceptible at ≤2 μg/ml) were the only antimicrobials tested with >94% susceptibility in all regions. Susceptibility rates for other commonly used were lower than expected and varied geographically. This *in vitro* data supports tigecycline as a potential candidate for clinical investigations into *S. maltophilia* infections.

*Stenotrophomonas maltophilia* is a Gram-negative bacillus, inherently multidrug resistant (MDR) and frequently recovered from environmental sources. It has been associated with severe nosocomial acquired bacteremia and pneumonia, usually among immunocompromised patients, as well as meningitis, endocarditis, and urinary tract, skin/soft tissue, and ocular infections. *S. maltophilia* infections are associated with high morbidity and mortality, with estimated crude mortality rates ranging from 20 to 70% and with the risk of mortality highest among patients receiving inappropriate initial antimicrobial therapy (5). Treatment of *S. maltophilia* infections represents a significant challenge because of the organism’s high levels of intrinsic resistance to many antimicrobial agents, difficulties in susceptibility testing, the development of resistance during therapy, and the paucity of clinical trials to determine optimal therapy (8, 12).

The combination trimethoprim-sulfamethoxazole (TMP/SMX) is the recognized antimicrobial of choice for the treatment of infections caused by *S. maltophilia* with ceftazidime, ticarcillin-clavulanate, minocycline, tigecycline, fluoroquinolones, and the polymyxins being described as alternative therapies. It is important to note that all recommended therapy options have been based on *in vitro* studies and anecdotal experience rather than appropriately structured clinical trials (11). Resistance to TMP/SMX has been described and varies geographically, being shown by as many as 10% of isolates in Europe (7). In addition, allergic reactions to the combination TMP/SMX are common and can be severe, which further compromises its application (1). Clearly, therapeutic alternatives are needed to treat infections caused by *S. maltophilia*.

Tigecycline binds to the 30S ribosomal subunit, resulting in inhibition of protein synthesis (13). It exhibits a wide range of activity against Gram-positive and -negative organisms, including MDR strains. Tigecycline is approved by the United States Food and Drug Administration (USFDA) for the treatment of complicated skin and skin structure infections (cSSSI), intra-abdominal infections, and, more recently, community-acquired bacterial pneumonia. Tigecycline has demonstrated good *in vitro* activity against *S. maltophilia* in several studies (6, 9, 14). The aim of this study was to assess antimicrobial resistance in *S. maltophilia* against commonly used agents by using the largest and most geographically diverse collection of contemporary isolates available, with the rationale being the paucity of such information in the face of a clear need for clinical and research options.

From January 2003 to December 2008, a total of 1,586 unique clinical *S. maltophilia* strains were recovered and identified from 119 medical centers located across Asia and the Pacific (Asian-Pacific), Europe, Latin America, and North America. Bacterial identification was confirmed by the central monitoring site (JMI Laboratories, North Liberty, IA) using standard algorithms (microscopy, culture characteristics, and oxidase reaction) followed by an automated system (Vitek 2; bioMerieux, Hazelwood, MO). MIC values were determined for all isolates based on the Clinical Laboratory Standards Institute (CLSI) broth microdilution method using commercially prepared and validated panels (TREK Diagnostic Systems, Cleveland, OH) in fresh cation-adjusted Mueller-Hinton broth (2). Tigecycline breakpoints established by the USFDA for *Enterobacteriaceae* (≤2 μg/ml for susceptibility and ≥8 μg/ml for resistance) as well as the polymyxin B breakpoints established by the CLSI for *P. aeruginosa* (≤2 μg/ml for susceptibility and ≥8 μg/ml for resistance), were applied for comparison only (Tygacil; Wyeth Pharmaceuticals, Philadelphia, PA). CLSI quality control ranges and interpretive criteria were used for comparator compounds (3).
TABLE 1. Regional MIC distributions for tigecycline tested against 1,586 S. maltophilia strains, stratified by geographic region

<table>
<thead>
<tr>
<th>Region (no. of strains tested)</th>
<th>≤0.12</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>&gt;4</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America (491)</td>
<td>2.2</td>
<td>16.5</td>
<td>49.7</td>
<td>79.8</td>
<td>94.5</td>
<td>98.4</td>
<td>100.0</td>
</tr>
<tr>
<td>Europe (447)</td>
<td>1.8</td>
<td>13.7</td>
<td>48.1</td>
<td>95.3</td>
<td>99.3</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Asian-Pacific (359)</td>
<td>1.4</td>
<td>12.5</td>
<td>57.9</td>
<td>87.5</td>
<td>96.1</td>
<td>99.2</td>
<td>100.0</td>
</tr>
<tr>
<td>Latin America (289)</td>
<td>1.7</td>
<td>15.2</td>
<td>52.3</td>
<td>87.5</td>
<td>96.5</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>All regions (1,586)</td>
<td>1.8</td>
<td>14.6</td>
<td>51.6</td>
<td>84.0</td>
<td>95.5</td>
<td>99.1</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* Susceptibility breakpoint established by the CLSI for Enterobacteriaceae (3).
tophilia are life threatening and have a high mortality, and the lack of evidence-based therapeutic options often forces clinicians to make difficult decisions regarding antimicrobial therapy. The role of tigecycline in the treatment of S. maltophilia infections warrants further investigation due to its high in vitro activity and potency. Synergies between tigecycline and TMP/SMX and also amikacin have been reported, and hence combination therapy would be a potential approach for clinical investigations and experimental therapy trials (4).

REFERENCES