Abstract (Revised)

Background: Ceftobiprole is a new cephalosporin with a mechanism of PBP binding that includes inhibition of staphyloccocal PBP2a, resulting in broad-spectrum activity against Gram positive (G+) and Gram negative (G-) pathogens. The objective of this study was to compare European methods for susceptibility testing of staphylococci and enterococci with MIC methods of the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST), which are widely used in Europe and the United States. Methods: Each site tested their MIC method: SFM and SRGA, BSAC, and CLSI broth microdilution. Differences in MICs were assessed with a geometric mean. Results: There was good correlation of ceftobiprole MICs by SFM, CLSI, and SRGA. Conclusions: There was good reproducibility of ceftobiprole and ceftazidime MICs in this multi-national MIC study.

Methods

- **SFM MIC Method:** Agar dilution using Mueller Hinton Agar (MHA) for staphylococci and green negative bacilli, MHA + 3% defibrinated sheep blood (SBB) for streptococci and Haemophilus Thick Media agar (HTM) for H. influenzae.
- **SRGA MIC Method:** Agar dilution using IsoSensitest (SA) for staphylococci and green negative bacilli and SA + 3% defibrinated horse blood (SB) and 20 mg/mL NAD for streptococci and H. influenzae.
- **BSAC MIC Method:** Agar dilution using IsoSensitest (SA) for staphylococci and green negative bacilli and SA + 3% defibrinated horse blood (SB) for streptococci and SA + 3% horse blood + 20 mg/mL NAD for H. influenzae.

**Table 1:**

<table>
<thead>
<tr>
<th>Testing Site/Method</th>
<th>n</th>
<th>Ceftobiprole (µg/mL)</th>
<th>Ceftazidime (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>France/SFM</td>
<td>124</td>
<td>0.13</td>
<td>123</td>
</tr>
<tr>
<td>France/CLSI</td>
<td>124</td>
<td>0.15</td>
<td>112</td>
</tr>
<tr>
<td>UK/CLSI</td>
<td>123</td>
<td>0.23</td>
<td>113</td>
</tr>
<tr>
<td>Germany/DIN/CLSI</td>
<td>124</td>
<td>0.14</td>
<td>114</td>
</tr>
<tr>
<td>Germany/CLSI/DIN</td>
<td>124</td>
<td>0.15</td>
<td>114</td>
</tr>
</tbody>
</table>

**Results**

- The geometric mean MICs of all strains by all methods ranged from 0.13-0.23 µg/mL.
- The geometric mean MICs of all strains by all methods ranged from 1.4-2.0 µg/mL.
- Overall essential agreement (within 1 doubling dilution) compared to CLSI for ceftobiprole was 90%; 90% - 91% at the German site, susceptible by SFM and CLSI at the French site, and non-susceptible by SFM and CLSI at the Swedish and the UK sites.

**Conclusions**

- There was good reproducibility of ceftobiprole and ceftazidime MICs in this multi-national MIC study.
- The geometric mean MICs of all strains were within one doubling dilution for all methods. Although there was lower correlation of ceftobiprole CLSI and BSAC MICs, the BSAC MICs were similar to the other country specific method MICs.
- The CLSI ceftobiprole MICs from the UK site were generally higher compared to the CLSI MICs from the other countries.
- Overall, there was good correlation of ceftobiprole MICs by SFM, SRGA, BSAC agar dilution and CLSI/DIN broth microdilution methodologies.

**Figure 1:** Geometric mean ceftobiprole MICs (µg/mL) by method of staphylococci and E. faecalis.

**Figure 2:** Geometric mean ceftobiprole MICs (µg/mL) by method of streptococci.

**Figure 3:** Geometric mean ceftobiprole MICs (µg/mL) by method of Enterobacteriaceae and H. influenzae.

**Figure 4:** Geometric mean ceftobiprole MICs (µg/mL) by method of Pseudomonas aeruginosa.