INTRODUCTION & PURPOSE

• Pneumonia is a major cause of morbidity and mortality in adults and children around the world.1-4 Although antibiotic resistance rates vary by geographic region, rates are rising worldwide, creating a need for new therapies to treat community-acquired bacterial pneumonia (CABP)5,6.

• Streptococcal pneumonia is the most commonly isolated bacterial pathogen in patients with CABP, with prevalences that vary by geographic region. Other causes of CABP include Haemophilus influenzae, Moraxella catarrhalis, and Staphylococcus aureus, as well as atypical pathogens.7,8

• Lefamulin (LEF), the first pleuromutilin antibiotic to be approved for intravenous (IV) and oral treatment of adults with CABP, selectively inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit at the A- and P-sites in the peptidyl transferase center of the 50S ribosome.9 (Figure 1)

• In patients with CABP, LEF demonstrated noninferiority to moxifloxacin in the IV-to-oral switch Lefamulin Evaluation Against Pneumonia (LEAP) 1 phase 3 study10 and in the LEAP 2 oral-only phase 3 study11 by the objective of this study was to evaluate the in vitro activity of LEF and comparators against a contemporary global set of gram-positive pathogens.

Figure 1. (A) Structure of Lefamulin and (B) Lefamulin in the Peptidyl Transferase Center of the Large Ribosomal Subunit.

METHODS

As part of the 2017 SENTRY Antimicrobial Surveillance Program, 4337 unique isolates (1 per patient) were collected from patients with community-acquired respiratory tract infections (40.0%), hospitalized patients with pneumonia (13.6%), bloodstream infections (23.2%), skin and soft tissue infections (18.7%), and other infections (4.5%).

• Isolates were collected from 98 sites in 34 countries – 36.8% of isolates were collected from the United States, 38.8% from Europe, 13.1% from the Asia-Pacific region, and 11.3% from Latin America.

• Minimum inhibitory concentration (MIC) for LEF and comparators was determined using Clinical and Laboratory Standards Institute (CLSI) broth microdilution methods12: susceptibility was evaluated using the CLSI (2019) breakpoints.

RESULTS

LEF showed potent antibacterial activity against all tested pathogens, and its activity was unaffected by resistance to other antibiotic classes.

Streptococcus pneumoniae

- S. pneumoniae isolates were largely susceptible to moxifloxacin (98.0%–100%) and amoxicillin-clavulanic acid (85.5%–94.8%).
- In contrast, only 38.2%–72.6% and 44.5%–71.9% were susceptible to azithromycin and LEF, respectively.

Table 1. Activity of Lefamulin and Comparators Against Streptococcus pneumoniae

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>MIC50/90 (µg/mL)</th>
<th>% Susceptible per CLSI (M100, 2019)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>USA* Europe† Latin America‡ Asia-Pacific §</td>
<td></td>
</tr>
<tr>
<td>S. pneumoniae (n=230)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LEF*</td>
<td>0.06/0.12</td>
<td>100.0 100.0 100.0 100.0</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>&gt;32/&gt;32</td>
<td>34.1 45.1 23.6 45.8</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.03/0.06</td>
<td>98.4 98.4 98.4 98.4</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.08/0.16</td>
<td>50.0 50.0 50.0 50.0</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.008/0.016</td>
<td>100.0 100.0 100.0 100.0</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.5/1</td>
<td>100.0 100.0 100.0 100.0</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1/1</td>
<td>100.0 100.0 100.0 100.0</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>2/8</td>
<td>97.6 98.8 100.0 91.7</td>
</tr>
</tbody>
</table>

• LEF activity was unaffected by resistance to other antibiotic classes, including macrolides, fluoroquinolones, and β-lactam antibiotics, or by geographic region.

• These in vitro data suggest that LEF may offer an important empiric monotherapy treatment option for CABP caused by these organisms, particularly in regions with high rates of resistance to antimicrobials commonly used for CABP.

CONCLUSIONS

- LEF demonstrated potent activity against this contemporary (2017) worldwide collection of gram-positive pathogens.
- LEF activity was unaffected by resistance to other antibiotic classes, including macrolides, fluoroquinolones, and β-lactam antibiotics, or by geographic region.

REFERENCES


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Lefamulin Activity Against Gram-Positive Pathogens Collected in the 2017 Global SENTRY Antimicrobial Surveillance Program

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Table 2. Activity of Lefamulin and Comparators Against β-hemolytic Streptococcus spp.

Table 4. Activity of Lefamulin and Comparators Against Coagulase-Negative Staphylococcus spp.