**Antimicrobial Activity of LB11058 Tested Against S. pneumoniae, H. influenzae and M. catarrhals**

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**ABSTRACT**

Background: LB11058 is a novel cephalosporin with a C-3 pyrimidinyl-substituted vinyl group and a C-7 aminothiazole (AT) moiety. This compound was derived by the JONES Group/JMI Laboratories, North Liberty, IA, from a parent cephalosporin through medicinal chemistry and bioassay-guided optimization. A series of LB11058 analogs were evaluated in vitro against selected bacterial pathogens. We report here the evaluation of LB11058 against recent clinical isolates collected from patients with CARTI worldwide.

Methods: A total of 955 isolates were tested, including 305 S. pneumoniae (SPN) (penicillin-resistant [PRP] and non-resistant [PEN]), 102 H. influenzae (H. influenzae), 103 M. catarrhals (MCa) and 279 methicillin-resistant Staphylococcus (MRSA) (MICr) isolates. LB11058 were determined by methods recommended by NCCLS (M7-A6).

Results: LB11058 was the most potent compound tested against SPN and H. influenzae more active than LB11058 (MIC50, 0.008-0.015 g/ml; range 0.008-16 g/ml), but activity varied according to the organism's β-lactamase, and it was similar to that of cefepime (MIC90, 0.06-2 g/ml). LB11058 showed excellent activity against the most significant pathogens (ceftriaxone) against the same isolates.

**CONCLUSIONS**

LB11058 was highly active against the three most common pathogens isolated from CARTI worldwide. Since LB11058 showed higher potency than the currently prescribed third-generation cephalosporins (ceftaxime) against S. pneumoniae, and retained potent activity against H. influenzae and M. catarrhals, this compound may represent an excellent therapeutic candidate for empiric therapy of CARTI and bacterial meningitis, especially in areas with high rates of antimicrobial resistance.

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**MATERIALS & METHODS**

**INTRODUCTION**

Community-acquired respiratory tract infections (CARTI) are the leading causes of primary care physician office visits and the majority of prescribed antimicrobials are currently prescribed third-generation cephalosporins (LB11058) against recent clinical isolates collected from patients with CARTI worldwide.

**Table 1. Antimicrobial activity of LB11058 and selected comparison drugs tested against Gram-positive species.**

<table>
<thead>
<tr>
<th>Organism/antimicrobial agent</th>
<th>MIC (µg/mL)</th>
<th>Range</th>
<th>% Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. tested</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S. pneumoniae</em> Penicillin-susceptible (102)</td>
<td>50%</td>
<td>90%</td>
<td>Range</td>
</tr>
<tr>
<td>Penicillin-intermediate (52)</td>
<td>0.03-0.06</td>
<td>80.2</td>
<td>44.2</td>
</tr>
<tr>
<td>Penicillin-susceptible (102)</td>
<td>0.06-0.25</td>
<td>93.1</td>
<td>100.0</td>
</tr>
<tr>
<td>C. Influenzae</td>
<td>0.12-2</td>
<td>98.1</td>
<td>99.0</td>
</tr>
<tr>
<td><em>M. catarrhals</em> Penicillin-susceptible (103)</td>
<td>0.03</td>
<td>80.2</td>
<td>44.2</td>
</tr>
<tr>
<td>Penicillin-resistant (102)</td>
<td>0.12-1</td>
<td>93.1</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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**ACKNOWLEDGMENTS**

The JONES Group/JMI Laboratories, North Liberty, IA

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**SELECTED REFERENCES**

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**Figure 1. Chemical structure of LB11058.**