Antimicrobial Spectrum and Potency of Ceftaroline Combined With NXL104
When Tested Against Enterobacteriaceae Collected From USA Hospitals

H. S. SADER, M. CASTANHEIRA, D. J. FARRELL, R. N. JONES
JMI Laboratories, North Liberty, Iowa, USA

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Introduction

The production of β-lactamases is the most important contributor for antimicrobial resistance among Gram-negative bacteria. These enzymes are widely spread among clinical isolates and bacteria. Furthermore, the enzymes encoding β-lactamases are often carried by plasmids that also bear resistance genes to other antibiotic classes. Thus, removing the therapeutic options to treat infections caused by β-lactam-producing bacteria is a major problem.

Ceftaroline, the active form of ceftaroline furoate, is a novel broad-spectrum bactericidal cephalosporin that inhibits β-lactamases (eg, ESBL, KPC, and AmpC). We hypothesized that ceftaroline combined with NXL104 (CXL; fixed 4-μg/mL concentration of NXL104) would be synergistic against a variety of strains producing class A and class C β-lactamases, and a variable level of activity against class D β-lactamases (eg, PEN, VIM, IMP, and CTX-M).

Results

The MICs of the β-lactamase enzyme-encoding genes

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC50 (μg/mL)</th>
<th>MIC90 (μg/mL)</th>
<th>%S / %R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftaroline</td>
<td>0.5</td>
<td>1</td>
<td>99.7 / 0.3</td>
</tr>
<tr>
<td>NXL104 alone</td>
<td>8</td>
<td>16</td>
<td>99.7 / 0.3</td>
</tr>
<tr>
<td>Ceftaroline + NXL104</td>
<td>0.06</td>
<td>0.12</td>
<td>100.0 / 0.0</td>
</tr>
</tbody>
</table>

In a study conducted by Sader et al. (2010), a total of 3258 Enterobacteriaceae isolates from the USA were tested against ceftaroline and NXL104. The results indicated that 99.7% of strains were inhibited at CXL MIC of 0.06-0.12 μg/mL.

Conclusions

- Ceftaroline was active against Enterobacteriaceae, including strains expressing broad-spectrum β-lactamase activity.
- Overall, the activity of this β-lactam/β-lactamase combination was comparable to that of the carbapenem. CXL was particularly active against Enterobacteriaceae strains with decreased susceptibility to carbapenems (MIC > 0.5 μg/mL and MIC > 2 μg/mL).
- The worldwide spread of β-lactamase-encoding genes among Enterobacteriaceae strains from nosocomial and community settings jeopardizes the use of β-lactam agents for the treatment of serious infections caused by these organisms. Our results demonstrated that CXL is a valuable option to treat infections caused by strains producing β-lactamase, including organisms producing β-lactamase-inhibitor cephalosporins, ESBLs, and KPC β-lactamases.

References


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