**INTRODUCTION**

Tamboribactam, (formerly NXR-5133), is a novel cyclic boronic-based broad-spectrum β-lactamase inhibitor with potent and selective direct inhibitory activity against serine- and metallo-β-lactamases (Ambler Classes A, B, C and D) [1]. Tamboribactam greatly enhances the activity of cefepime against many difficult-to-treat organisms, in combination with ceftazidime and carbenapenem-resistant Enterobacteriales and Pseudomonas aeruginosa. In this study, we evaluated the in vitro activity of the investigational combination tamboribactam-cefepime and comparator agents against recent clinical isolates of Enterobacteriales collected during 2018-2020 surveillance.

**METHODS**

MICs of cefepime with tamboribactam and comparator agents against Enterobacteriales were determined following CLSI M07-A11 guidelines [2] against 13,730 Enterobacteriales isolates collected globally (Figure 1, Figure 2). Quality control (QC) testing was performed each day of testing as specified by the CLSI [2]. Isolates were from community and hospital infections collected from 266 sites in 56 countries from 2018 to 2020. Isolates were sourced from (n) percent of total respiratory tract infections (4,550/33.1%), urinary tract infections (3,849/28.0%), skin/soft tissue infections (2,346/17.7%), and central line associated bloodstream infections (4,550/33.1%). OXA-48 group genes via PCR and Sanger sequencing. Seventy-four OXA-48 group genes were identified in 14% (N=207) and VIM (n=22). Note organisms could also possess AmpC-type enzymes, or OSBLs, but no carbapenemases.

**RESULTS**

In the current study, we evaluated the in vitro activity of the investigational combination tamboribactam-cefepime and comparator agents against Enterobacteriales, with tamboribactam-cefepime significantly restoring the in vitro activity of cefepime against Enterobacteriales, including isolates monoresistant to cefepime and cefepime-resistant, and demonstrating approved BL/BLI combinations and expressing synergy with multiple classes of β-lactams, and supporting the continued development of tamboribactam in a potential combination therapy for challenging infections due to resistant Gram-negative pathogens.

**REFERENCES**


**ACKNOWLEDGMENTS**

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**Figure 1. Distribution of 13,730 Enterobacteriales isolates by species**

<table>
<thead>
<tr>
<th>Species</th>
<th>%S</th>
<th>%I</th>
<th>%R</th>
<th>MIC</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacter cloaceae</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
<tr>
<td>Citrobacter amalonaticus</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
<tr>
<td>Citrobacter braakii</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>84.2</td>
<td>4.7</td>
<td>5.1</td>
<td>0.06</td>
<td>≤0.12</td>
</tr>
</tbody>
</table>

**Figure 2. Distribution of 13,730 Enterobacteriales isolates by region**

**Figure 3. MIC distribution of cefepime-taniborbactam and select comparator agents against 13,730 Enterobacteriales**

**Figure 4. MIC distribution of cefepime-taniborbactam against resistant Enterobacteriales**

**Figure 5. MIC distribution of cefepime-taniborbactam against molecularly characterized Enterobacteriales**

**Antimicrobial Activity of Cefepime in Combination with Taniborbactam Against Clinical Isolates of Enterobacteriales from 2018-2020 Global Surveillance**

**RESULTS SUMMARY**

- Tamboribactam-cefepime showed potent in vitro activity against all Enterobacteriales, with MIC50/90 values of 0.06/0.25 µg/mL and ≥99% inhibited at MIC values of ≤8 µg/mL at the provisional susceptible breakpoint of ≤8 µg/mL (Table 1, Figure 3).
- Cefepime-taniborbactam activity was maintained against resistant subsets of Enterobacteriales, with MIC50 values of 0.02 µg/mL against cefepime-non-susceptible, 8 µg/mL against meropenem-susceptible and 4 µg/mL against tamboribactam-non-susceptible isolates (Table 1, Figure 4).
- Cefepime-taniborbactam maintained activity against ESBL, KPC, and VIM-IMPA harboring isolates with MIC50 values of 1.0 µg/mL, 2 µg/mL, and 0.5 µg/mL, respectively, ≥99.62% inhibition was observed in 21/24 ESBL, and colimuria, and polymyxin MIC values of 0.06/0.25 µg/mL and ≥99% inhibited at MIC values of ≤8 µg/mL at the provisional susceptible breakpoint of ≤8 µg/mL (Table 1, Figure 4).
- Cefepime-taniborbactam inhibited 76.0% of isolates expressing NDM (n=207) or VIM (n=22) MBLs. Whole genome sequence analysis suggested likely explanations for the loss of the non-IMP harboring isolates exhibiting cefepime-taniborbactam MIC values ≤16 µg/mL, including penicillin-binding protein overexpression in 12/39 (31.6%) isolates observed in 21/24 ES, coli, and permeability defects and/or efflux up-regulation in 39/39 (100%) K. pneumoniae.

**REFERENCES**

