Background

ETX2514 is a novel β-lactamase inhibitor with broad-spectrum activity against metallo-β-lactamases. Sulbactam-ETX2514 (ETX2514SUL) was highly active against this collection of ABC isolates. In addition, ETX2514SUL demonstrated potent antibacterial activity against recent, geographically diverse clinical isolates of ABC, including MDR isolates. These clinical isolates were collected in 2017 from geographically diverse medical centers in the United States, Europe, Latin America, and the Asia-Pacific region. Susceptibility testing was performed in a standardized manner according to CLSI guidelines, and data analysis was performed using CLSI and ECOFF breakpoint criteria. Select isolates were subjected to whole genome sequencing with an Illumina MiSeq system and genomic analysis using CLC Genomics Workbench v9.5.

Methods

ETX2514SUL was the most active agent against the metallo-β-lactamase NDM-1, which ETX2514 does not inhibit.

• Sulbactam-ETX2514 potency was consistent across Acinetobacter species, geographical regions and sources of infection.

• Sulbactam-ETX2514 maintained a MIC90 of 4 mg/L, which was subjected to whole genome sequencing.

• Of 23 isolates encoded NDM-1, which ETX2514 does not inhibit.

• 14 of 23 isolates encoded the blaNDM (Oxford/Pasteur) whole genome sequence. Sulbactam-ETX2514 maintained a MIC90 of 4 mg/L among carbapenem and colistin non-susceptible isolates.

• These data support development of ETX2514 in combination with sulbactam for the treatment of infections caused by multidrug-resistant A. baumannii calcoaceticus complex isolates.

Profile of Select Isolates with Reduced Susceptibility to ETX2514SUL

<table>
<thead>
<tr>
<th>Species</th>
<th>N</th>
<th>MIC50 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. baumannii</td>
<td>665</td>
<td>4</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>A. calcoaceticus</td>
<td>146</td>
<td>4</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>A. pitii</td>
<td>11</td>
<td>4</td>
<td>64</td>
<td>64</td>
</tr>
</tbody>
</table>

Disclosures

S. McLeod, S. Moussa, M. Hackel, R. Tommasi, and A. Miller are employees of Enantas Therapeutics, Inc. M. Miller is an employee of IMAX, Inc.

References


* background

ETX2514 is a novel β-lactamase inhibitor (β-LI) from a series of diazabicyclooctane (DAB) β-LIs. ETX2514SUL was tested by dilution of sulbactam in the presence of 4 mg/L ETX2514. ETX2514SUL demonstrated potent antibacterial activity against recent, geographically diverse, multidrug-resistant Gram-negative bacteria (MDR-GNB).

ETX2514SUL (sulbactam-ETX2514) is a β-lactamase inhibitor combination conjugated to clinical development for the treatment of resistant A. baumannii infections.

ETX2514 is a novel β-lactamase inhibitor (β-LI) from a series of diazabicyclooctanes with potent broad-spectrum activity against class A, C, and D beta-lactamases. Substrates are in vivo with antibacterial activity against carbapenem-resistant strains, through inhibition of IMP.

Disclosures

S. McLeod, S. Moussa, R. Tommasi and A. Miller are employees of Enantas Therapeutics, Inc. M. Miller is an employee of IMAX, Inc.

References