The Novel β-lactamase Inhibitor Enmetazobactam is More Potent than Tazobactam against ESBL-producing Enterobacteriaceae

A. Belley1, I. Morrissey2, S. Hawser3, M. Huband2, S. Bajaksouzian4, M.R. Jacobs4, K. Papp-Wallace5, R.A. Bonomo5, P. Kechtle1
1Allecra Therapeutics SAS; 2IHMA Europe Sàrl; 3JMI Laboratories Inc.; 4University Hospitals, Cleveland Medical Center; 5Louis Stokes Cleveland VA Medical Center

Abstract

Background: New carbapenem-sparing therapies are needed for infections caused by extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae. Cefepime (FEP) combined with the novel ESBL inhibitor enmetazobactam (EMT, formerly AAI101) is in phase 3 development for the treatment of adult patients with cUTI/AoP. In this study, the in vitro activity of EMT relative to tazobactam (TZB) was compared against ESBL-producing and -resistant Enterobacteriaceae. Methods: Both broth microdilution assays were performed following CLSI guidelines. Isolates tested were Escherichia coli isogenic strains (15) expressing diverse ESBLs (CTX-M, SHV, TEM) and/or OXA-48, and E. coli expressing TEM (strain C436) and K. pneumoniae (strain ATCC 700603) expressing CTX-M-14. Results: Against the ESBL-producing E. coli, colistin reduced the MIC of EMT by 4 to 8 µg/ml when compared with meropenem. EMT exhibited similar potency against ESBL-resistant Enterobacteriaceae. EMT was significantly more potent against all isolates than TZB. Background:

- Use of carbapenems, a "last resort" class of β-lactamases, is recommended for the treatment of infections caused by ESBL-producing Enterobacteriaceae. However, the availability of these antibiotics is limited due to the development of resistance. New carbapenem-sparing therapies are needed for infections caused by ESBL-producing Enterobacteriaceae.

Methods

- Isolation and identification of clinical isolates
- Susceptibility testing using broth microdilution
- Determination of minimal inhibitory concentrations (MICs)

Results

Table 1. Cefepime-enmetazobactam exhibits potent antibacterial activity against a diversity of ESBL-producing isogenic strains (n=15) of E. coli

<table>
<thead>
<tr>
<th>Organism group</th>
<th>Antibacterial agent</th>
<th>MIC (µg/ml)</th>
<th>Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>Cefepime</td>
<td>≤0.06</td>
<td>99.1</td>
</tr>
<tr>
<td></td>
<td>Meropenem</td>
<td>≤0.06</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Piperacillin-tazobactam</td>
<td>≤0.06</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2. Cefepime-enmetazobactam exhibits potent antibacterial activity against clinical isolates of ESBL-producing E. coli and K. pneumoniae

<table>
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Conclusions

- Enmetazobactam restores the in vitro activity of cefepime against ESBL-producing clinical isolates and isogenic strains of E. coli and K. pneumoniae expressing a diversity of β-lactamases.

References


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