In vitro activity of eravacycline and comparators against Acinetobacter baumannii, including carbapenem-resistant strains, and Stenotrophomonas maltophilia isolated from patients in Europe

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Introduction
Eravacycline is a novel, fully-synthetic fluoroacetamide antibiotic of the tetracycline class with broad-spectrum activity in development for the treatment of serious infections, including those caused by MDR pathogens. Eravacycline has been evaluated in phase 2 studies for the treatment of CAI and for UTI, including pyelonephritis. It is important to evaluate the activity of eravacycline against European clinical isolates of key pathogens because eravacycline will be under review by the European Medicines Agency for potential approval in Europe.

The purpose of this study was to evaluate the in vitro activity of eravacycline and comparators against Acinetobacter baumannii and Stenotrophomonas maltophilia, including strains with a carbapenem-resistant (CR) phenotype, isolated from patients in Europe.

Methods
In this study, a total of 248 clinical isolates (150 A. baumannii and 99 S. maltophilia) were collected from 2013-2014, including CR isolates.

- Minimum inhibitory concentration (MIC) endpoints were determined by broth microdilution according to CLSI guidelines.
- Quality control testing was performed each day of testing as specified by the CLSI using E. coli ATCC 25922 and E. coli ATCC 35218.
- Antibiotic susceptibility was determined using EUCAST breakpoints (2), when available.
- CR was defined as resistance to imipenem.

Results
The eravacycline MIC\textsubscript{90} for all A. baumannii and S. maltophilia isolates was 0.51 mg/L. The eravacycline MIC\textsubscript{90} for CR A. baumannii isolates was also 0.51 mg/L. Tigecycline and colistin MIC\textsubscript{90} for all A. baumannii and S. maltophilia isolates was 0.25 mg/L and 1/4 mg/L, respectively for CR isolates. The eravacycline MIC\textsubscript{90} was 0.52 mg/L. For S. maltophilia, the eravacycline MIC\textsubscript{90} for CR isolates was 1/4 mg/L.

- Summary of MIC\textsubscript{90} for A. baumannii and S. maltophilia isolates are shown in Table 1. There were no CR S. maltophilia isolates.

Conclusions
- Overall, the eravacycline MIC\textsubscript{50} for A. baumannii (including the CR subset) and S. maltophilia was 1 mg/L, and was found to be 2-4 fold more potent than tigecycline and colistin, comparatively.
- Based on MIC\textsubscript{90} values, the potency of eravacycline was 2-4 fold greater than that of tigecycline.
- The origin of the bacterial isolates was widely diverse throughout Europe, with the source of infection for the majority of the isolates coming from bodily fluids, respiratory, gastrointestinal, and the genitourinary regions.
- Eravacycline shows promising activity against A. baumannii, including CR-resistant isolates, and S. maltophilia from European patients.

Table 1. Cumulative MIC\textsubscript{90} distribution for eravacycline for A. baumannii and S. maltophilia including drug resistant phenotypes (CR)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of isolates (cumulative %) inhibited at eravacycline MIC (mg/L) of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>A. baumannii</td>
<td>8</td>
</tr>
<tr>
<td>S. maltophilia</td>
<td>0</td>
</tr>
</tbody>
</table>

References

Figure 1. Country of origin (N, %) for the 249 clinical isolates tested

Figure 2. MIC distribution of eravacycline, tigecycline, and colistin for A. baumannii (N=99)

Figure 3. MIC distribution of eravacycline, tigecycline, and colistin for S. maltophilia (N=150)

Figure 4. MIC distribution of eravacycline, tigecycline, and colistin for CR A. baumannii (N=150)

Figure 5. Isolate counts by source of infection (N=249)