**In Vitro Activity of Eravacycline and Comparators Against Acinetobacter baumannii, Including Carbapenem-Resistant Strains, and Stenotrophomonas maltophilia Isolated from Patients in the US**

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**Abstract**

**Background:** Eravacycline (ERV) is a novel, fully-synthetic fluoroquinolone antibiotic of the tetracycline class in development for the treatment of serious infections, including those caused by multidrug-resistant (MDR) pathogens. The purpose of this study was to evaluate in vitro activity of ERV and comparators against Acinetobacter baumannii (AB), including strains with a carbapenem-resistant (CR) phenotype, and Stenotrophomonas maltophilia (SM) isolated from US patients.

**Methods:** Non-duplicate, non-convective, single-gram colony isolates of AB and SM were collected from US patients in 2013-2014. MICs for ERV and comparators against 380 isolates from both species were determined by CLSI broth microdilution. Susceptibility was determined with CLSI 2015 breakpoints, where available. CR in AB (CRAB) was defined as resistance to imipenem.

**Results:** ERV activity against AB and SM was determined in the following Table. ERV MIC<sub>90</sub> for all AB and SM isolates was 1 mg/L and 2 mg/L for CRAB. TGC, imipenem (IPM), and colistin (CST) MIC<sub>90</sub> for AB were 4, 2, and 2 mg/L, respectively, and remained constant for CRAB. Susceptibility to CST for all AB was 99%, while for CRAB was 10%. Susceptibility to IPM for all AB and CRAB was poor (94.5%, 0% respectively). TGC, IPM, and CST MIC<sub>90</sub> for SM were 2, 4, and 4 mg/L, respectively.

**Conclusions:** Overall, ERV MIC<sub>90</sub> for AB and SM was 1 mg/L (2 mg/L for CRAB), and was 2-4-fold more potent than TGC or CST, and up to 4-fold more potent than IPM. ERV shows promising activity against AB and SM, including CRAB, isolated from US patients.

**Introduction**

Gram-negative bacteria are common causes of intra-abdominal infections, urinary tract infections, and other serious infections. Moreover, resistance amongst Gram-negative pathogens is increasing. Eravacycline is a novel, fully-synthetic fluoroquinolone antibiotic of the tetracycline class in development for the treatment of serious infections, including those caused by multidrug-resistant (MDR) pathogens. ERV is in phase 3 clinical development for the treatment of complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI), including pyelonephritis. The pharmacokinetics and pharmacodynamics of eravacycline have been studied in animals and during clinical trials. Two doses of eravacycline were used in clinical trials of SM that produced favorable results in terms of efficacy, safety and pharmacokinetic evaluations: 1.5 mg/kg IPM-1 and 1 mg/kg IPM-2. In phase 1 multiple ascending dose study in healthy volunteers, the <sup>14</sup>C-ERV delivery was 2.2-2.3 mg/L at day 1, respectively, and 1.9 and 1.8 mg/L at day 10, respectively, based on a four-compartment model (2). The AUC<sub>1-10</sub> values were 87.2 and 127 mg·h/L for the 1.5 mg/kg IPM-1 dose and 1 mg/kg IPM-2 dose, respectively (3).

Renal clearance of 3.0-3.5 L/h was reported in healthy volunteers with approximately 10% excreted unchanged in the urine. In healthy subjects who received multiple IV doses of 1.5 mg/kg IPM over 60 minutes, eravacycline concentrations in urine collected from 0-6 h were 6.9 ± 1.2 mg/L on day 1 and 13.3 ± 3.4 mg/L on day 10 (2). 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 the US.

**Methods**

- A total of 380 clinical isolates (149 A. baumannii and 31 S. maltophilia) were collected from various body sites from 2013-2014, including CR isolates (breakdown by site of infection is given in Figure 1).
- Minimal inhibitory concentration (MIC) endpoints were determined by broth microdilution according to CLSI guidelines (4).
- Quality control testing was performed each day of testing as specified by the CLSI using E. coli ATCC 25922, E. coli ATCC 25921 and P. aeruginosa ATCC 27853.
- Antibiotic susceptibility was determined using CLSI 2015 breakpoints (5), where available.
- Carbapenem-resistant (CR) was defined as resistance to imipenem.

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>MIC (mg/L)</th>
<th>%S / %I / %R</th>
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<tbody>
<tr>
<td>AB</td>
<td>1</td>
<td>100% / 0% / 0%</td>
</tr>
<tr>
<td>SM</td>
<td>1</td>
<td>100% / 0% / 0%</td>
</tr>
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</table>

**Results**

The eravacycline MIC<sub>90</sub> values for all A. baumannii and S. maltophilia isolates were ≤0.25 mg/L. The eravacycline MIC<sub>90</sub> values for CR A. baumannii were 0.5 mg/L (Table 1).

The antimicrobial activity of eravacycline and comparators is shown in Table 2. MIC distributions for eravacycline, tigecycline, colistin, and imipenem for A. baumannii, CR A. baumannii, and S. maltophilia are shown in Figures 3, 4, and 5, respectively.

**Conclusions**

- Eravacycline was active against isolates of Acinetobacter baumannii, including carbapenem-resistant strains, and Stenotrophomonas maltophilia collected within the US.

**References**