Global in vitro activity of eravacycline and comparators against Enterobacteriaceae, Acinetobacter baumannii, Stenotrophomonas maltophilia, Staphylococcus aureus and Enterococcus spp. including multidrug-resistant (MDR) isolates from 2016

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Introduction

Eravacycline is a novel, fully-synthetic fluoroquinolone antibiotic currently under review by the EMA and FDA for the treatment of complicated intra-abdominal infections. The purpose of this study was to evaluate the activity of eravacycline and comparators against global isolates of Enterobacteriaceae, Acinetobacter baumannii, Stenotrophomonas maltophilia, Staphylococcus aureus (including methicillin-resistant S. aureus, MRSA) and Enterococcus spp., including those that are multidrug-resistant (MDR).

Methods

• A total of 6719 clinical isolates collected in 2016 from genito-urinary, gastro-intestinal, body fluids, and respiratory sources were tested.

• Global distribution of the clinical isolates are shown in Figure 1.

• MDR was defined as resistance to ≥ 3 from cephalosporin, cefotaxime/ceftriaxone/ceftriaxone (any one),第三代头孢, gentamicin, a carbapenem (meropenem or ertapenem), levofloxacin, piperacillin-tazobactam, tigecycline or tigecycline.

• Minimal inhibitory concentration (MIC) values were determined by broth microdilution according to CLSI guidelines

• Quality control testing was performed each day of testing as specified by the CLSI using Escherichia coli ATCC 25922, E. coli ATCC 35218, Klebsiella pneumoniae ATCC 700603, Pseudomonas aeruginosa ATCC 27853, and E. feacalis ATCC 29212 and S. aureus ATCC 29213.

• Antibiotic susceptibility was determined using CLSI 2016 breakpoints.

Results

• Susceptibility data, MIC\textsubscript{\text{MIC}} values, and MIC ranges for eravacycline and comparators are shown in Tables 1 - 8.

• The susceptibility range of MDR Enterobacteriaceae was from 22% for ceftriaxone to 93% for meropenem, with 81.1% of isolates susceptible to tigecycline (Table 2).

• Against Enterobacteriaceae, the MIC\textsubscript{\text{MIC}} for eravacycline was 4-fold lower than tigecycline (Table 1).

• Similarly, against MDR Enterobacteriaceae (Table 2), including versus specific strains (Table 3) eravacycline was observed to be at least 2-fold more potent than tigecycline and at least 8-fold more potent than minocycline.

• 80.1% and 93.8% of MRSA were susceptible to tigecycline and tetracycline, respectively (Table 5).

• The MIC\textsubscript{\text{MIC}} of eravacycline was at least 4-fold lower than tigecycline against S. aureus, including MRSA (Table 5).

• Versus A. baumannii, eravacycline demonstrated 8-fold greater potency compared to tigecycline and minocycline (Table 8).

Conclusions

• Eravacycline demonstrated potent in vitro activity against Enterobacteriaceae, including MDR phenotypes, as well as clinically important Gram-positive organisms and S. maltophilia collected globally in 2016.

• Eravacycline demonstrated lower MIC\textsubscript{\text{MIC}} values compared to tigecycline against Enterobacteriaceae, S. aureus, Enterococcus spp. and S. maltophilia, including MDR organisms.

• This global surveillance investigation highlights eravacycline’s broad spectrum potency against Gram-negative and Gram-positive bacteria, including MDR strains and further underscores its potential benefit for treatment of polymicrobial infections caused by resistant pathogens.

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Figure 1. Percent distribution of all isolates by geographic origin

Table 1. Susceptibility of Enterobacteriaceae (n = 3,317) to eravacycline and comparators.

| Organism | Drug Breakpoints (S|I|R) | %S | %I | %R | MIC<sub>50</sub> | MIC<sub>90</sub> | Minimum | Maximum |
|----------|------------------------|-----|-----|-----|----------------|----------------|---------|---------|
| E. coli  | Levofloxacin <=2 | 4 | >=8 | 29.4 | 16 | 64 | 0.03 | > 64 |
|         | Meropenem <=2 | 4 | >=8 | 32.4 | 64 | > 64 | <= 0.03 | > 64 |
|         | Ceftazidime <=8 | 16 | >=32 | 30.8 | 64 | > 64 | 0.12 | > 64 |
|         | Ampicillin <=8 | -- | >=16 | 65.7 | 2 > 8 | 0.5 > 8 | > 8 |
|         | Penicillin <=0.12 | -- | >=0.25 | 32.03 | 2 > 8 | <= 0.12 | > 2 |
|         | Linezolid <=4 | -- | >=8 | 100 | 24 | <= 0.5 | 2 |

References


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