Presentation 005
Monday

In Vitro Activity of Eravacycline and Comparators Against *Enterobacteriaceae*, Including Strains Resistant to Carbapenems or 3rd/4th Generation Cephalosporins in the US

Y Doi[1], GR Corey[2], I Morrissey[3], T Grossman[4], K Luepke[4], P Scoble[4], J Sutcliffe[4]

[1]University of Pittsburgh Medical Center; Pittsburgh, PA; [2]Duke University Medical Center, Durham, NC [3]IHMA Europe Sarl, Monthey, Switzerland [4]Tetraphase Pharmaceuticals, Watertown, MA

Contact:
Tetraphase Pharmaceuticals
Medical Information (TPMI)
medinfo@tphase.com
617-715-3600

Abstract

Background: Eravacycline (ERV) is a novel, fully-synthetic fluorocycline 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 the *in vitro* activity of ERV and comparators against *Enterobacteriaceae* (ENT), including isolates resistant to carbapenems (CR) or 3rd/4th generation cephalosporins (GC-R) in the US.

Materials/methods: Clinical isolates were collected from various body sites in patients in US hospitals from 2013-14. MIC results for ERV and comparators against 2,723 ENT isolates were determined by CLSI broth microdilution. Susceptibility was determined with CLSI 2015 breakpoints, except for tigecycline (TGC) where FDA breakpoints were used. GC-R was defined as resistant to ceftriaxone, cefotaxime, ceftazidime, or cefepime (FEP). CR was defined as resistant to imipenem (IPM).

Results: The ERV $MIC_{50/90}$ values for all ENT were 0.5/2 mg/L. The ERV $MIC_{50/90}$ values of GC-R and CR isolates were 0.5/2 and 1/2 mg/L, respectively. ERV and comparator MIC results (mg/L) for *Escherichia coli, Klebsiella pneumoniae*, and *Serratia marcescens* are shown in the table below. Most GC-R ENT were susceptible to TGC (91.8%), however susceptibilities decreased in CR isolates (61.4%).

Organism (N)	ERV	TGC	IPM	FEP
	$MIC_{50/90}$	$MIC_{50/90}$	$MIC_{50/90}$	$MIC_{50/90}$
E. coli (349)	0.12/0.25	0.25/0.5	≤0.25/0.5	≤0.25/4
GC-R (50)	0.25/0.5	0.25/0.5	≤0.25/1	16/>16
K. pneumoniae (350)	0.5/1	0.5/2	≤0.25/1	≤0.25/4
GC-R (50)	1/2	1/2	0.5/8	16/>16
CR (20)	0.5/2	1/2	>8/>8	>16/>16
S. marcescens (347)	1/2	2/2	1/2	≤0.25/0.5
GC-R (26)	2/2	2/2	1/4	1/16
CR (6)	1/2	1/2	4/>8	≤0.25/>16

$MIC_{50/90}$, minimal inhibitory concentration required to inhibit growth of 50/90% of isolates (mg/L)

Conclusion: Overall, ERV MIC90 for ENT isolates ranged from 0.25-2 mg/L, and was the same or within two-fold for GC-R and CR isolates. Potency of ERV was comparable to 2-fold greater than TGC. ERV potency was up to 4-fold and 8-fold greater for IPM for FEP, respectively. ERV shows promising activity against ENT, including those with resistant phenotypes, isolated from US patients.

Introduction

Gram-negative bacteria are common causes of intra-abdominal infections and urinary tract infections, and resistance amongst these pathogens is increasing. Eravacycline (ERV) is a novel, fully-synthetic fluorocycline 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 cIAI that produced favorable results in terms of efficacy, safety and pharmacokinetic evaluations: 1.5 mg/kg q24h and 1 mg/kg q12h (1, 2). In a phase 1 multiple-ascending dose study in healthy volunteers, the C_{max} values after a 60-minute infusion were 2.7 and 2.1 mg/L at day 1, respectively, and 1.9 and 1.8 mg/L at day 10, respectively, based on a four-compartment model (3). AUC_{ss} values were 8.7 and 12.7 mg·hr/L for the 1.5 mg/kg q24h dose and 1 mg/kg q12h dose, respectively (3).

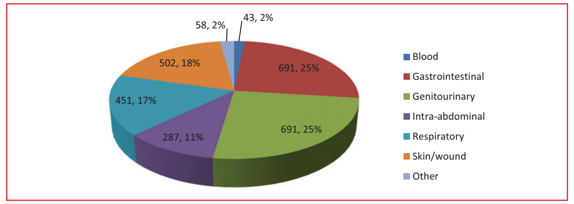
Renal clearance of 3.0-3.5 L/h was reported in healthy volunteers with approximately 16% excreted unchanged in the urine. In healthy subjects who received multiple IV doses of 1.5 mg/kg q24h over 60 minutes, eravacycline concentrations in urine collected from 0–8 h were 6.9 ± 1.2 mg/L on day 1 and 13.3 ± 3.4 mg/L on day 10 (2).

The purpose of this study was to assess the *in vitro* activity of eravacycline and comparators against *Enterobacteriaceae*, including isolates resistant to carbapenems (CR) or 3rd/4th generation cephalosporins (GC-R) in the US.

Methods

- A total of 2,723 clinical isolates, collected from various body sites in 2013-2014 from 43 US hospitals, were tested (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 *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853.
- Antibiotic susceptibility was determined using CLSI 2015 breakpoints (5), with the exception of tigecycline (TGC), where FDA breakpoints were used (6).
- GC-R was defined as resistant to ceftriaxone, cefotaxime, ceftazidime, or cefepime.
- CR was defined as resistant to imipenem (IPM).

Figure 1. Isolate counts (n, %) by source of infection (N=2,723)



Other includes HEENT (Head, Ears, Eyes, Nose, and Throat), Instruments (Catheters/Drains/Tubes), Bone, Bodily Fluids (Aspirate, CSF), Lymph & Muscle Tissue

Results

- ERV MICs against *Enterobacteriaceae* from US hospitals ranged from 0.06 to 8 mg/L, with $MIC_{50/90}$ values of 0.5/2 mg/L against all isolates combined (Table 1).
- Similar ERV MIC distribution was observed against *Enterobacter* spp., *Klebsiella* spp. and *Citrobacter* spp., but ERV MIC distribution was slightly lower against *Escherichia coli* (range 0.06 to 2 mg/L) and slightly higher against indole-positive *Proteeae* or *Proteus mirabilis* (range 0.25 to 8 mg/L) and *Serratia marcescens* (range 0.5 to 8 mg/L) (Table 1).
- Nevertheless ERV MIC_{90} values were no higher than 2 mg/L against all *Enterobacteriaceae* (Table 1), including GC-R (Table 2) and CR (Table 3) isolates, except for GC-R indole-positive *Proteeae* or *Proteus mirabilis* (Table 2) where ERV MIC_{90} values were 4 mg/L.
- Based on MIC_{90} values, the potency of ERV was up to 2-fold greater than that of TGC against *Enterobacteriaceae* pathogens (Table 1) including GC-R (Table 2) and CR (Table 3) isolates.
- ERV MIC distribution against GC-R isolates was identical to the combined population, but higher against CR isolates (Figure 2).

Figure 2. MIC distribution for eravacycline against all *Enterobacteriaceae*, 3rd/4th generation cephalosporin-resistant (GC-R) *Enterobacteriaceae* and imipenem-resistant (CR) *Enterobacteriaceae*

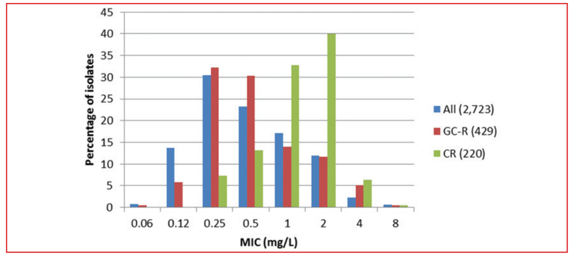


Table 1. Antimicrobial activity of eravacycline and comparator agents against *Enterobacteriaceae*

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{90}	Range	%S	%I	%R
***Enterobacteriaceae* (2723)**						
Aztreonam	≤0.5	>16	≤0.5 - >16	86.5	1.1	12.5
Cefepime	≤0.25	1	≤0.25 - >16	94.0	2.7	3.3
Ceftazidime	≤0.5	>16	≤0.5 - >16	87.2	1.1	11.7
Ceftriaxone	≤0.5	32	≤0.5 - >32	82.7	1.9	15.4
Colistin	1	>4	≤0.12 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.06 - 8**	**--**	**--**	**--**
Gentamicin	0.5	2	≤0.25 - >8	93.0	1.0	6.0
Imipenem	0.5	2	≤0.25 - >8	77.3	14.6	8.1
Levofloxacin	≤0.25	>4	≤0.25 - >4	87.0	1.8	11.3
Piperacillin/tazobactam	2	32	≤0.5 - >64	88.0	9.1	2.9
Tetracycline	2	>8	≤0.25 - >8	61.6	5.9	32.6
Tigecycline	0.5	2	0.03 - 16	92.2	6.3	1.5
***Enterobacter* spp (699)**						
Aztreonam	≤0.5	>16	≤0.5 - >16	73.8	1.4	24.8
Cefepime	≤0.25	2	≤0.25 - >16	93.3	4.9	1.9
Ceftazidime	≤0.5	>16	≤0.5 - >16	73.8	0.6	25.6
Ceftriaxone	≤0.5	>32	≤0.5 - >32	69.0	1.9	29.2
Colistin	0.5	1	≤0.12 - >4	--	--	--
Eravacycline	**0.5**	**1**	**0.12 - 8**	**--**	**--**	**--**
Gentamicin	0.5	1	≤0.25 - >8	96.4	0.7	2.9
Imipenem	1	2	≤0.25 - >8	75.8	21.8	2.4
Levofloxacin	≤0.25	1	≤0.25 - >4	96.0	1.3	2.7
Piperacillin/tazobactam	4	64	≤0.5 - >64	76.3	19.9	3.9
Tetracycline	2	8	0.5 - >8	88.0	3.9	8.2
Tigecycline	0.5	1	0.03 - 8	97.1	2.2	0.7
***Klebsiella* spp (697)**						
Aztreonam	≤0.5	>16	≤0.5 - >16	88.8	0.6	10.6
Cefepime	≤0.25	1	≤0.25 - >16	93.3	2.2	4.6
Ceftazidime	≤0.5	2	≤0.5 - >16	91.5	1.0	7.5
Ceftriaxone	≤0.5	4	≤0.5 - >32	88.5	0.9	10.6
Colistin	1	1	≤0.12 - >4	--	--	--
Eravacycline	**0.25**	**1**	**0.06 - 8**	**--**	**--**	**--**
Gentamicin	0.5	1	≤0.25 - >8	96.3	1.2	2.6
Imipenem	≤0.25	0.5	≤0.25 - >8	94.8	2.3	2.9
Levofloxacin	≤0.25	2	≤0.25 - >4	90.2	1.7	8.0
Piperacillin/tazobactam	2	32	≤0.5 - >64	89.0	6.3	4.7
Tetracycline	2	>8	≤0.25 - >8	84.5	5.2	10.3
Tigecycline	0.5	2	0.12 - 16	96.6	2.7	0.7
***Escherichia coli* (349)**						
Aztreonam	≤0.5	16	≤0.5 - >16	86.3	2.3	11.5
Cefepime	≤0.25	4	≤0.25 - >16	88.3	2.6	9.2
Ceftazidime	≤0.5	8	≤0.5 - >16	87.7	2.6	9.7
Ceftriaxone	≤0.5	>32	≤0.5 - >32	85.7	0.3	14.0
Colistin	0.5	1	0.25 - 4	--	--	--
Eravacycline	**0.12**	**0.25**	**0.06 - 2**	**--**	**--**	**--**
Gentamicin	1	>8	≤0.25 - >8	81.1	0.9	18.1
Imipenem	≤0.25	0.5	≤0.25 - 1	100	0	0
Levofloxacin	≤0.25	>4	≤0.25 - >4	64.8	0.3	35.0
Piperacillin/tazobactam	2	8	≤0.5 - >64	94.3	5.2	0.6
Tetracycline	2	>8	1 - >8	62.5	1.7	35.8
Tigecycline	0.25	0.5	0.12 - 2	100		
***Serratia marcescens* (347)**						
Aztreonam	≤0.5	1	≤0.5 - >16	96.0	0.9	3.2
Cefepime	≤0.25	0.5	≤0.25 - >16	98.3	0.6	1.2
Ceftazidime	≤0.5	≤0.5	≤0.5 - >16	97.7	0.3	2.0
Ceftriaxone	≤0.5	2	≤0.5 - >32	88.8	3.8	7.5
Colistin	>4	>4	1 - >4	--	--	--
Eravacycline	**1**	**2**	**0.5 - 8**	**--**	**--**	**--**
Gentamicin	1	1	≤0.25 - >8	98.0	0.6	1.4
Imipenem	1	2	≤0.25 - >8	87.6	10.7	1.7
Levofloxacin	≤0.25	2	≤0.25 - >4	93.7	1.2	5.2
Piperacillin/tazobactam	2	16	≤0.5 - >64	90.8	8.7	0.6
Tetracycline	>8	>8	2 - >8	1.7	20.5	77.8
Tigecycline	2	2	0.5 - 16	96.8	2.0	1.2
***Proteus mirabilis* (258)**						
Aztreonam	≤0.5	≤0.5	≤0.5 - >16	98.1	0	1.9
Cefepime	≤0.25	0.5	≤0.25 - >16	94.6	3.5	1.9
Ceftazidime	≤0.5	≤0.5	≤0.5 - >16	96.9	0.8	2.3
Ceftriaxone	≤0.5	1	≤0.5 - 32	91.9	3.5	4.7
Colistin	>4	>4	4 - >4	--	--	--
Eravacycline	**1**	**2**	**0.25 - 8**	**--**	**--**	**--**
Gentamicin	2	>8	≤0.25 - >8	86.4	1.9	11.6
Imipenem	2	4	≤0.25 - >8	19.8	42.3	38.0
Levofloxacin	≤0.25	>4	≤0.25 - >4	75.2	1.9	22.9
Piperacillin/tazobactam	≤0.5	1	≤0.5 - >64	98.5	0.8	0.8
Tetracycline	>8	>8	0.5 - >8	3.1	0.4	96.5
Tigecycline	2	4	0.25 - 8	55.0	38.0	7.0
***Citrobacter* spp (206)**						
Aztreonam	≤0.5	16	≤0.5 - >16	83.5	1.0	15.5
Cefepime	≤0.25	1	≤0.25 - >16	98.5	1.0	0.5
Ceftazidime	≤0.5	>16	≤0.5 - >16	83.0	1.0	16.0
Ceftriaxone	≤0.5	>32	≤0.5 - >32	82.0	1.0	17.0
Colistin	1	1	≤0.12 - >4	--	--	--
Eravacycline	**0.25**	**0.5**	**0.06 - 4**	**--**	**--**	**--**
Gentamicin	1	2	≤0.25 - >8	96.1	0	3.9
Imipenem	0.5	2	≤0.25 - >8	88.8	10.2	1.0
Levofloxacin	≤0.25	1	≤0.25 - >4	95.6	2.4	1.9
Piperacillin/tazobactam	2	32	≤0.5 - >64	87.9	6.3	5.8
Tetracycline	1	>8	≤0.25 - >8	89.3	0.5	10.2
Tigecycline	0.5	1	0.06 - 4	99.5	0.5	0
Indole-positive *Proteeae* (167)						
Aztreonam	≤0.5	1	≤0.5 - >16	95.8	1.2	3.0
Cefepime	≤0.25	0.5	≤0.25 - >16	96.4	1.8	1.8
Ceftazidime	≤0.5	2	≤0.5 - >16	92.8	2.4	4.8
Ceftriaxone	≤0.5	4	≤0.5 - 32	84.4	4.8	10.8
Colistin	>4	>4	>4 - >4	--	--	--
Eravacycline	**1**	**2**	**0.25 - 8**	**--**	**--**	**--**
Gentamicin	2	>8	≤0.25 - >8	86.2	2.4	11.4
Imipenem	2	4	≤0.25 - 8	16.8	37.1	46.1
Levofloxacin	≤0.25	>4	≤0.25 - >4	75.5	7.2	17.4
Piperacillin/tazobactam	≤0.5	4	≤0.5 - >64	98.2	1.2	0.6
Tetracycline	>8	>8	1 - >8	33.5	10.8	55.7
Tigecycline	2	4	0.25 - 8	75.5	19.2	5.4

"--" = No breakpoint defined

Table 2. Antimicrobial activity of eravacycline and comparator agents against 3rd/4th generation cephalosporin-resistant (GC-R) *Enterobacteriaceae*

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{50}	Range	%S	%I	%R
***Enterobacteriaceae* (429)**						
Aztreonam	>16	>16	≤0.5 - >16	16.1	6.1	77.9
Cefepime	2	>16	≤0.25 - >16	63.4	15.6	21.0
Ceftazidime	>16	>16	≤0.5 - >16	21.5	4.2	74.4
Ceftriaxone	32	>32	≤0.5 - >32	1.6	0.9	97.4
Colistin	0.5	>4	≤0.12 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.06 - 8**	**--**	**--**	**--**
Gentamicin	0.5	>8	≤0.25 - >8	74.4	4.4	21.2
Imipenem	1	4	≤0.25 - >8	77.9	10.0	12.1
Levofloxacin	0.5	>4	≤0.25 - >4	64.8	4.2	31.0
Piperacillin/tazobactam	32	>64	≤0.5 - >64	36.8	46.2	17.0
Tetracycline	4	>8	1 - >8	58.3	8.6	33.1
Tigecycline	1	2	0.12 - 8	91.8	6.5	1.6
***Enterobacter* spp (206)**						
Aztreonam	>16	>16	≤0.5 - >16	12.1	4.9	83.0
Cefepime	1	4	≤0.25 - >16	77.2	16.5	6.3
Ceftazidime	>16	>16	≤0.5 - >16	11.2	1.9	86.9
Ceftriaxone	32	>32	1 - >32	1.0	0	99.0
Colistin	0.5	1	≤0.12 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.12 - 8**	**--**	**--**	**--**
Gentamicin	0.5	8	≤0.25 - >8	87.9	2.4	9.7
Imipenem	1	2	≤0.25 - >8	85.9	9.7	4.4
Levofloxacin	≤0.25	4	≤0.25 - >4	88.8	3.4	7.8
Piperacillin/tazobactam	32	>64	≤0.5 - >64	21.8	65.1	13.1
Tetracycline	4	>8	1 - >8	77.2	8.7	14.1
Tigecycline	0.5	2	0.25 - 8	93.7	5.3	1.0
***Klebsiella* spp (77)**						
Aztreonam	>16	>16	≤0.5 - >16	5.2	1.3	93.5
Cefepime	4	>16	≤0.25 - >16	39.0	19.5	41.6
Ceftazidime	>16	>16	≤0.5 - >16	29.9	2.6	67.5
Ceftriaxone	>32	>32	1 - >32	3.9	0	96.1
Colistin	1	1	0.25 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.06 - 4**	**--**	**--**	**--**
Gentamicin	1	>8	≤0.25 - >8	72.7	10.4	16.9
Imipenem	0.5	>8	≤0.25 - >8	71.4	6.5	22.1
Levofloxacin	>4	>4	≤0.25 - >4	35.1	5.2	59.7
Piperacillin/tazobactam	64	>64	2 - >64	27.3	32.5	40.3
Tetracycline	4	>8	1 - >8	58.4	10.4	31.2
Tigecycline	1	2	0.25 - 4	92.2	7.8	0
***Escherichia coli* (50)**						
Aztreonam	>16	>16	1 - >16	4.0	16.0	80.0
Cefepime	16	>16	≤0.25 - >16	22.0	14.0	64.0
Ceftazidime	16	>16	≤0.5 - >16	16.0	16.0	68.0
Ceftriaxone	>32	>32	≤0.5 - >32	2.0	0	98.0
Colistin	0.5	1	0.25 - 1	--	--	--
Eravacycline	**0.25**	**0.5**	**0.06 - 1**	**--**	**--**	**--**
Gentamicin	>8	>8	≤0.25 - >8	28.0	4.0	68.0
Imipenem	≤0.25	1	≤0.25 - 1	100	0	0
Levofloxacin	>4	>4	≤0.25 - >4	8.0	0	92.0
Piperacillin/tazobactam	4	64	≤0.5 - >64	80.0	18.0	2.0
Tetracycline	>8	>8	1 - >8	26.0	0	74.0
Tigecycline	0.25	0.5	0.12 - 1	100	0	0
***Citrobacter* spp (36)**						
Aztreonam	>16	>16	1 - >16	5.6	5.6	88.9
Cefepime	1	2	≤0.25 - >16	91.7	5.6	2.8
Ceftazidime	>16	>16	≤0.5 - >16	2.8	5.6	91.7
Ceftriaxone	>32	>32	2 - >32	0	2.8	97.2
Colistin	1	1	0.5 - 2	--	--	--
Eravacycline	**0.25**	**1**	**0.12 - 2**	**--**	**--**	**--**
Gentamicin	1	>8	0.5 - >8	86.1	0	13.9
Imipenem	1	2	≤0.25 - >8	83.3	13.9	2.8
Levofloxacin	≤0.25	4	≤0.25 - >4	86.1	8.3	5.6
Piperacillin/tazobactam	32	>64	≤0.5 - >64	33.3	36.1	30.6
Tetracycline	2	>8	1 - >8	72.2	2.8	25.0
Tigecycline	0.5	1	0.25 - 2	100	0	0
***Serratia marcescens* (26)**						
Aztreonam	8	>16	≤0.5 - >16	46.2	11.5	42.3
Cefepime	1	16	≤0.25 - >16	76.9	7.7	15.4
Ceftazidime	1	>16	≤0.5 - >16	69.2	3.9	26.9
Ceftriaxone	16	>32	4 - >32	0	0	100
Colistin	>4	>4	1 - >4	--	--	--
Eravacycline	**2**	**2**	**0.5 - 4**	**--**	**--**	**--**
Gentamicin	1	>8	≤0.25 - >8	73.1	7.7	19.2
Imipenem	1	4	0.5 - >8	76.9	11.5	11.5
Levofloxacin	1	>4	≤0.25 - >4	73.1	3.9	23.1
Piperacillin/tazobactam	32	64	2 - >64	38.5	53.9	7.7
Tetracycline	>8	>8	4 - >8	3.9	30.8	65.4
Tigecycline	2	2	0.5 - 4	96.2	3.9	0.0
Indole-positive *Proteeae* (19)						
Aztreonam	≤0.5	>16	≤0.5 - >16	63.2	10.5	26.3
Cefepime	0.5	>16	≤0.25 - >16	79.0	5.3	15.8
Ceftazidime	2	>16	≤0.5 - >16	57.9	0	42.1
Ceftriaxone	8	32	2 - 32	0	5.3	94.7
Colistin	>4	>4	>4 - >4	--	--	--
Eravacycline	**2**	**4**	**0.5 - 4**	**--**	**--**	**--**
Gentamicin	2	>8	0.5 - >8	63.2	10.5	26.3
Imipenem	4	8	2 - 8	0	36.8	63.2
Levofloxacin	≤0.25	>4	≤0.25 - >4	63.2	10.5	26.3
Piperacillin/tazobactam	1	64	≤0.5 - >64	84.2	10.5	5.3
Tetracycline	>8	>8	1 - >8	31.6	10.5	57.9
Tigecycline	2	8	1 - 8	63.2	26.3	10.5
***Proteus mirabilis* (15)**						
Aztreonam	≤0.5	>16	≤0.5 - >16	80.0	0	20.0
Cefepime	8	>16	1 - >16	26.7	40.0	33.3
Ceftazidime	2	>16	≤0.5 - >16	53.3	6.7	40.0
Ceftriaxone	8	16	≤0.5 - 32	6.7	13.3	80.0
Colistin	>4	>4	>4 - >4	--	--	--
Eravacycline	**2**	**4**	**0.25 - 4**	**--**	**--**	**--**
Gentamicin	>8	>8	2 - >8	40.0	0.0	60.0
Imipenem	4	8	1 - >8	13.3	20.0	66.7
Levofloxacin	>4	>4	≤0.25 - >4	13.3	6.7	80.0
Piperacillin/tazobactam	1	8	≤0.5 - 32	93.3	6.7	0
Tetracycline	>8	>8	>8 - >8	0	0	100
Tigecycline	4	8	1 - 8	46.7	33.3	20.0

"--" = No breakpoint defined

Table 3. Antimicrobial activity of eravacycline and comparator agents against imipenem-resistant (CR) *Enterobacteriaceae*

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{50}	MIC_{50}	%S	%I	%R
***Enterobacteriaceae* (220)**						
Aztreonam	≤0.5	>16	≤0.5 - >16	83.6	0.9	15.5
Cefepime	≤0.25	16	≤0.25 - >16	83.2	4.6	12.3
Ceftazidime	≤0.5	>16	≤0.5 - >16	80.5	1.8	17.7
Ceftriaxone	≤0.5	>32	≤0.5 - >32	73.2	4.6	22.3
Colistin	>4	>4	0.25 - >4	--	--	--
Eravacycline	**1**	**2**	**0.25 - 8**	**--**	**--**	**--**
Gentamicin	2	>8	≤0.25 - >8	83.2	3.6	13.2
Imipenem	4	8	4 - >8	0	0	100
Levofloxacin	≤0.25	>4	≤0.25 - >4	71.4	4.1	24.6
Piperacillin/tazobactam	≤0.5	>64	≤0.5 - >64	84.6	3.2	12.3
Tetracycline	>8	>8	1 - >8	28.2	5.9	65.9
Tigecycline	2	4	0.25 - 8	61.4	31.4	7.3
***Proteus mirabilis* (98)**						
Aztreonam	≤0.5	1	≤0.5 - >16	95.9	0	4.1
Cefepime	≤0.25	2	≤0.25 - >16	90.8	6.1	3.1
Ceftazidime	≤0.5	2	≤0.5 - >16	93.9	2.0	4.1
Ceftriaxone	≤0.5	2	≤0.5 - 32	86.7	5.1	8.2
Colistin	>4	>4	>4 - >4	--	--	--
Eravacycline	**2**	**2**	**0.25 - 4**	**--**	**--**	**--**
Gentamicin	2	>8	1 - >8	83.7	2.0	14.3
Imipenem	4	8	4 - >8	0	0	100
Levofloxacin	≤0.25	>4	≤0.25 - >4	74.5	2.0	23.5
Piperacillin/tazobactam	≤0.5	2	≤0.5 - >64	95.9	2.0	2.0
Tetracycline	>8	>8	2 - >8	2.0	1.0	96.9
Tigecycline	4	8	0.25 - 8	37.8	51.0	11.2
Indole-positive *Proteeae* (77)						
Aztreonam	≤0.5	1	≤0.5 - >16	94.8	2.6	2.6
Cefepime	≤0.25	1	≤0.25 - >16	96.1	2.6	1.3
Ceftazidime	≤0.5	8	≤0.5 - >16	89.6	2.6	7.8
Ceftriaxone	≤0.5	4	≤0.5 - 16	79.2	6.5	14.3
Colistin	>4	>4	>4 - >4	--	--	--
Eravacycline	**1**	**2**	**0.25 - 8**	**--**	**--**	**--**
Gentamicin	2	>8	≤0.25 - >8	84.4	0	15.6
Imipenem	4	4	4 - 8	0	0	100
Levofloxacin	≤0.25	>4	≤0.25 - >4	77.9	7.8	14.3
Piperacillin/tazobactam	≤0.5	4	≤0.5 - >64	97.4	1.3	1.3
Tetracycline	8	>8	1 - >8	45.5	6.5	48.1
Tigecycline	2	4	0.25 - 8	72.7	20.8	6.5
***Klebsiella* spp (20)**						
Aztreonam	>16	>16	≤0.5 - >16	15.0	0	85.0
Cefepime	>16	>16	≤0.25 - >16	15.0	0	85.0
Ceftazidime	>16	>16	≤0.5 - >16	15.0	0	85.0
Ceftriaxone	>32	>32	≤0.5 - >32	15.0	0	85.0
Colistin	1	1	0.5 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.25 - 2**	**--**	**--**	**--**
Gentamicin	1	8	≤0.25 - >8	75.0	20.0	5.0
Imipenem	>8	>8	4 - >8	0	0	100
Levofloxacin	>4	>4	≤0.25 - >4	15.0	0	85.0
Piperacillin/tazobactam	>64	>64	2 - >64	15.0	0	85.0
Tetracycline	4	>8	2 - >8	70.0	15.0	15.0
Tigecycline	1	2	0.5 - 4	95.0	5.0	0
***Enterobacter* spp (17)**						
Aztreonam	2	>16	≤0.5 - >16	52.9	0	47.1
Cefepime	≤0.25	>16	≤0.25 - >16	70.6	11.8	17.7
Ceftazidime	4	>16	≤0.5 - >16	52.9	0	47.1
Ceftriaxone	8	>32	≤0.5 - >32	47.1	0	52.9
Colistin	0.5	1	0.25 - >4	--	--	--
Eravacycline	**0.5**	**2**	**0.25 - 4**	**--**	**--**	**--**
Gentamicin	0.5	8	≤0.25 - >8	88.2	5.9	5.9
Imipenem	4	>8	4 - >8	0	0	100
Levofloxacin	≤0.25	>4	≤0.25 - >4	82.4	5.9	11.8
Piperacillin/tazobactam	32	>64	2 - >64	47.1	23.5	29.4
Tetracycline	4	>8	2 - >8	58.8	5.9	35.3
Tigecycline	1	4	0.25 - 4	88.2	11.8	0

"--" = No breakpoint defined

Conclusions

- Overall, ERV MIC_{90} values for ENT isolates ranged from 0.25-2 mg/L, and was the same or within two-fold for GC-R and CR isolates.
- Potency of ERV was equal to or two-fold greater than TGC.
- ERV shows promising activity against ENT, including those with resistant phenotypes, isolated from US patients.

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