Poster #1825

In vitro global surveillance of eravacycline and comparators against Enterobacteriaceae, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, including multidrug-resistant (MDR) isolates, over a three-year period (2013-15)

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Introduction

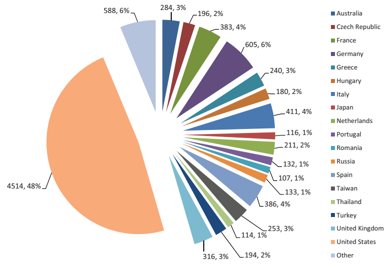
Gram-negative bacteria are common causes of intra-abdominal infections and urinary tract infections, and resistance amongst these pathogens is increasing.[1] Eravacycline (ERV) is a novel, fully-synthetic fluorocycline antibiotic of the tetracycline class in development for the treatment of serious infections, 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 purpose of this study was to evaluate activity of ERV and comparators against global isolates of Enterobacteriaceae (ENT), *A. baumannii* (AB), and *S. maltophilia* (SM), including those resistant to carbapenems (CR) or 3rd/4th generation cephalosporins (ESC-R), over a three-year surveillance period.

Methods

- A total of 9363 clinical isolates, collected from 2013-2015 from 205 hospitals, were tested.
- Clinical isolates were from global locations, with 48% from countries within North America (specifically, the United States), 41% from within Europe, 7% from within Asia, and 4% from within the South Pacific (Fig. 1).
- Most isolates were collected from respiratory, GI, GU, and bodily fluid sources followed by skin/wound infections (Fig. 2).
- Minimal inhibitory concentration (MIC) endpoints were determined by broth microdilution according to CLSI guidelines.[2]
- Quality control testing was performed each day of testing as specified by the CLSI using *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218 and *P. aeruginosa* ATCC 27853.
- Antibiotic susceptibility was determined using CLSI 2015 breakpoints[3], with the exception of tigecycline (TGC), where FDA breakpoints were used.[4]
- MDR was defined as resistant to at least 1 agent in 3 or more antibiotic categories.
- ESC-R was defined as resistant to ceftriaxone, cefotaxime, ceftazidime, or cefepime.
- CR was defined as resistant to imipenem (2013-2014 isolates) or meropenem (2015 isolates).

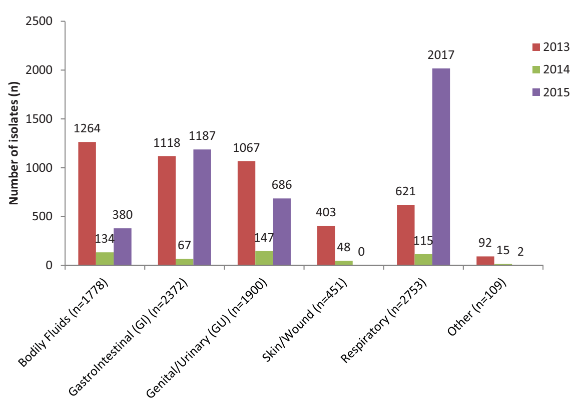
Figure 1. Isolate counts (n, %) by country of origin for the 9,363 isolates collected from 2013-2015



Countries included as "Other" (Austria, Croatia, Denmark, Hong Kong, Ireland, Latvia, Lithuania, New Zealand, Serbia, Singapore, Sweden, and Switzerland) had less than 56 isolates each.

Methods (cont'd)

Figure 2. Isolate counts by source of infection and year for the 9,363 isolates collected in 2013 (n=4,565), 2014 (n=526) and 2015 (n=4,272)



Other includes Blood, Lymph, HEENT (Head, Eyes, Ears, Nose, and Throat), Instruments (Catheters/Drains/Tubes), Muscle, Reproductive Site, and Bone

Results

- ERV $MIC_{50/90}$ values for combined ENT were 0.5/2 mg/L (Table 1). The MIC_{90} values against MDR (Table 2) and ESC-R (Table 3) were identical to the combined population.
  - Amongst most ENT pathogens, ERV MIC_{90} values increased by 1 doubling-dilution for resistant phenotypes (Tables 1-4).
  - MIC_{90} values were no higher than 2 mg/L for ENT isolates with the following exceptions: MDR and ESC-R *S. marcescens*, MDR and ESC-R *Proteus mirabilis*, MDR Indole-positive *Proteeae*, and CR *Enterobacter* spp. had ERV MIC_{90} values of 4 mg/L.
- ERV $MIC_{50/90}$ values for combined AB were 0.5/2 mg/L (Table 1), and 1/2 mg/L for MDR, ESC-R, and CR AB (Tables 2-4).
- ERV $MIC_{50/90}$ values for combined SM were 1/2 mg/L (Table 1) and 2/8 mg/L for MDR SM (Table 2).
- Based on MIC_{90} values, the potency of ERV was up to 4-fold greater than that of TGC against these Gram-negative organisms.
- Cumulative MIC distribution patterns for ENT organisms were relatively consistent over the three-year period (Fig. 3). A one doubling-dilution shift was seen for SM and AB in the 0.12 – 1 mg/L ranges from 2013 to 2015. For both organisms, the number of 2014 isolates was low compared with 2015.

Results (cont'd)

Table 1. Summary antimicrobial activity of eravacycline and comparator agents against Enterobacteriaceae (n=7576), *S. maltophilia* (n=690), and *A. baumannii* (n=1097) isolates collected from 2013-2015

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{90}	Range Min	Max	%S
Enterobacteriaceae (7576)					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	84.9%
Cefepime	≤ 0.25	2	≤ 0.008	> 16	91.9%
Ceftazidime	≤ 0.5	> 16	≤ 0.03	> 128	85.4%
Ceftriaxone	≤ 0.5	> 4	≤ 0.015	> 32	80.6%
Colistin	0.5	> 4	≤ 0.12	> 4	--
Eravacycline	0.5	2	0.06	> 16	--
Gentamicin	0.5	4	≤ 0.12	> 16	92%
Levofloxacin	≤ 0.25	> 4	≤ 0.004	> 8	87.7%
Piperacillin/tazobactam	2	32	≤ 0.25	> 128	87.9%
Tetracycline	2	32	≤ 0.25	> 64	61.8%
Tigecycline	0.5	4	≤ 0.015	> 32	88.7%
***Klebsiella* spp.[a] (1898)**					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	84.7%
Cefepime	≤ 0.25	4	≤ 0.008	> 16	88.9%
Ceftazidime	≤ 0.5	16	≤ 0.03	> 128	88.4%
Ceftriaxone	≤ 0.5	> 4	≤ 0.015	> 32	84.4%
Colistin	0.5	1	≤ 0.12	> 4	--
Eravacycline	0.25	1	0.06	8	--
Gentamicin	0.5	1	≤ 0.12	> 16	93.3%
Levofloxacin	≤ 0.25	4	0.008	> 8	89.3%
Piperacillin/tazobactam	2	64	≤ 0.25	> 128	87.3%
Tetracycline	2	> 8	≤ 0.25	> 64	83.8%
Tigecycline	0.5	2	0.12	16	96.6%
***Enterobacter* spp.[b] (1683)**					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	72.2%
Cefepime	≤ 0.25	2	≤ 0.008	> 16	92%
Ceftazidime	≤ 0.5	> 16	0.06	> 128	71.3%
Ceftriaxone	≤ 0.5	32	≤ 0.015	> 32	66.9%
Colistin	0.5	1	≤ 0.12	> 4	--
Eravacycline	0.5	1	0.12	8	--
Gentamicin	0.5	1	≤ 0.12	> 16	95.3%
Levofloxacin	≤ 0.25	1	≤ 0.004	> 8	95.1%
Piperacillin/tazobactam	4	64	≤ 0.25	> 128	76.2%
Tetracycline	2	8	0.5	> 64	87.1%
Tigecycline	0.5	1	0.03	8	96.6%
***Escherichia coli* (996)**					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	83.8%
Cefepime	≤ 0.25	16	≤ 0.008	> 16	85.8%
Ceftazidime	≤ 0.5	16	≤ 0.03	> 128	85.7%
Ceftriaxone	≤ 0.5	> 4	≤ 0.015	> 32	82%
Colistin	0.5	1	0.25	4	--
Eravacycline	0.12	0.25	0.06	2	--
Gentamicin	1	> 8	≤ 0.12	> 16	83.2%
Levofloxacin	≤ 0.25	8	0.008	> 8	67.8%
Piperacillin/tazobactam	2	16	≤ 0.25	> 128	92.5%
Tetracycline	2	> 64	≤ 0.25	> 64	58.9%
Tigecycline	0.25	0.5	0.12	4	99.4%
***Citrobacter* spp.[c] (895)**					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	83.2%
Cefepime	≤ 0.25	1	0.015	> 16	96.3%
Ceftazidime	≤ 0.5	> 16	≤ 0.03	> 128	83.6%
Ceftriaxone	≤ 0.5	> 4	≤ 0.015	> 32	82.1%
Colistin	0.5	1	≤ 0.12	> 4	--
Eravacycline	0.25	0.5	0.06	4	--
Gentamicin	0.5	1	≤ 0.12	> 16	97.4%
Levofloxacin	≤ 0.25	0.5	0.008	> 8	96.3%
Piperacillin/tazobactam	2	32	≤ 0.5	> 128	87.3%
Tetracycline	1	8	≤ 0.25	> 64	89.6%
Tigecycline	0.5	1	≤ 0.015	4	97.9%
***Serratia marcescens* (719)**					
Aztreonam	≤ 0.5	2	≤ 0.03	> 16	93.3%
Cefepime	≤ 0.25	0.5	0.03	> 16	95.4%
Ceftazidime	≤ 0.5	1	0.06	> 128	96.1%
Ceftriaxone	≤ 0.5	2	0.03	> 32	87.3%
Colistin	> 4	> 4	0.5	> 4	--
Eravacycline	1	2	0.12	8	--
Gentamicin	1	2	≤ 0.12	> 16	96.2%
Levofloxacin	≤ 0.25	2	0.015	> 8	93.7%
Piperacillin/tazobactam	2	16	≤ 0.5	> 128	91.4%
Tetracycline	> 8	> 64	2	> 64	1.8%
Tigecycline	2	2	0.25	16	92.5%
***Proteus mirabilis* (717)**					
Aztreonam	≤ 0.5	≤ 0.5	≤ 0.03	> 16	98.7%
Cefepime	≤ 0.25	1	0.015	> 16	95.4%
Ceftazidime	≤ 0.5	≤ 0.5	≤ 0.03	64	95.8%
Ceftriaxone	≤ 0.5	1	≤ 0.015	> 32	91.6%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	2	2	0.25	> 16	--
Gentamicin	2	> 8	≤ 0.12	> 16	85.2%
Levofloxacin	≤ 0.25	> 4	0.008	> 8	80.3%
Piperacillin/tazobactam	≤ 0.5	1	≤ 0.25	> 128	98.3%
Tetracycline	> 8	64	0.5	> 64	2.4%
Tigecycline	4	8	0.25	> 32	32.6%
Indole-positive *Proteeae*[d] (668)					
Aztreonam	≤ 0.5	1	≤ 0.03	> 16	96.7%
Cefepime	≤ 0.25	0.5	0.015	> 16	95.8%
Ceftazidime	≤ 0.5	4	≤ 0.03	> 16	91.9%
Ceftriaxone	≤ 0.5	> 4	≤ 0.015	> 32	80.7%
Colistin	> 4	> 4	0.5	> 4	--
Eravacycline	1	2	0.12	16	--
Gentamicin	2	8	≤ 0.12	16	88.9%
Levofloxacin	≤ 0.25	> 4	0.008	> 4	84%
Piperacillin/tazobactam	≤ 0.5	2	≤ 0.25	> 64	98.1%
Tetracycline	> 8	> 8	0.5	> 64	31.3%
Tigecycline	2	4	0.25	32	74.1%
***S. maltophilia* (690)**					
Aztreonam	> 64	> 64	1	> 64	--
Cefepime	32	64	0.5	> 64	--
Ceftazidime	16	> 64	≤ 0.5	> 64	39.3%
Ceftriaxone	> 64	> 64	1	> 64	--
Colistin	1	8	≤ 0.12	> 32	--
Eravacycline	1	2	0.03	16	--
Gentamicin	64	> 64	≤ 0.25	> 64	--
Levofloxacin	1	8	0.12	64	75.5%
Piperacillin/tazobactam	128	> 128	2	> 128	--
Tetracycline	16	32	1	> 64	--
Tigecycline	1	4	0.06	16	--
***A. baumannii* (1097)**					
Aztreonam	32	> 64	≤ 0.5	> 64	--
Cefepime	> 16	> 64	≤ 0.25	> 64	28.4%
Ceftazidime	> 16	> 64	≤ 0.5	> 64	28.3%
Ceftriaxone	> 32	> 64	≤ 0.5	> 64	10.8%
Colistin	1	2	≤ 0.03	> 32	94.9%
Eravacycline	0.5	2	0.03	8	--
Gentamicin	> 8	> 64	≤ 0.03	> 64	38.6%
Levofloxacin	> 4	64	≤ 0.03	> 64	25.3%
Piperacillin/tazobactam	> 64	> 128	0.25	> 128	23.3%
Tetracycline	> 8	> 64	≤ 0.25	> 64	26.2%
Tigecycline	2	4	0.06	> 16	--

[a]Includes *K. pneumoniae* (983) and *K. oxytoca* (915); [b]Includes *E. cloacae* (935), *E. aerogenes* (743), and *E. asburiae* (5); [c]Includes *C. freundii* (507) and *C. koseri* (388); [d]Includes *Morganella morganii* (216), *Proteus vulgaris* (317), *Providencia rettgeri* (51), and *P. stuartii* (84)

Table 2. Summary antimicrobial activity of eravacycline and comparator agents against MDR Enterobacteriaceae (n=1235), *S. maltophilia* (n=36), and *A. baumannii* (n=801) isolates collected from 2013-2015

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{90}	Range Min	Max	%S
Enterobacteriaceae (1235)					
Aztreonam	> 16	> 16	≤ 0.03	> 16	34.1%
Cefepime	2	> 16	0.015	> 16	55.6%
Ceftazidime	> 16	128	≤ 0.03	> 128	36.8%
Ceftriaxone	> 4	> 32	≤ 0.015	> 32	24%
Colistin	0.5	> 4	0.25	> 4	--
Eravacycline	0.5	2	0.06	> 16	--
Gentamicin	2	> 16	≤ 0.12	> 16	59.4%
Levofloxacin	4	> 8	0.008	> 8	48%
Piperacillin/tazobactam	16	> 128	≤ 0.25	> 128	54.1%
Tetracycline	> 8	> 64	0.5	> 64	30.1%
Tigecycline	1	8	0.12	> 32	77.9%
***Klebsiella* spp.[a] (266)**					
Aztreonam	> 16	> 16	≤ 0.03	> 16	8.3%
Cefepime	> 16	> 16	0.015	> 16	25.2%
Ceftazidime	> 16	> 128	≤ 0.03	> 128	23.7%
Ceftriaxone	> 4	> 32	0.03	> 32	6.4%
Colistin	0.5	1	0.25	> 4	--
Eravacycline	0.5	2	0.12	8	--
Gentamicin	2	> 16	≤ 0.12	> 16	56.8%
Levofloxacin	> 4	> 8	0.03	> 8	33.8%
Piperacillin/tazobactam	> 64	> 128	1	> 128	32%
Tetracycline	8	> 64	0.5	> 64	42.9%
Tigecycline	1	2	0.12	16	91.4%
***Enterobacter* spp.[b] (296)**					
Aztreonam	> 16	> 16	≤ 0.03	> 16	11.2%
Cefepime	2	> 16	0.03	> 16	62.5%
Ceftazidime	> 16	128	0.12	> 128	11.2%
Ceftriaxone	> 4	> 32	0.06	> 32	7.8%
Colistin	0.5	1	0.25	> 4	--
Eravacycline	0.5	2	0.12	8	--
Gentamicin	0.5	> 8	≤ 0.12	> 16	75.7%
Levofloxacin	0.5	> 4	0.008	> 8	77.7%
Piperacillin/tazobactam	64	128	≤ 0.25	> 128	29.1%
Tetracycline	4	> 64	1	> 64	53.4%
Tigecycline	1	4	0.25	8	86.2%
***Escherichia coli* (244)**					
Aztreonam	16	> 16	0.06	> 16	40.2%
Cefepime	4	> 16	0.015	> 16	46.3%
Ceftazidime	8	32	0.06	> 128	45.1%
Ceftriaxone	> 4	> 32	0.03	> 32	34.4%
Colistin	0.5	1	0.25	2	--
Eravacycline	0.25	0.5	0.06	2	--
Gentamicin	> 8	> 16	≤ 0.12	> 16	43.9%
Levofloxacin	> 4	> 8	0.015	> 8	19.3%
Piperacillin/tazobactam	4	64	≤ 0.5	> 128	79.5%
Tetracycline	> 8	> 64	1	> 64	15.2%
Tigecycline	0.5	1	0.12	4	99.2%
***Citrobacter* spp.[c] (106)**					
Aztreonam	> 16	> 16	≤ 0.03	> 16	13.2%
Cefepime	1	> 16	0.015	> 16	75.5%
Ceftazidime	32	> 128	0.12	> 128	13.2%
Ceftriaxone	> 4	> 32	0.06	> 32	10.4%
Colistin	0.5	1	0.25	> 4	--
Eravacycline	0.25	1	0.12	4	--
Gentamicin	0.5	> 8	≤ 0.12	> 16	82.1%
Levofloxacin	≤ 0.25	8	0.015	> 8	76.4%
Piperacillin/tazobactam	> 64	> 128	2	> 128	24.5%
Tetracycline	2	> 64	1	> 64	54.7%
Tigecycline	0.5	2	0.25	4	91.5%
***Serratia marcescens* (58)**					
Aztreonam	> 16	> 16	0.12	> 16	32.8%
Cefepime	2	> 16	0.06	> 16	50%
Ceftazidime	4	32	0.25	> 128	56.9%
Ceftriaxone	> 4	> 32	0.12	> 32	17.2%
Colistin	> 1	> 4	0.5	> 4	--
Eravacycline	2	4	0.5	8	--
Gentamicin	2	> 16	≤ 0.12	> 16	58.6%
Levofloxacin	2	8	0.12	> 8	62.1%
Piperacillin/tazobactam	8	> 128	1	> 128	60.3%
Tetracycline	> 8	> 64	4	> 64	1.7%
Tigecycline	2	4	0.5	8	74.1%
***Proteus mirabilis* (171)**					
Aztreonam	≤ 0.5	4	≤ 0.03	> 16	94.7%
Cefepime	≤ 0.25	8	0.015	> 16	81.9%
Ceftazidime	≤ 0.5	16	≤ 0.03	64	83%
Ceftriaxone	≤ 0.5	16	≤ 0.015	> 32	67.8%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	2	4	0.25	> 16	--
Gentamicin	4	> 16	0.25	> 16	55%
Levofloxacin	> 4	> 8	0.03	> 8	40.4%
Piperacillin/tazobactam	1	8	≤ 0.25	> 128	93.6%
Tetracycline	> 8	64	4	> 64	0.6%
Tigecycline	8	8	0.5	> 32	16.4%
Indole-positive *Proteeae*[d] (94)					
Aztreonam	≤ 0.5	> 16	≤ 0.03	> 16	77.7%
Cefepime	≤ 0.25	16	0.06	> 16	76.6%
Ceftazidime	2	> 16	0.06	> 16	63.8%
Ceftriaxone	4	16	≤ 0.015	> 32	37.2%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	2	4	0.25	16	--
Gentamicin	> 8	> 8	0.25	16	38.3%
Levofloxacin	4	> 4	0.03	> 4	42.6%
Piperacillin/tazobactam	2	32	≤ 0.25	> 64	87.2%
Tetracycline	> 8	16	1	64	3.2%
Tigecycline	2	8	0.5	32	57.5%
***S. maltophilia* (36)**					
Aztreonam	> 64	> 64	4	> 64	--
Cefepime	32	> 64	8	> 64	--
Ceftazidime	> 64	> 64	4	> 64	2.8%
Ceftriaxone	> 64	> 64	64	> 64	--
Colistin	2	16	0.25	> 32	--
Eravacycline	2	8	0.5	16	--
Gentamicin	> 64	> 64	1	> 64	--
Levofloxacin	32	32	8	64	0%
Piperacillin/tazobactam	> 128	> 128	64	> 128	--
Tetracycline	32	64	8	> 64	--
Tigecycline	4	8	0.5	16	44.4%
***A. baumannii* (801)**					
Aztreonam	32	> 64	1	> 64	--
Cefepime	> 16	> 64	1	> 64	4.9%
Ceftazidime	64	> 64	2	> 64	3.5%
Ceftriaxone	> 64	> 64	4	> 64	0.9%
Colistin	1	2	≤ 0.03	> 32	93.6%
Eravacycline	1	2	0.06	8	--
Gentamicin	> 8	> 64	≤ 0.03	> 64	17.7%
Levofloxacin	> 4	64	0.06	> 64	1.5%
Piperacillin/tazobactam	> 128	> 128	≤ 0.5	> 128	1.8%
Tetracycline	> 8	> 64	1	> 64	4.4%
Tigecycline	2	4	0.25	> 16	--

[a]Includes *K. pneumoniae* (204) and *K. oxytoca* (62); [b]Includes *E. cloacae* (210) and *E. aerogenes* (86); [c]Includes *C. freundii* (101) and *C. koseri* (5); [d]Includes *M. morganii* (38), *P. vulgaris* (25), *P. rettgeri* (3), and *P. stuartii* (28)

Table 3. Summary antimicrobial activity of eravacycline and comparator agents against 3rd/4th generation cephalosporin-resistant (ESC-R) Enterobacteriaceae (n=1406) and *A. baumannii* (n=801) isolates collected from 2013-2015

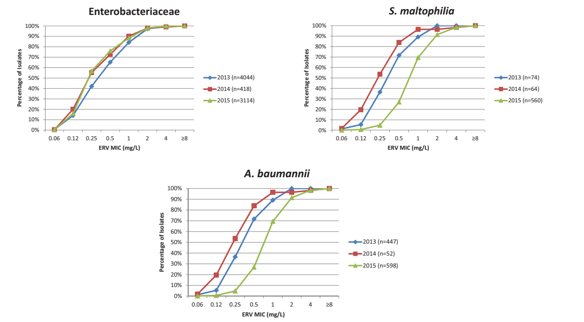
Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{90}	Range Min	Max	%S
Enterobacteriaceae (1406)					
Aztreonam	> 16	> 16	≤ 0.03	> 16	20.3%
Cefepime	2	> 16	0.03	> 16	57.3%
Ceftazidime	> 16	128	≤ 0.03	> 128	22.8%
Ceftriaxone	8	> 32	0.25	> 32	1.9%
Colistin	0.5	> 4	≤ 0.12	> 4	--
Eravacycline	0.5	2	0.06	16	--
Gentamicin	1	> 8	≤ 0.12	> 16	72.8%
Levofloxacin	0.5	8	0.008	> 8	64.8%
Piperacillin/tazobactam	32	128	≤ 0.25	> 128	44.7%
Tetracycline	4	> 64	0.5	> 64	53.3%
Tigecycline	1	4	0.12	32	88.2%
***Klebsiella* spp.[a] (287)**					
Aztreonam	> 16	> 16	0.25	> 16	4.9%
Cefepime	16	> 16	0.03	> 16	27.2%
Ceftazidime	> 16	> 128	≤ 0.03	> 128	25.1%
Ceftriaxone	> 4	> 32	0.5	> 32	2.1%
Colistin	0.5	1	0.25	> 4	--
Eravacycline	0.5	2	0.06	8	--
Gentamicin	1	> 16	≤ 0.12	> 16	61%
Levofloxacin	> 4	> 8	0.03	> 8	42.2%
Piperacillin/tazobactam	64	> 128	1	> 128	32.8%
Tetracycline	8	> 64	0.5	> 64	49.5%
Tigecycline	1	2	0.12	16	92.3%
***Enterobacter* spp.[b] (536)**					
Aztreonam	> 16	> 16	0.06	> 16	13.3%
Cefepime	1	16	0.03	> 16	75%
Ceftazidime	> 16	128	0.25	> 128	10.1%
Ceftriaxone	16	> 32	0.25	> 32	0.9%
Colistin	0.5	1	≤ 0.12	> 4	--
Eravacycline	0.5	2	0.12	8	--
Gentamicin	0.5	> 8	≤ 0.12	> 16	85.8%
Levofloxacin	≤ 0.25	> 4	0.008	> 8	87.1%
Piperacillin/tazobactam	32	128	≤ 0.25	> 128	26.9%
Tetracycline	4	> 8	1	> 64	75.6%
Tigecycline	1	2	0.12	8	93.3%
***Escherichia coli* (181)**					
Aztreonam	> 16	> 16	0.12	> 16	12.2%
Cefepime	16	> 16	0.06	> 16	23.2%
Ceftazidime	16	32	0.25	> 128	22.1%
Ceftriaxone	8	> 32	≤ 0.5	> 32	1.7%
Colistin	0.5	1	0.25	2	--
Eravacycline	0.25	0.5	0.06	1	--
Gentamicin	4	> 16	≤ 0.25	> 16	51.4%
Levofloxacin	> 4	> 8	0.015	> 8	20.4%
Piperacillin/tazobactam	4	64	≤ 0.5	> 128	81.8%
Tetracycline	> 8	> 64	1	> 64	27.6%
Tigecycline	0.25	0.5	0.12	4	99.5%
***Citrobacter* spp.[c] (157)**					
Aztreonam	> 16	> 16	≤ 0.03	> 16	6.4%
Cefepime	1	16	0.03	> 16	79%
Ceftazidime	> 16	> 128	≤ 0.5	> 128	7%
Ceftriaxone	16	> 32	1	> 32	0.6%
Colistin	0.5	1	≤ 0.12	4	--
Eravacycline	0.25	1	0.12	4	--
Gentamicin	1	4	≤ 0.12	> 16	90.5%
Levofloxacin	≤ 0.25	4	0.015	> 8	86%
Piperacillin/tazobactam	64	> 128	≤ 0.5	> 128	32.5%
Tetracycline	2	32	1	> 64	74.5%
Tigecycline	0.5	2	0.25	4	94.3%
***Serratia marcescens* (75)**					
Aztreonam	16	> 16	0.12	> 16	36%
Cefepime	2	> 16	0.12	> 16	56%
Ceftazidime	4	> 16	0.25	> 128	62.7%
Ceftriaxone	> 4	> 32	0.25	> 32	4%
Colistin	> 4	> 4	0.5	> 4	--
Eravacycline	2	4	0.5	8	--
Gentamicin	1	> 16	≤ 0.12	> 16	66.7%
Levofloxacin	2	> 4	0.03	> 8	72%
Piperacillin/tazobactam	32	128	1	> 128	48%
Tetracycline	> 8	32	4	> 64	2.7%
Tigecycline	2	4	0.5	4	84%
***Proteus mirabilis* (58)**					
Aztreonam	1	8	≤ 0.03	> 16	89.7%
Cefepime	2	> 16	0.06	> 16	53.5%
Ceftazidime	4	> 16	0.06	64	51.7%
Ceftriaxone	> 4	32	0.25	> 32	10.3%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	2	4	0.25	4	--
Gentamicin	> 8	> 16	0.25	> 16	39.7%
Levofloxacin	> 4	> 8	0.03	> 8	27.6%
Piperacillin/tazobactam	1	8	≤ 0.25	64	94.8%
Tetracycline	> 8	> 64	> 8	> 64	0%
Tigecycline	4	8	1	16	24.1%
Indole-positive *Proteeae*[d] (112)					
Aztreonam	0.5	> 16	≤ 0.03	> 16	80.4%
Cefepime	0.25	16	0.03	> 16	76.8%
Ceftazidime	2	> 16	≤ 0.03	> 16	59.8%
Ceftriaxone	> 4	16	≤ 0.5	> 32	2.7%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	1	2	0.25	16	--
Gentamicin	2	> 8	0.25	> 8	71.4%
Levofloxacin	≤ 0.25	> 4	0.015	> 4	72.3%
Piperacillin/tazobactam	0.5	32	≤ 0.25	> 64	89.3%
Tetracycline	> 8	32	1	> 64	30.4%
Tigecycline	2	4	0.5	32	62.5%
***A. baumannii* (801)**					
Aztreonam	64	> 64	1	> 64	--
Cefepime	> 16	> 64	0.5	> 64	4.7%
Ceftazidime	64	> 64	2	> 64	2.6%
Ceftriaxone	> 64	> 64	8	> 64	0.5%
Colistin	1	2	≤ 0.03	> 32	93.9%
Eravacycline	1	2	0.06	8	--
Gentamicin	> 8	> 64	≤ 0.03	> 64	19.1%
Levofloxacin	> 4	64	0.06	> 64	3.3%
Piperacillin/tazobactam	> 128	> 128	0.25	> 128	2.1%
Tetracycline	> 8	> 64	1	> 64	5.6%
Tigecycline	2	4	0.25	> 16	--

[a]Includes *K. pneumoniae* (207) and *K. oxytoca* (80); [b]Includes *E. cloacae* (313), *E. aerogenes* (222), and *E. asburiae* (1); [c]Includes *C. freundii* (144) and *C. koseri* (13); [d]Includes *M. morganii* (31), *P. vulgaris* (63), *P. rettgeri* (2), and *P. stuartii* (16)

Table 4. Summary antimicrobial activity of eravacycline and comparator agents against CR isolates collected from 2013-2015

Organism (n)/ Antimicrobial Agent	MIC (mg/L) MIC_{50}	MIC_{90}	Range Min	Max	%S
***Klebsiella* spp. (67)**					
Aztreonam	> 16	> 16	0.25	> 16	13.4%
Cefepime	> 16	> 16	0.12	> 16	14.9%
Ceftazidime	> 16	> 128	≤ 0.5	> 128	11.9%
Ceftriaxone	> 4	> 32	0.25	> 32	9%
Colistin	0.5	4	0.25	> 4	--
Eravacycline	0.5	2	0.12	4	--
Gentamicin	2	> 16	≤ 0.25	> 16	64.2%
Levofloxacin	> 4	> 8	≤ 0.25	> 8	17.9%
Piperacillin/tazobactam	> 64	> 128	2	> 128	6%
Tetracycline	8	> 64	2	> 64	47.8%
Tigecycline	1	2	0.5	8	92.5%
***Enterobacter* spp. (51)**					
Aztreonam	> 16	> 16	≤ 0.5	> 16	31.4%
Cefepime	2	> 16	≤ 0.25	> 16	52.9%
Ceftazidime	> 16	> 128	≤ 0.5	> 128	29.4%
Ceftriaxone	> 4	> 32	≤ 0.5	> 32	25.5%
Colistin	0.5	1	0.25	> 4	--
Eravacycline	0.5	4	0.25	4	--
Gentamicin	0.5	> 8	≤ 0.12	> 16	80.4%
Levofloxacin	≤ 0.25	> 4	0.03	> 8	78.4%
Piperacillin/tazobactam	> 64	> 128	1	> 128	25.5%
Tetracycline	4	32	1	> 64	51%
Tigecycline	1	4	0.25	8	78.4%
***Serratia marcescens* (13)**					
Aztreonam	> 16	> 16	≤ 0.5	> 16	30.8%
Cefepime	8	> 16	≤ 0.25	> 16	30.8%
Ceftazidime	16	> 128	≤ 0.5	> 128	38.5%
Ceftriaxone	> 4	> 32	≤ 0.5	> 32	23.1%
Colistin	> 4	> 4	> 1	> 4	--
Eravacycline	1	2	1	4	--
Gentamicin	2	> 8	1	> 16	69.2%
Levofloxacin	2	> 4	0.12	> 8	76.9%
Piperacillin/tazobactam	> 64	> 128	1	> 128	30.8%
Tetracycline	> 8	32	8	32	0%
Tigecycline	1	4	1	4	84.6%
***A. baumannii* (707)**					
Aztreonam	64	> 64	8	> 64	--
Cefepime	32	> 64	2	> 64	3.3%
Ceftazidime	64	> 64	2	> 64	3.5%
Ceftriaxone	> 64	> 64	8	> 64	0.6%
Colistin	1	2	0.25	> 32	92.8%
Eravacycline	1	2	0.06	8	--
Gentamicin	> 8	> 64	0.06	> 64	17.8%
Levofloxacin	8	64	0.06	> 64	1.7%
Piperacillin/tazobactam	> 128	> 128	16	> 128	0.3%
Tetracycline	16	> 64	1	> 64	4.5%
Tigecycline	2	4	0.25	> 16	--

Figure 3. ERV MIC distribution (cumulative %) against all Enterobacteriaceae, all *A. baumannii*, and all *S. maltophilia* by year



Conclusions

- ERV demonstrated consistent and potent activity against ENT, AB, and SM over a recent 3-year time period (2013-2015).
- ERV shows promising activity against globally-isolated Gram-negative organisms, including those with resistant phenotypes.

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ID Week 2016, October 26-30, New Orleans, LA