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Activity of Eravacycline and Comparators against 6,380 Pathogens Isolated from Canadian Hospitals: CANWARD 2014 and 2015

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ABSTRACT

Background: Eravacycline (ERV) is a novel, fully synthetic fluorocycline antibiotic of the tetracycline class with broad-spectrum activity being developed for the treatment of serious infections, including those caused by multidrug-resistant (MDR) pathogens. The activity of this synthetic fluorocycline was compared to a variety of comparators including meropenem (MER) and piperacillin-tazobactam (PTZ) against Gram-negative and Gram-positive pathogens causing infections in Canadian hospitals.

Methods: From January 2014 - October 2015, inclusive, 13 sentinel hospitals submitted pathogens from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units as part of an ongoing national surveillance program in Canadian hospitals. 6,380 total isolates were collected for 2014 and 2015. Susceptibility testing was performed using CLSI broth microdilution methods.

Results: The activity (µg/mL) of ERV, MER and PTZ against select pathogens is described below:

Organism (# isolates)	ERV MIC_{50}/MIC_{90}	MER MIC_{50}/MIC_{90}	PTZ MIC_{50}/MIC_{90}
S. agalactiae (115)	0.03/0.06	≤0.06/≤0.06	≤1/≤1
S.pneumoniae (282)	0.008/0.015	≤0.06/≤0.06	≤1/≤1
S. pyogenes (86)	0.015/0.03	≤0.06/≤0.06	≤1/≤1
SPN - PenR (10)	0.008/0.015	0.5/1	4/4
MSSA (1222)	0.06/0.12	0.12/0.25	≤1/≤1
MRSA[a] (301)	0.06/0.12	4/32	32/128
CA-MRSA (115)	0.06/0.12	2/8	16/64
HA-MRSA (161)	0.06/0.25	16/32	64/128
S. epidermidis (130)	0.06/0.25	0.5/16	≤1/16
E. faecalis (204)	0.06/0.12	4/8	4/4
E. faecium (85)	0.03/0.06	>32/>32	>512/>512
VRE (17)	0.03/0.12	>32/>32	>512/>512
C. freundii (19)	0.25/2	≤0.03/≤0.03	2/64
E. aerogenes (33)	0.25/0.5	≤0.03/0.06	4/32
E. cloacae (175)	0.5/1	≤0.03/0.12	2/64
E. coli (1179)	0.12/0.5	≤0.03/≤0.03	≤1/4
E. coli-ESBL (141)	0.25/0.5	≤0.03/≤0.03	2/16
K. oxytoca (88)	0.25/0.5	≤0.03/≤0.03	≤1/128
K. pneumoniae (380)	0.25/0.5	≤0.03/≤0.03	2/8
M. morganii (20)	1/2	0.06/0.12	≤1/≤1
P. mirabilis (91)	1/2	0.06/0.12	≤1/≤1
S. marcescens (83)	1/2	0.06/0.06	≤1/4
A. baumannii (28)	0.06/ 0.5	0.25/1	≤1/16
H. influenzae (250)	0.12/0.25	0.5/8	4/64
P. aeruginosa (707)	8/16	0.5/8	4/64
S. maltophilia (118)	1/4	>32/>32	256/>512

MSSA-methicillin-susceptible *Staphylococcus aureus*, MR-methicillin resistant, VRE-vancomycin-resistant enterococci, SPN-*Streptococcus pneumoniae*, ESBL-extended spectrum beta lactamase producing.
[a]Based upon oxacillin susceptibility.

Conclusions: Eravacycline displayed broad-spectrum activity against recent pathogens from Canadian hospitals including MRSA, VRE, ESBL-producing Enterobacteriaceae and *A. baumannii*.

INTRODUCTION

Eravacycline is a synthetic, broad-spectrum intravenous and oral fluorocycline antibiotic for the treatment of multidrug-resistant infections [1]. It has completed enrollment in Phase 3 clinical trials for the treatment of complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI) [1,2]. The activity of eravacycline was compared to comparators, including meropenem (MER) and piperacillin-tazobactam (PTZ) against Gram-negative and Gram-positive pathogens causing infections in Canadian hospitals.

PURPOSE

To determine the *in vitro* activity of eravacycline along with comparators versus Gram-negative and Gram-positive pathogens isolated from patients in Canadian hospitals from January 2014 to October 2015.

MATERIALS & METHODS

Study Background and Bacterial Isolates

The isolates tested in this study were obtained from January 2014 to October 2015, inclusive, from an ongoing cross-Canada surveillance study (CANWARD; www.can-r.ca) organized by the investigators [3]. The goal of the CANWARD study was to assess pathogens and antimicrobial resistance patterns associated with lower respiratory tract, skin/skin structure, urinary, and bacteremic infections in Canadian patients on medical wards, surgical wards, intensive care units, and presenting to emergency rooms and hospital clinics [3]. In CANWARD 2014 and 2015, 13 sentinel hospital sites in Canada were recruited. These centres were in major population centres in 8 of the 10 provinces in Canada. These sites were geographically distributed in a population based fashion: (British Columbia [1 site], Alberta [1 site], Saskatchewan [1 site], Manitoba [1 site], Ontario [4 sites in 2014, 3 sites in 2015], Quebec [3 sites in 2014, 4 sites in 2015], Maritimes [2 sites]).

All isolates of MRSA were typed using staphylococcal protein A (*spa*) typing to assess whether the isolates were community-associated or healthcare-associated [3]. Isolates with a *spa* type associated with CMRSA7 or CMRSA10 were considered CA-MRSA. Isolates with a *spa* type associated with CMRSA1, CMRSA2, CMRSA4, CMRSA5, CMRSA3/6, CMRSA8 or CMRSA9 were considered HA-MRSA [3].

Potential *E. coli* or *Klebsiella* spp. ESBL-producers were identified as isolates with a ceftriaxone and/or ceftazidime MIC of 1 µg/mL or greater and confirmed using the CLSI double disk diffusion method, as previously described [3].

Antimicrobial Susceptibility Testing Methodology

Isolates were tested for antimicrobial susceptibilities using in-house prepared (Department of Clinical Microbiology, Health Sciences Centre, Winnipeg, Canada) 96-well broth microdilution panels according to CLSI (2015) guidelines [3,4]. The antimicrobial agents tested were obtained as laboratory grade powders from their respective manufacturers.

Stock solutions were prepared and dilutions made, as described by the CLSI [4] in cation-adjusted Mueller-Hinton broth (MHB). Following 2 subcultures from frozen stock, the MICs of the antimicrobial agents for the isolates were determined by the CLSI broth microdilution method. Colony counts were performed periodically to confirm inocula. Quality control was performed using ATCC organisms including: *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853.

CONCLUSIONS

- Eravacycline demonstrated *in vitro* activity versus Gram-negative bacilli.
- Eravacycline demonstrated potent *in vitro* activity against Enterobacteriaceae including ESBL-producing *E. coli* and *K. pneumoniae* and its activity was unaffected by the presence of ESBL phenotype.
- Compared to tigecycline, eravacycline was 4 fold more active versus *P. mirabilis* and 4 fold more active versus *Acinetobacter baumannii.*
- Eravacycline demonstrated potent *in vitro* activity against *Stenotrophomonas maltophilia.*

- Eravacycline was the most potent agent versus Gram-positive cocci.
- Eravacycline demonstrated potent *in vitro* activity against MSSA and MRSA, including both CA-MRSA and HA-MRSA.
- Eravacycline demonstrated potent *in vitro* activity against all streptococci.
- Eravacycline demonstrated potent *in vitro* activity against *E. faecalis* and *E. faecium,* including VRE.

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RESULTS

Bacterial Isolates Collected

6,380 clinical isolates were collected for CANWARD 2014 and 2015.

- 2546 (39.9%) were from blood, 2554 (40.0%) from respiratory sources, 646 (10.1%) were from urine, and 634 (10.0%) were from wounds
- 3513 (55.1%) collected from male patients; 2866 (44.9%) female patients (1 isolate unknown: 0.02%)
- 887 (13.9%) from patients ≤ 17 years of age, 2694 (42.2%) 18-64 years, and 2798 (43.9%) ≥ 65 years (1 isolate unknown: 0.02%)
- 2098 (32.9%) were from patients on medical wards, 1447 (22.7%) from emergency rooms, 1151 (18.0%) from intensive care units, 1203 (18.9%) from hospital clinics, and 481 (7.5%) from surgical wards
- 5,644 Gram-negative and Gram-positive pathogens were tested with eravacycline and the results are listed below:

Table 1. ***In vitro*** **activities of eravacycline and comparators versus Gram-negative bacilli**

Organism (no. tested)/ antimicrobial agent	MIC (µg/mL) 50%	90%	Range	% S	% I	% R
Escherichia coli ALL (1179)						
Eravacycline	0.12	0.5	0.03 - 2	NA[a]	NA	NA
Ceftazidime	≤ 0.25	4	≤ 0.25 - > 32	91.6	1.6	6.8
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 0.5	100		
Piperacillin-Tazobactam	≤ 1	4	≤ 1 - > 512	97.6	1.1	1.3
Ceftriaxone	≤ 0.25	32	≤ 0.25 - > 64	87.4	0.3	12.3
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	74.5	0.2	25.4
Tigecycline[b]	0.25	0.5	0.12 - 4	99.8	0.2	
Escherichia coli ESBL pos (141)						
Eravacycline	0.25	0.5	0.06 - 1	NA[a]	NA	NA
Ceftazidime	16	> 32	0.5 - > 32	39	10.6	50.4
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 0.5	100		
Piperacillin-Tazobactam	2	16	≤ 1 - > 512	92.2	3.5	4.3
Ceftriaxone	> 64	> 64	0.5 - > 64	4.3	1.4	94.3
Ciprofloxacin	> 16	> 16	≤ 0.06 - > 16	16.3		83.7
Tigecycline[b]	0.25	0.5	0.12 - 1	100		
Escherichia coli ESBL neg (1037)						
Eravacycline	0.12	0.25	0.03 - 2	NA[a]	NA	NA
Ceftazidime	≤ 0.25	0.5	≤ 0.25 - > 32	98.7	0.4	0.9
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 0.12	100		
Piperacillin-Tazobactam	≤ 1	4	≤ 1 - > 512	98.4	0.8	0.9
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - > 64	98.6	0.2	1.2
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	82.4	0.2	17.4
Tigecycline[b]	0.25	0.5	0.12 - 4	99.8	0.2	
Klebsiella pneumoniae ALL (380)						
Eravacycline	0.25	0.5	0.06 - 8	NA[a]	NA	NA
Ceftazidime	≤ 0.25	1	≤ 0.25 - > 32	94.5	1.1	4.5
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 16	99.2		0.8
Piperacillin-Tazobactam	2	8	≤ 1 - > 512	97.1	1.1	1.8
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - > 64	93.7		6.3
Ciprofloxacin	≤ 0.06	0.5	≤ 0.06 - > 16	92.9	1.3	5.8
Tigecycline[b]	0.5	1	0.12 - 16	95.5	4.2	0.3
Klebsiella pneumoniae ESBL pos (21)						
Eravacycline	0.5	2	0.25 - 2	NA[a]	NA	NA
Ceftazidime	32	> 32	1 - > 32	19	14.3	66.7
Meropenem	≤ 0.03	0.25	≤ 0.03 - 16	90.5		9.5
Piperacillin-Tazobactam	16	> 512	2 - > 512	61.9	9.5	28.6
Ceftriaxone	64	> 64	≤ 0.25 - > 64	4.8		95.2
Ciprofloxacin	4	> 16	≤ 0.06 - > 16	23.8	14.3	61.9
Tigecycline[b]	0.5	2	0.5 - 4	90.5	9.5	
Enterobacter cloacae (175)						
Eravacycline	0.5	1	0.06 - 8	NA[a]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	74.9		25.1
Meropenem	≤ 0.03	0.12	≤ 0.03 - 4	98.9	0.6	0.6
Piperacillin-Tazobactam	2	64	≤ 1 - 256	85.1	8.6	6.3
Ceftriaxone	≤ 0.25	> 64	≤ 0.25 - > 64	70.9	4	25.1
Ciprofloxacin	≤ 0.06	0.12	≤ 0.06 - > 16	94.9	1.7	3.4
Tigecycline[b]	0.5	1	0.12 - 8	94.3	2.9	2.9
Serratia marcescens (83)						
Eravacycline	1	2	0.5 - 8	NA[a]	NA	NA
Ceftazidime	≤ 0.25	1	≤ 0.25 - 2	100		
Meropenem	0.06	0.06	≤ 0.03 - 8	98.8	0	1.2
Piperacillin-Tazobactam	≤ 1	4	≤ 1 - 32	98.8	1.2	
Ceftriaxone	≤ 0.25	0.5	≤ 0.25 - 4	98.8		1.2
Ciprofloxacin	≤ 0.06	0.5	≤ 0.06 - 1	100		
Tigecycline[b]	1	2	1 - 4	94	6	
Klebsiella oxytoca (88)						
Eravacycline	0.25	0.5	0.06 - 1	NA[a]	NA	NA
Ceftazidime	≤ 0.25	0.5	≤ 0.25 - 32	97.7	1.1	1.1
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 0.5	100		
Piperacillin-Tazobactam	≤ 1	128	≤ 1 - > 512	87.5	2.3	10.2
Ceftriaxone	≤ 0.25	2	≤ 0.25 - 64	88.6	3.4	8
Ciprofloxacin	≤ 0.06	≤ 0.06	≤ 0.06 - 0.5	100		
Tigecycline[b]	0.25	0.5	0.12 - 4	98.9	1.1	

Organism (no. tested)/ antimicrobial agent	MIC (µg/mL) 50%	90%	Range	% S	% I	% R
Stenotrophomonas maltophilia (118)						
Eravacycline	1	4	0.25 - 16	NA[a]	NA	NA
Ceftazidime	> 32	> 32	2 - > 32	23.7	5.1	71.2
Meropenem	> 32	> 32	1 - > 32	NA	NA	NA
Piperacillin-Tazobactam	256	> 512	8 - > 512	NA	NA	NA
Ceftriaxone	> 64	> 64	2 - > 64	NA	NA	NA
Ciprofloxacin	4	16	0.5 - > 16	NA	NA	NA
Tigecycline[b]	1	4	0.25 - 16	NA	NA	NA
Proteus mirabilis (91)						
Eravacycline	1	2	0.5 - 4	NA[a]	NA	NA
Ceftazidime	≤ 0.25	≤ 0.25	≤ 0.25 - 16	97.8	1.1	1.1
Meropenem	0.06	0.12	≤ 0.03 - 0.25	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 0.12 - 2	100		
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - > 64	96.7	1.1	2.2
Ciprofloxacin	≤ 0.06	0.25	≤ 0.06 - 16	93.4	2.2	4.4
Tigecycline[b]	4	8	0.5 - 8	17.6	56	26.4
Acinetobacter baumannii (28)						
Eravacycline	0.06	0.5	0.03 - 1	NA[a]	NA	NA
Ceftazidime	8	16	2 - > 32	85.7	10.7	3.6
Meropenem	0.25	1	0.25 - 2	100		
Piperacillin-Tazobactam	≤ 1	16	≤ 1 - 64	92.9	7.1	
Ceftriaxone	8	32	4 - > 64	50	46.4	3.6
Ciprofloxacin	0.25	0.25	≤ 0.06 - 1	100		
Tigecycline[b]	0.25	2	0.12 - 4	NA	NA	NA
Enterobacter aerogenes (33)						
Eravacycline	0.25	0.5	0.125 - 1	NA[a]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	75.8		24.2
Meropenem	≤ 0.03	0.06	≤ 0.03 - 0.25	100		
Piperacillin-Tazobactam	4	32	≤ 1 - 64	81.8	18.2	
Ceftriaxone	≤ 0.25	64	≤ 0.25 - > 64	75.8		24.2
Ciprofloxacin	≤ 0.06	0.25	≤ 0.06 - 2	97	3	
Tigecycline[b]	0.5	1	0.25 - 1	100		
Citrobacter freundii (19)						
Eravacycline	0.25	2	0.12 - 2	NA[a]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	73.7		26.3
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - 0.06	100		
Piperacillin-Tazobactam	2	64	≤ 1 - 512	84.2	10.5	5.3
Ceftriaxone	≤ 0.25	64	≤ 0.25 - 64	73.7		26.3
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	84.2		15.8
Tigecycline[b]	0.5	2	0.25 - 4	94.7	5.3	
Morganella morganii (20)						
Eravacycline	1	2	0.12 - 2	NA[a]	NA	NA
Ceftazidime	≤ 0.25	8	≤ 0.25 - 16	85	10	5
Meropenem	0.06	0.12	≤ 0.03 - 0.12	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 2	100		
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - 2	95	5	0
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	85		15
Tigecycline[b]	1	2	0.12 - 4	95	5	
Haemophilus influenzae (250)						
Eravacycline	0.12	0.25	≤ 0.03 - 0.25	NA[a]	NA	NA
Ceftazidime	0.12	0.25	≤ 0.03 - 2	100		
Meropenem	≤ 0.06	0.12	≤ 0.06 - 0.25	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 2	99.2		0.8
Ceftriaxone	≤ 0.06	≤ 0.06	≤ 0.06 - 2	100		
Ciprofloxacin	≤ 0.015	≤ 0.015	≤ 0.015 - > 0.5	100		
Tigecycline[b]	0.25	0.5	≤ 0.03 - 1	62		38
Pseudomonas aeruginosa (707)						
Eravacycline	8	16	0.06 - >16	NA[a]	NA	NA
Ceftazidime	2	16	≤ 0.25 - > 32	81.6	8.6	9.8
Meropenem	0.5	8	≤ 0.03 - > 32	75	9	16
Piperacillin-Tazobactam	4	64	≤ 1 - 512	84.4	8.5	7.1
Ceftriaxone	16	> 64	≤ 0.25 - > 64	NA	NA	NA
Ciprofloxacin	0.25	4	≤ 0.06 - > 16	76.8	8.3	14.9
Tigecycline[b]	16	> 16	0.25 - > 16	NA	NA	NA

[a] NA – not applicable. [b] Interpretive breakpoints defined by FDA (tigecycline) where applicable

Table 2. ***In vitro*** **activities of eravacycline and comparators versus Gram-positive cocci**

Organism (no. tested)/ antimicrobial agent	MIC (µg/mL) 50%	90%	Range	% S	% I	% R
Staphylococcus aureus MSSA (1222)						
Eravacycline	0.06	0.12	≤ 0.015 - 0.5	NA[a]	NA	NA
Ceftazidime	16	16	2 - > 32	NA	NA	NA
Meropenem	0.12	0.25	≤ 0.03 - 16	NA	NA	NA
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 4	NA	NA	NA
Ceftriaxone	4	4	≤ 0.25 - 16	NA	NA	NA
Ciprofloxacin	0.5	2	≤ 0.06 - > 16	87.4	2.9	9.7
Tigecycline[b]	0.12	0.25	≤ 0.03 - 1	99.9		
Staphylococcus aureus MRSA (301)						
Eravacycline	0.06	0.12	≤ 0.015 - 1	NA[a]	NA	NA
Ceftazidime	> 32	> 32	16 - > 32	NA	NA	NA
Meropenem	4	32	0.25 - > 32	NA	NA	NA
Piperacillin-Tazobactam	32	128	≤ 1 - 256	NA	NA	NA
Ceftriaxone	> 64	> 64	8 - > 64	NA	NA	NA
Ciprofloxacin	16	> 16	≤ 0.06 - > 16	23.9	0.7	75.4
Tigecycline[b]	0.12	0.25	≤ 0.03 - 1	97.7		
CA-MRSA (115)						
Eravacycline	0.06	0.12	≤ 0.015 - 0.12	NA[a]	NA	NA
Ceftazidime	> 32	> 32	16 - > 32	NA	NA	NA
Meropenem	2	8	0.25 - 32	NA	NA	NA
Piperacillin-Tazobactam	16	64	2 - 256	NA	NA	NA
Ceftriaxone	64	> 64	16 - > 64	NA	NA	NA
Ciprofloxacin	16	16	≤ 0.06 - > 16	26.1	1.7	72.2
Tigecycline[b]	0.12	0.25	≤ 0.03 - 0.25	100		
HA-MRSA (161)						
Eravacycline	0.06	0.25	≤ 0.015 - 1	NA[a]	NA	NA
Ceftazidime	> 32	> 32	16 - > 32	NA	NA	NA
Meropenem	16	32	0.5 - > 32	NA	NA	NA
Piperacillin-Tazobactam	64	128	2 - 256	NA	NA	NA
Ceftriaxone	> 64	> 64	8 - > 64	NA	NA	NA
Ciprofloxacin	> 16	> 16	0.25 - > 16	12.4		87.6
Tigecycline[b]	0.25	0.5	0.06 - 1	95.7		
Staphylococcus epidermidis (130)						
Eravacycline	0.06	0.25	≤ 0.015 – 1	NA[a]	NA	NA
Ceftazidime	16	> 32	1 - > 32	NA	NA	NA
Meropenem	0.5	16	≤ 0.03 - > 32	NA	NA	NA
Piperacillin-Tazobactam	≤ 1	16	≤ 1 - 64	NA	NA	NA
Ceftriaxone	4	> 64	≤ 0.25 - > 64	NA	NA	NA
Ciprofloxacin	0.25	> 16	≤ 0.06 - > 16	59.2		40.8
Tigecycline[b]	0.12	0.25	≤ 0.03 - 1	NA	NA	NA
Enterococcus faecalis (204)						
Eravacycline	0.06	0.12	≤ 0.015 - 0.12	NA[a]	NA	NA
Ceftazidime	> 32	> 32	16 - > 32	NA	NA	NA
Meropenem	4	8	0.5 - 16	NA	NA	NA
Piperacillin-Tazobactam	4	4	≤ 1 - > 512	NA	NA	NA
Ceftriaxone	> 64	> 64	1 - > 64	NA	NA	NA
Ciprofloxacin	1	> 16	0.25 - > 16	77	6.9	16.2
Tigecycline[b]	0.12	0.25	≤ 0.03 - 1	99.5		

Organism (no. tested)/ antimicrobial agent	MIC (µg/mL) 50%	90%	Range	% S	% I	% R
Enterococcus faecium (85)						
Eravacycline	0.03	0.06	≤ 0.015 - 0.12	NA[a]	NA	NA
Ceftazidime	> 32	> 32	16 - > 32	NA	NA	NA
Meropenem	> 32	> 32	1 - > 32	NA	NA	NA
Piperacillin-Tazobactam	> 512	> 512	2 - > 512	NA	NA	NA
Ceftriaxone	> 64	> 64	0.5 - > 64	NA	NA	NA
Ciprofloxacin	> 16	> 16	0.5 - > 16	5.9	1.2	92.9
Tigecycline[b]	0.12	0.12	≤ 0.03 - 0.25	NA	NA	NA
VRE (17)						
Eravacycline	0.03	0.12	0.03 - 0.12	NA[a]	NA	NA
Ceftazidime	> 32	> 32	> 32 - > 32	NA	NA	NA
Meropenem	> 32	> 32	> 32 - > 32	NA	NA	NA
Piperacillin-Tazobactam	> 512	> 512	> 512 - > 512	NA	NA	NA
Ceftriaxone	> 64	> 64	> 64 - > 64	NA	NA	NA
Ciprofloxacin	> 16	> 16	> 16 - > 16			100
Tigecycline[b]	0.12	0.12	0.12 - 0.12	NA	NA	NA
Streptococcus agalactiae (115)						
Eravacycline	0.03	0.06	≤ 0.004 - 0.06	NA[a]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 - 0.12	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - ≤ 1	NA	NA	NA
Ceftriaxone	≤ 0.12	≤ 0.12	≤ 0.12 - ≤ 0.12	100		
Ciprofloxacin	0.5	1	0.25 - > 16	NA	NA	NA
Tigecycline[b]	0.06	0.12	0.03 - 0.12	100		
Streptococcus pneumoniae (282)						
Eravacycline	0.008	0.015	≤ 0.004 - 0.12	NA[a]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 – 1	92.9	5.3	1.8
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 – 4	NA	NA	NA
Ceftriaxone	≤ 0.12	0.25	≤ 0.12 – 1	100		
Ciprofloxacin	1	2	≤ 0.06 - 8	NA	NA	NA
Tigecycline[b]	0.03	0.03	≤ 0.015 - 0.12	99.6		
Streptococcus pneumoniae PenR (10)						
Eravacycline	0.008	0.015	≤ 0.004 - 0.015	NA[a]	NA	NA
Meropenem	0.5	1	0.5 - 1		60	40
Piperacillin-Tazobactam	4	4	2 - 4	NA	NA	NA
Ceftriaxone	1	1	0.5 - 1	100		
Ciprofloxacin	2	2	1 - 4	90		10
Tigecycline[b]	0.03	0.03	≤ 0.015 - 0.03	100		
Streptococcus pyogenes (86)						
Eravacycline	0.015	0.03	≤ 0.004 - 0.06	NA[a]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 - ≤ 0.06	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - ≤ 1	NA	NA	NA
Ceftriaxone	≤ 0.12	≤ 0.12	≤ 0.12 - ≤ 0.12	100		
Ciprofloxacin	0.5	1	0.12 - 2	NA	NA	NA
Tigecycline[b]	0.03	0.06	≤ 0.015 - 0.12	100		

CA-MRSA – community associated MRSA; HA-MRSA – healthcare associated MRSA; VRE - vancomycin resistant enterococcus.
[a] NA – not applicable. [b] Interpretive breakpoints defined by FDA (tigecycline) where applicable.

Table 3. Distribution of eravacycline MICs versus Gram-negative organisms

Organism agent	Number of isolates for which the eravacycline MIC (µg/mL) was: ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	≥64
E. coli ALL		2	172	459	401	133	10	2					
E. coli ESBL pos			13	30	52	43	3						
E. coli ESBL neg		2	159	429	349	89	7	2					
K. pneumoniae ALL			4	15	195	129	23	8	5	1			
K. pneumoniae ESBL					5	11	2	3					
E. cloacae			1	10	69	63	22	4	4	2			
E. aerogenes				2	16	14	1						
S. marcescens						11	51	18	2	1			
K. oxytoca			6	28	45	7	2						
S. maltophilia					10	35	46	13	9	4	1		
P. mirabilis						3	55	27	6				
A. baumannii		4	15	4	2	2	1						
C. freundii				2	10	3	2	2					
M. Morganii				1	1	3	10	5					
H. Influenzae		10[a]	36	139	65								

[a] Lowest dilution tested

Table 4. Distribution of eravacycline MICs versus Gram-positive organisms

Organism agent	Number of isolates for which the eravacycline MIC (µg/mL) was: ≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	≥64
S. aureus MSSA	24	386	624	165	18	5							
S. aureus MRSA	3	58	137	73	16	8	6						
CA-MRSA	1	29	62	23									
HA-MRSA	2	27	67	38	13	8	6						
S. epidermidis	21	33	24	34	13	4	1						
E. faecalis	16	76	83	29									
E. faecium	14	39	26	6									
VRE	2	8	4	3									
S. agalactiae	24	64	27										
S. pneumoniae	276	5		1									
S. pneumoniae PenR	10												
S. pyogenes	53	32	1										

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