ASM Microbe 2019
SATURDAY-AAR-790

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Activity of Eravacycline and Comparators Against 15,872 Bacterial Pathogens Isolated from Patients Receiving Care in Canadian Hospitals: CANWARD 2014-18

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Introduction

Eravacycline is a synthetic, broad-spectrum intravenous fluorocycline antibiotic for the treatment of multidrug-resistant infections [1]. It has completed Phase 3 clinical trials for the treatment of complicated intra-abdominal infections (cIAI) [1,2] and has received FDA approval for this indication. 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.

The purpose of this study was 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 2018.

Materials and Methods

Study Background and Bacterial Isolates
The isolates tested in this study were obtained from January 2014 to October 2018, 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]. 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 (2018) 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. MICs for eravacycline and tigecycline were interpreted using EUCAST breakpoints. MICs for all other comparator were interpreted using CLSI breakpoints [5].

Acknowledgements

The authors would like to thank the participating CANWARD centres, investigators and laboratory site staff for their support. Financial support for the CANWARD study was provided in part by the University of Manitoba, the National Microbiology Laboratory, and Tetraphase Inc.

References

1. Zhanel GG, Cheung D, Adam H, Zelenitsky S, Golden A, Schweizer F, Gorityala B, Lagacé-Wiens PR, Walkty A, Gin AS, Hoban DJ and Karlowsky JA. Review of eravacycline: A novel fluorocycline antibacterial agents. Drugs 2016 Apr;76(5):567-88.
2. Solomkin JS, Gardovskis J, Lawrence K, Montravers P, Sway A, Evans D, Tsai L. IGNITE 4: Results of a Phase 3, randomized, multicentre, prospective, trial of eravacycline vs meropenem, in a treatment of complicated intra-abdominal infections. Clinical Infectious Diseases 2018. Dec 18.
3. Zhanel GG, Adam H, Baxter M, Fuller J, Nichol K, Denisuik AJ, Golden A, Hink R, Lagacé-Wiens P, Walkty A, Mulvey M, Schweizer F, Bay D, Hoban DJ, Karlowsky JA, the Canadian Antimicrobial Resistance Alliance (CARA). 42,936 pathogens from Canadian hospitals: 10 years of results (2007-2016) from the CANWARD surveillance study. Journal of Antimicrobial Chemotherapy 2019 (in press).
4. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically - Eleventh Edition: Approved Standard M07-A11. CLSI, Wayne, PA, USA, 2018.
5. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. M100, 28th Edition. CLSI, Wayne, PA, USA, 2018.

Results

Table 1. *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 (2865)						
Eravacycline[a]	0.06	0.12	≤ 0.015 - 1	99.1		0.9
Ceftazidime	16	16	2 - > 32	NA[b]	NA	NA
Meropenem	0.12	0.25	≤ 0.03 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	≤ 1	2	≤ 1 - 64	NA[b]	NA	NA
Ceftriaxone	4	4	≤ 0.25 - > 64	NA[b]	NA	NA
Ciprofloxacin	0.5	2	≤ 0.06 - > 16	87.4	3.2	9.4
Tigecycline[a]	0.12	0.25	≤ 0.03 - 2	99.6		0.4
Staphylococcus aureus MRSA (663)						
Eravacycline[a]	0.06	0.25	≤ 0.015 - 1	92.9		7.1
Ceftazidime	> 32	> 32	16 - > 32	NA[b]	NA	NA
Meropenem	4	32	0.12 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	32	128	≤ 1 - 512	NA[b]	NA	NA
Ceftriaxone	> 64	> 64	4 - > 64	NA[b]	NA	NA
Ciprofloxacin	16	> 16	≤ 0.06 - > 16	25.3	0.3	74.4
Tigecycline[a]	0.25	0.5	≤ 0.03 - 2	97.4		2.6
CA-MRSA (311)						
Eravacycline[a]	0.06	0.12	≤ 0.015 - 0.5	99.4		0.6
Ceftazidime	> 32	> 32	16 - > 32	NA[b]	NA	NA
Meropenem	4	8	0.12 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	32	64	≤ 1 - 512	NA[b]	NA	NA
Ceftriaxone	64	> 64	8 - > 64	NA[b]	NA	NA
Ciprofloxacin	16	> 16	≤ 0.06 - > 16	29.3	0.6	70.1
Tigecycline[a]	0.12	0.25	≤ 0.03 - 1	99.7		0.3
HA-MRSA (318)						
Eravacycline[a]	0.12	0.5	≤ 0.015 - 1	86.2		13.8
Ceftazidime	> 32	> 32	16 - > 32	NA[b]	NA	NA
Meropenem	16	> 32	0.12 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	64	128	≤ 1 - 256	NA[b]	NA	NA
Ceftriaxone	> 64	> 64	4 - > 64	NA[b]	NA	NA
Ciprofloxacin	> 16	> 16	0.25 - > 16	15.1		84.9
Tigecycline[a]	0.25	0.5	≤ 0.03 - 2	95.0		5.0
Staphylococcus epidermidis (372)						
Eravacycline	0.12	0.5	≤ 0.015 - 2	NA[b]	NA	NA
Ceftazidime	16	> 32	1 - > 32	NA[b]	NA	NA
Meropenem	1	16	≤ 0.03 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	≤ 1	4	≤ 1 - 128	NA[b]	NA	NA
Ceftriaxone	8	64	≤ 0.25 - > 64	NA[b]	NA	NA
Ciprofloxacin	1	> 16	≤ 0.06 - > 16	50.5	1.1	48.4
Tigecycline	0.12	0.25	≤ 0.03 - 1	NA[b]	NA	NA
Enterococcus faecalis (475)						
Eravacycline[a]	0.06	0.12	≤ 0.015 - 0.25	99.6		0.4
Ceftazidime	> 32	> 32	16 - > 32	NA[b]	NA	NA
Meropenem	4	8	0.25 - 32	NA[b]	NA	NA
Piperacillin-Tazobactam	4	4	≤ 1 - > 512	NA[b]	NA	NA
Ceftriaxone	> 64	> 64	0.5 - > 64	NA[b]	NA	NA
Ciprofloxacin	1	> 16	≤ 0.06 - > 16	71.4	11.6	17.1
Tigecycline[a]	0.12	0.25	≤ 0.03 - 1	98.5		1.5
Enterococcus faecium (213)						
Eravacycline[a]	0.06	0.12	≤ 0.015 - 0.5	99.1		0.9
Ceftazidime	> 32	> 32	16 - > 32	NA[b]	NA	NA
Meropenem	> 32	> 32	1 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	> 512	> 512	≤ 1 - > 512	NA[b]	NA	NA
Ceftriaxone	> 64	> 64	0.5 - > 64	NA[b]	NA	NA
Ciprofloxacin	> 16	> 16	0.5 - > 16	6.1	0.9	93.0
Tigecycline[a]	0.12	0.12	≤ 0.03 - 0.5	99.1		0.9
VRE (50)						
Eravacycline[a]	0.06	0.12	≤ 0.015 - 0.5	98.0		2.0
Ceftazidime	> 32	> 32	> 32 - > 32	NA[b]	NA	NA
Meropenem	> 32	> 32	> 32 - > 32	NA[b]	NA	NA
Piperacillin-Tazobactam	> 512	> 512	512 - > 512	NA[b]	NA	NA
Ceftriaxone	> 64	> 64	> 64 - > 64	NA[b]	NA	NA
Ciprofloxacin	> 16	> 16	16 - > 16			100
Tigecycline[a]	0.12	0.12	≤ 0.03 - 0.5	98.0		2.0
Streptococcus agalactiae (255)						
Eravacycline	0.03	0.06	≤ 0.004 - 0.06	NA[b]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 - 0.12	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - ≤ 1	NA[b]	NA	NA
Ceftriaxone	≤ 0.12	≤ 0.12	≤ 0.12 - 0.5	100		
Ciprofloxacin	0.5	1	0.25 - > 16	NA[b]	NA	NA
Tigecycline[a]	0.06	0.12	≤ 0.015 - 0.12	100		0
Streptococcus pneumoniae (634)						
Eravacycline	0.015	0.015	≤ 0.004 - 0.12	NA[b]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 - 1	94.6	3.8	1.6
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 4	NA[b]	NA	NA
Ceftriaxone	≤ 0.12	0.25	≤ 0.12 - 1	100		
Ciprofloxacin	1	2	≤ 0.06 - > 16	99.1		0.9
Tigecycline	0.03	0.03	≤ 0.015 - 0.12	NA[b]	NA	NA
Streptococcus pneumoniae PenR (28)						
Eravacycline	0.015	0.03	≤ 0.004 - 0.03	NA[b]	NA	NA
Meropenem	0.5	1	≤ 0.06 - 1	28.6	39.3	32.1
Piperacillin-Tazobactam	4	4	2 - 4	NA[b]	NA	NA
Ceftriaxone	1	1	0.25 - 1	100		
Ciprofloxacin	2	2	0.5 - 8	92.9		7.1
Tigecycline	0.03	0.03	≤ 0.015 - 0.06	NA[b]	NA	NA
Streptococcus pyogenes (212)						
Eravacycline	0.03	0.03	≤ 0.004 - 0.12	NA[b]	NA	NA
Meropenem	≤ 0.06	≤ 0.06	≤ 0.06 - 0.25	100	-	-
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 4	NA[b]	NA	NA
Ceftriaxone	≤ 0.12	≤ 0.12	≤ 0.12 - 0.25	100	-	-
Ciprofloxacin	0.5	1	0.12 - > 16	NA[b]	NA	NA
Tigecycline[a]	0.03	0.06	≤ 0.015 - 0.25	99.5		0.5

CA-MRSA – community associated MRSA; HA-MRSA – healthcare associated MRSA; VRE – vancomycin resistant enterococcus S, susceptible; I, intermediate; R, resistant

[a] Interpretative breakpoints defined by EUCAST (eravacycline, tigecycline) where applicable.
[b] NA – not available.

Table 2. *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 (2993)						
Eravacycline[a]	0.25	0.5	0.03 - 2	97.8		2.2
Ceftazidime	≤ 0.25	8	≤ 0.25 - > 32	89.9	2.0	8.2
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - > 32	100		
Piperacillin-Tazobactam	2	4	≤ 1 - > 512	96.7	1.6	1.7
Ceftriaxone	≤ 0.25	32	≤ 0.25 - > 64	87.0	0.4	12.6
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	73.5	1.3	25.2
Tigecycline[a]	0.25	0.5	≤ 0.03 - 2	96.3		3.7
Escherichia coli ESBL pos (344)						
Eravacycline[a]	0.25	0.5	0.06 - 2	92.4		7.6
Ceftazidime	16	> 32	0.5 - > 32	28.2	13.7	58.1
Meropenem	≤ 0.03	0.06	≤ 0.03 - 1	100		
Piperacillin-Tazobactam	4	16	≤ 1 - > 512	91.6	4.1	4.4
Ceftriaxone	> 64	> 64	0.5 - > 64	1.7	1.5	96.8
Ciprofloxacin	> 16	> 16	≤ 0.06 - > 16	12.2	0.6	87.2
Tigecycline[a]	0.25	1	0.12 - 2	89.2		10.8
Escherichia coli ESBL neg (2648)						
Eravacycline[a]	0.25	0.5	0.03 - 2	98.5		1.5
Ceftazidime	≤ 0.25	0.5	≤ 0.25 - > 32	97.9	0.5	1.7
Meropenem	≤ 0.03	≤ 0.03	≤ 0.03 - > 32	100		
Piperacillin-Tazobactam	2	4	≤ 1 - > 512	97.3	1.3	1.4
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - > 64	98.0	0.3	1.7
Ciprofloxacin	≤ 0.06	> 16	≤ 0.06 - > 16	81.4	1.4	17.2
Tigecycline[a]	0.25	0.5	≤ 0.03 - 2	97.2		2.8
Klebsiella pneumoniae ALL (1001)						
Eravacycline	0.5	1	0.06 - > 16	NA[b]	NA	NA
Ceftazidime	≤ 0.25	2	≤ 0.25 - > 32	92.6	0.9	6.5
Meropenem	≤ 0.03	0.06	≤ 0.03 - > 32	99.1	0.1	0.8
Piperacillin-Tazobactam	4	16	≤ 1 - > 512	94.8	2.0	3.2
Ceftriaxone	≤ 0.25	0.5	≤ 0.25 - > 64	91.2	0.1	8.7
Ciprofloxacin	≤ 0.06	1	≤ 0.06 - > 16	86.0	3.2	10.8
Tigecycline	0.5	1	0.12 - > 16	NA[b]	NA	NA
Klebsiella pneumoniae ESBL pos (77)						
Eravacycline	0.5	2	0.25 - 4	NA[b]	NA	NA
Ceftazidime	> 32	> 32	1 - > 32	20.8	6.5	72.7
Meropenem	≤ 0.03	1	≤ 0.03 - > 32	90.9	1.3	7.8
Piperacillin-Tazobactam	16	> 512	2 - > 512	59.7	15.6	24.7
Ceftriaxone	> 64	> 64	≤ 0.25 - > 64	3.9		96.1
Ciprofloxacin	4	> 16	≤ 0.06 - > 16	9.1	7.8	83.1
Tigecycline	1	4	0.5 - 4	NA[b]	NA	NA
Enterobacter cloacae (477)						
Eravacycline	0.5	1	0.03 - 8	NA[b]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	74.4	0.8	24.7
Meropenem	0.06	0.12	≤ 0.03 - 4	99.6	0.2	0.2
Piperacillin-Tazobactam	2	64	≤ 1 - > 512	83.0	8.8	8.2
Ceftriaxone	≤ 0.25	> 64	≤ 0.25 - > 64	71.7	1.9	26.4
Ciprofloxacin	≤ 0.06	0.12	≤ 0.06 - > 16	93.7	1.0	5.2
Tigecycline	0.5	1	0.12 - 8	NA[b]	NA	NA
Serratia marcescens (260)						
Eravacycline	2	4	0.5 - 16	NA[b]	NA	NA
Ceftazidime	0.5	1	≤ 0.25 - > 32	98.5	0.4	1.2
Meropenem	0.06	0.12	≤ 0.03 - 8	99.2	0.4	0.4
Piperacillin-Tazobactam	2	4	≤ 1 - 128	98.5	0.8	0.8
Ceftriaxone	≤ 0.25	1	≤ 0.25 - > 64	93.5	1.9	4.6
Ciprofloxacin	≤ 0.06	1	≤ 0.06 - 16	85.8	3.5	10.8
Tigecycline	2	2	1 - 16	NA[b]	NA	NA
Klebsiella oxytoca (281)						
Eravacycline	0.25	0.5	0.06 - 2	NA[b]	NA	NA
Ceftazidime	≤ 0.25	1	≤ 0.25 - > 32	97.9		2.1
Meropenem	≤ 0.03	0.06	≤ 0.03 - 0.12	100		
Piperacillin-Tazobactam	2	32	≤ 1 - > 512	89.0	1.8	9.3
Ceftriaxone	≤ 0.25	4	≤ 0.25 - > 64	87.5	2.1	10.3
Ciprofloxacin	≤ 0.06	≤ 0.06	≤ 0.06 - > 16	97.9	0.7	1.4
Tigecycline	0.5	1	0.12 - 4	NA[b]	NA	NA
Stenotrophomonas maltophilia (351)						
Eravacycline	1	4	0.12 - 16	NA[b]	NA	NA
Ceftazidime	> 32	> 32	0.5 - > 32	22.5	4.8	72.6
Meropenem	> 32	> 32	1 - > 32	NA[a]	NA	NA
Piperacillin-Tazobactam	256	> 512	≤ 1 - > 512	NA[a]	NA	NA
Ceftriaxone	> 64	> 64	1 - > 64	NA[a]	NA	NA
Ciprofloxacin	4	16	0.12 - > 16	NA[a]	NA	NA
Tigecycline	1	4	0.12 - 16	NA[b]	NA	NA
Proteus mirabilis (211)						
Eravacycline	2	4	0.5 - 8	NA[b]	NA	NA
Ceftazidime	≤ 0.25	≤ 0.25	≤ 0.25 - 16	98.6	0.9	0.5
Meropenem	0.06	0.12	≤ 0.03 - 1	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 0.12 - 64	99.1	0.9	
Ceftriaxone	≤ 0.25	≤ 0.25	≤ 0.25 - > 64	98.1	0.9	0.9
Ciprofloxacin	≤ 0.06	2	≤ 0.06 - > 16	86.7	0.5	12.8
Tigecycline	4	8	1 - 16	NA[b]	NA	NA
Acinetobacter baumannii (74)						
Eravacycline	0.12	0.5	0.03 - 16	NA[b]	NA	NA
Ceftazidime	8	16	2 - > 32	74.3	16.2	9.5
Meropenem	0.5	2	0.12 - > 32	94.6	1.4	4.1
Piperacillin-Tazobactam	4	64	≤ 1 - > 512	77.0	13.5	9.5
Ceftriaxone	16	64	4 - > 64	40.5	48.6	10.8
Ciprofloxacin	0.25	0.5	≤ 0.06 - > 16	94.6		5.4
Tigecycline	0.5	2	0.12 - 16	NA[b]	NA	NA
Klebsiella aerogenes (95)						
Eravacycline	0.5	0.5	0.12 - 4	NA[b]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	68.4	3.2	28.4
Meropenem	0.06	0.12	≤ 0.03 - 32	98.9		1.1
Piperacillin-Tazobactam	4	64	≤ 1 - 256	75.8	18.9	5.3
Ceftriaxone	≤ 0.25	64	≤ 0.25 - > 64	67.4		32.6
Ciprofloxacin	≤ 0.06	0.12	≤ 0.06 - 8	93.7	2.1	4.2
Tigecycline	0.5	1	0.25 - 4	NA[b]	NA	NA
Citrobacter freundii (44)						
Eravacycline	0.5	1	0.12 - 2	NA[b]	NA	NA
Ceftazidime	0.5	> 32	≤ 0.25 - > 32	77.3		22.7
Meropenem	≤ 0.03	0.06	≤ 0.03 - 0.25	100		
Piperacillin-Tazobactam	2	256	≤ 1 - > 512	79.5	6.8	13.6
Ceftriaxone	≤ 0.25	> 64	≤ 0.25 - > 64	75.0		25.0
Ciprofloxacin	≤ 0.06	2	≤ 0.06 - > 16	75.0	4.5	20.5
Tigecycline	0.5	2	0.25 - 4	NA[b]	NA	NA
Morganella morganii (58)						
Eravacycline	1	2	0.12 - 4	NA[b]	NA	NA
Ceftazidime	≤ 0.25	8	≤ 0.25 - > 32	87.9	5.2	6.9
Meropenem	0.12	0.25	≤ 0.03 - 0.5	100		
Piperacillin-Tazobactam	≤ 1	2	≤ 1 - 256	98.3		1.7
Ceftriaxone	≤ 0.25	1	≤ 0.25 - > 64	93.1	3.4	3.4
Ciprofloxacin	≤ 0.06	16	≤ 0.06 - > 16	70.7	1.7	27.6
Tigecycline	2	4	0.12 - 16	NA[b]	NA	NA
Haemophilus influenzae (641)						
Eravacycline	0.12	0.25	≤ 0.03 - 1	NA[b]	NA	NA
Ceftazidime	0.12	0.25	≤ 0.03 - 16	99.8		0.2
Meropenem	≤ 0.06	0.12	≤ 0.06 - 0.5	100		
Piperacillin-Tazobactam	≤ 1	≤ 1	≤ 1 - 2	99.7		0.3
Ceftriaxone	≤ 0.06	≤ 0.06	≤ 0.06 - 2	100		
Ciprofloxacin	≤ 0.015	≤ 0.015	≤ 0.015 - > 0.5	100		

S, susceptible; I, intermediate; R, resistant

[a] Interpretative breakpoints defined by EUCAST (eravacycline, tigecycline) where applicable.
[b] NA – not available.

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

Organism	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	Total
S. aureus MSSA	25	438	1482	828	66	20	6					2865
S. aureus MRSA	4	61	294	221	36	34	13					663
CA-MRSA	1	32	157	107	12	2						311
HA-MRSA	3	28	127	97	19	31	13					318
S. epidermidis	23	80	82	66	76	38	6	1				372
E. faecalis	19	108	226	120	2							475
E. faecium	15	80	95	21	1	1						213
VRE	3	21	16	9		1						50
S. agalactiae	28[a]	161	66									255
S. pneumoniae	584[a]	48	1	1								634
S. pneumoniae PenR	23[a]	5										28
S. pyogenes	80[a]	120	11	1								212

[a] Lowest dilution tested

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

Organism	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	Total
E. coli ALL		2	183	905	1361	475	64	3				2993
E. coli ESBL pos			13	47	131	127	25	1				344
E. coli ESBL neg		2	170	858	1230	347	39	2				2648
K. pneumoniae ALL			4	18	322	512	85	40	16	2	2[b]	1001
K. pneumoniae ESBL pos					14	32	14	12	5			77
E. cloacae		1	2	11	104	263	67	16	8	5		477
K. aerogenes				2	29	56	4	3	1			95
S. marcescens						11	116	106	23	3	1	260
K. oxytoca			6	34	188	41	9	3				281
S. maltophilia				4	21	68	140	62	39	15	2	351
P. mirabilis						4	71	80	50	6		211
A. baumannii		4	28	19	11	6	5				1	74
C. freundii				2	19	17	2	4				44
M. morganii				1	1	7	22	24	3			58
H. influenzae		13[a]	42	273	289	23	1					641

[a] Lowest dilution tested; [b] Isolates had an MIC of >16 µg/mL.

Conclusions

1. Eravacycline demonstrated *in vitro* activity versus Gram-negative bacilli.
2. 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.
3. Compared to tigecycline, eravacycline was 4 fold more active versus *Acinetobacter baumannii.*
4. Eravacycline demonstrated potent *in vitro* activity against *Stenotrophomonas maltophilia.*
5. Eravacycline was potent versus Gram-positive cocci.
6. Eravacycline demonstrated potent *in vitro* activity against MSSA, MRSA including both CA-MRSA and HA-MRSA.
7. Eravacycline demonstrated potent *in vitro* activity against all streptococci.
8. Eravacycline demonstrated potent *in vitro* activity against *E. faecalis* and *E. faecium,* including VRE.