

Introduction

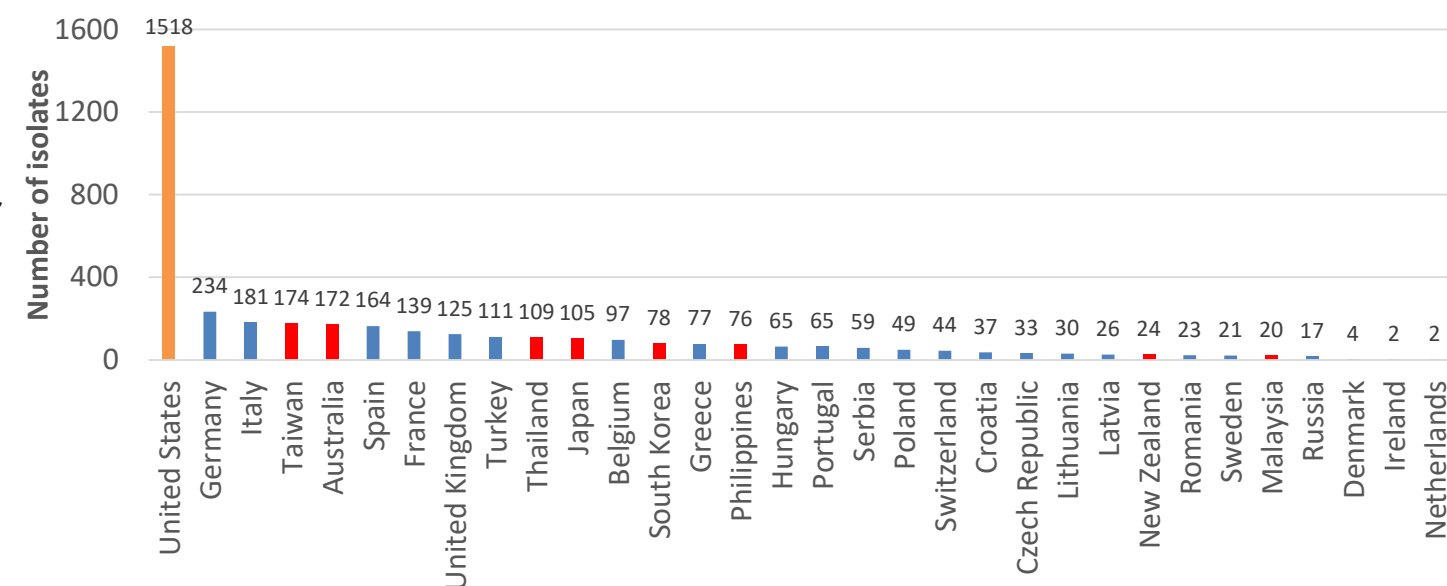
Eravacycline is a novel, fully-synthetic, fluorocycline antibiotic that is approved by the Food and Drug Administration (FDA) for the treatment of complicated intra-abdominal infections (cIAI) caused by susceptible microorganisms including *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii*, *Enterobacter cloacae*, *K. oxytoca*, *Enterococcus faecalis*, *E. faecium*, *Staphylococcus aureus*, *Streptococcus anginosus* group, *Clostridium perfringens*, *Bacteroides* species, and *Parabacteroides distasonis* in patients 18 years or older. The current study evaluated the *in vitro* activity of eravacycline and comparators against Gram-negative pathogens collected worldwide as part of an ongoing global surveillance program.

Methods & Materials

Clinical *Enterobacteriaceae* and *Acinetobacter baumannii* isolates were collected in 2018 from hospitals in 32 countries. In brief, totals of 758, 1,605 and 1,518 were from the Asia/Pacific, Europe and USA regions. Minimum inhibitory concentration (MIC) results for eravacycline and comparators were determined by the Clinical and Laboratory Standards Institute (CLSI) methods (1). Antibiotic susceptibility was determined and interpreted following CLSI guidelines (2) except for eravacycline and tigecycline where FDA breakpoints were used (3). European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints are available for eravacycline & tigecycline against *Escherichia coli* and tigecycline against *Citrobacter koseri* (4) and analysis using these was also performed for comparative purposes. Multi-drug-resistance (MDR) was defined as resistance (CLSI/FDA breakpoints) to ≥3 antibiotics from aztreonam, a carbapenem (meropenem or ertapenem), cefepime/cefotaxime/ceftazidime/ceftriaxone (any one), gentamicin, levofloxacin, piperacillin-tazobactam, tetracycline or tigecycline (5).

Results

Figure 1. Distribution of All Isolates by Country*



*Total of 3,881 isolates, Asia/Pacific (n=758), Europe (n=1,605) and the USA (n=1,518); Isolates from USA in orange, Asia-Pacific in red and Europe in blue

Table 3. Susceptibility of *Acinetobacter baumannii* and carbapenem-resistant *A. baumannii* (CRAB) to Eravacycline and Comparators

Organism	Drug	%S*	MIC ₅₀	MIC ₉₀	MIN MIC	MAX MIC
<i>Acinetobacter baumannii</i> (n=496)	Amikacin	55.2	8	>64	≤0.5	>64
	Ampicillin Sulbactam	42.5	32	>64	≤1	>64
	Aztreonam	NB	64	>64	2	>64
	Cefepime	34.1	64	>64	≤0.25	>64
	Ceftazidime	39.5	64	>64	1	>64
	Ceftriaxone	18.2	>64	>64	1	>64
	Colistin	NSB	0.5	1	≤0.12	>8
	Eravacycline	NB	0.5	1	≤0.015	4
	Gentamicin	44.2	16	>16	≤0.12	>16
	Levofloxacin	40.3	8	>32	≤0.12	>32
	Meropenem	42.5	>16	>16	≤0.12	>16
	Minocycline	66.9	1	16	≤0.12	>32
	Piperacillin Tazobactam	35.9	>128	>128	≤0.12	>128
Tetracycline	36.9	16	>32	≤0.12	>32	
Tigecycline	NB	2	4	0.03	>4	
Trimethoprim Sulfa	47.4	4	>32	≤0.06	>32	
CRAB (n=280)	Amikacin	23.2	>64	>64	1	>64
	Ampicillin Sulbactam	3.9	64	>64	4	>64
	Aztreonam	NB	64	>64	16	>64
	Cefepime	1.1	>64	>64	4	>64
	Ceftazidime	3.6	>64	>64	4	>64
	Ceftriaxone	0.4	>64	>64	8	>64
	Colistin	NSB	0.5	2	≤0.12	>8
	Eravacycline	NB	0.5	1	0.03	4
	Gentamicin	12.9	>16	>16	0.25	>16
	Levofloxacin	2.9	16	>32	≤0.12	>32
	Meropenem	0.0	>16	>16	8	>16
	Minocycline	45.4	8	16	≤0.12	>32
	Piperacillin Tazobactam	1.8	>128	>128	≤0.12	>128
Tetracycline	6.4	>32	>32	1	>32	
Tigecycline	NB	2	4	0.12	>4	
Trimethoprim Sulfa	18.6	>32	>32	≤0.06	>32	

*%S, percent susceptible; MIC₅₀ = concentration required to inhibit 50% of the population; MIC₉₀ = concentration required to inhibit 90% of the population; NSB, colistin does not have a susceptible breakpoint; NB, no defined breakpoints.

Table 1. Susceptibility of combined *Enterobacteriaceae* and MDR *Enterobacteriaceae* to Eravacycline and Comparators

Organism	Drug	%S*	MIC ₅₀	MIC ₉₀	MIN MIC	MAX MIC	
<i>Enterobacteriaceae</i> (n=3,385)	Aztreonam	77.5	0.12	>16	≤0.03	>16	
	Cefepime	88.2	0.06	4	≤0.008	>16	
	Cefotaxime	74.9	0.12	>64	≤0.015	>64	
	Ceftazidime	78.3	0.25	128	≤0.03	>128	
	Ceftazidime-avibactam	99.0	0.12	0.5	≤0.03	>8	
	Ceftriaxone	74.6	0.12	>4	≤0.015	>4	
	Colistin	NSB	0.25	0.5	≤0.03	>8	
	Eravacycline (FDA)	92.6	0.25	0.5	≤0.015	>16	
	Ertapenem	93.2	0.015	0.5	≤0.008	>8	
	Gentamicin	91.8	0.5	2	≤0.12	>16	
	Levofloxacin	84.4	0.06	4	≤0.004	>4	
	Meropenem	97.7	0.03	0.06	≤0.004	>16	
	Minocycline	85.6	2	8	≤0.12	>16	
	Piperacillin Tazobactam	81.8	2	128	≤0.25	>128	
	Tetracycline	81.1	1	>16	≤0.25	>16	
	Tigecycline (FDA)	95.5	0.5	2	≤0.015	>8	
	Trimethoprim Sulfa	83.2	0.12	>4	≤0.06	>4	
	MDR <i>Enterobacteriaceae</i> (n=681)	Aztreonam	16.6	>16	>16	≤0.03	>16
		Cefepime	44.8	4	>16	0.03	>16
Cefotaxime		13.5	>64	>64	≤0.015	>64	
Ceftazidime		22.6	64	>128	0.12	>128	
Ceftazidime-avibactam		95.0	0.25	1	≤0.03	>8	
Ceftriaxone		12.0	>4	>4	0.03	>4	
Colistin		NSB	0.25	1	0.06	>16	
Eravacycline (FDA)		80.9	0.25	1	0.06	>16	
Ertapenem		71.4	0.25	8	≤0.008	>8	
Gentamicin		62.4	1	>16	≤0.12	>16	
Levofloxacin		40.5	1	>4	≤0.004	>4	
Meropenem		89.1	0.06	2	0.015	>16	
Minocycline		62.4	4	>16	0.25	>16	
Piperacillin Tazobactam		38.5	64	>128	1	>128	
Tetracycline		43.5	16	>16	≤0.25	>16	
Tigecycline (FDA)		91.5	0.5	2	0.12	>8	
Trimethoprim Sulfa		42.1	>4	>4	≤0.06	>4	

Table 2. Susceptibility of individual species of *Enterobacteriaceae* to Eravacycline and Comparators

Organism	Drug	%S*	MIC ₅₀	MIC ₉₀	MIN MIC	MAX MIC	
<i>Klebsiella pneumoniae</i> (n=533)	Aztreonam	74.5	0.12	>16	≤0.03	>16	
	Cefepime	75.2	0.06	>16	≤0.008	>16	
	Cefotaxime	73.9	0.06	>64	≤0.015	>64	
	Ceftazidime	73.9	0.25	128	0.06	>128	
	Ceftazidime-avibactam	97.6	0.12	0.5	≤0.03	>8	
	Ceftriaxone	73.6	0.06	>4	≤0.015	>4	
	Colistin	NSB	0.25	0.5	0.12	>8	
	Eravacycline (FDA)	84.1	0.25	1	0.12	>16	
	Ertapenem	90.4	0.015	0.5	≤0.008	>8	
	Gentamicin	83.1	0.25	>16	≤0.12	>16	
	Levofloxacin	72.8	0.12	>4	≤0.004	>4	
	Meropenem	93.1	0.03	0.12	0.015	>16	
	Minocycline	73.7	2	>16	0.5	>16	
	Piperacillin Tazobactam	79.9	4	>128	≤0.25	>128	
	Tetracycline	71.5	2	>16	0.5	>16	
	Tigecycline (FDA)	91.2	0.5	2	0.25	>8	
	Trimethoprim Sulfa	72.1	0.25	>4	≤0.06	>4	
	<i>Klebsiella aerogenes</i> (n=494)	Aztreonam	71.4	0.25	>16	≤0.03	>16
		Cefepime	93.3	0.06	2	0.015	>16
Cefotaxime		66.0	0.25	32	0.06	>64	
Ceftazidime		69.1	0.5	>128	0.12	>128	
Ceftazidime-avibactam		98.9	0.25	0.5	0.06	>8	
Ceftriaxone		66.2	0.25	>4	0.03	>4	
Colistin		NSB	0.25	0.5	0.06	>8	
Eravacycline (FDA)		92.9	0.25	0.5	0.06	4	
Ertapenem		95.2	0.015	0.5	≤0.008	>8	
Gentamicin		90.9	0.5	2	≤0.12	>16	
Levofloxacin		84.2	0.12	1	0.008	>8	
Meropenem		98.7	0.03	0.06	0.015	>16	
Minocycline		85.9	2	8	0.25	>16	
Piperacillin Tazobactam		75.8	4	128	0.5	>128	
Tetracycline		85.7	1	>16	0.5	>16	
Tigecycline (FDA)		97.6	0.5	2	0.12	>8	
Trimethoprim Sulfa		82.9	0.06	>4	≤0.06	>4	
<i>Citrobacter freundii</i> (n=462)		Aztreonam	95.9	0.06	0.25	≤0.03	>16
		Cefepime	98.4	0.03	0.12	0.015	>16
	Cefotaxime	95.6	0.06	0.5	≤0.015	>64	
	Ceftazidime	96.2	0.12	1	0.06	>128	
	Ceftazidime-avibactam	99.7	0.12	0.25	≤0.03	>8	
	Ceftriaxone	96.7	0.06	0.25	≤0.015	>4	
	Colistin	NSB	0.25	0.25	0.12	>16	
	Eravacycline (FDA)	98.6	0.25	0.25	0.12	1	
	Ertapenem	98.9	0.008	0.015	≤0.008	>4	
	Gentamicin	97.5	0.25	0.5	≤0.12	>16	
	Levofloxacin	97.8	0.03	0.12	0.008	>4	
	Meropenem	100.0	0.015	0.03	0.008	0.5	
	Minocycline	96.4	1	4	0.25	>16	
	Piperacillin Tazobactam	95.9	2	16	0.5	>128	
	Tetracycline	96.2	1	4	0.5	>16	
	Tigecycline (FDA)	97.8	0.25	1	0.12	>4	
	Tigecycline (EUCAST)	82.2	0.25	1	0.12	>4	
	Trimethoprim Sulfa	95.9	0.12	0.25	≤0.06	>4	
	<i>Escherichia coli</i> (n=515)	Aztreonam	78.8	0.12	>16	≤0.03	>16
Cefepime		80.8	0.06	>16	≤0.008	>16	
Cefotaxime		76.3	0.06	>64	≤0.015	>64	
Ceftazidime		81.2	0.25	32	0.06	>128	
Ceftazidime-avibactam		100.0	0.06	0.25	≤0.03	>8	
Ceftriaxone		76.7	0.06	>4	≤0.015	>4	
Colistin		NSB	0.25	0.5	0.03	>8	
Eravacycline (FDA)		98.8	0.12	0.25	≤0.015	2	
Eravacycline (EUCAST)		98.8	0.12	0.25	≤0.015	2	
Ertapenem		98.1	0.015	0.06	≤0.008	>8	
Gentamicin		87.6	0.5	>16	≤0.12	>16	
Levofloxacin		66.0	0.12	>4	≤0.004	>4	
Meropenem		99.6	0.015	0.03	0.004	>8	
Minocycline		82.1	1	16	≤0.12	>16	
Piperacillin Tazobactam		89.9	2	32	≤0.25	>128	
Tetracycline		57.5	2	>16	0.5	>16	
Tigecycline (FDA)		99.2	0.25	1	≤0.015	>4	
Tigecycline (EUCAST)		85.1	0.25	1	≤0.015	>4	
Trimethoprim Sulfa		63.7	0.12	>4	≤0.06	>4	
<i>Enterobacter cloacae</i> (n=508)	Aztreonam	68.5	0.25	>16	≤0.03	>16	
	Cefepime	83.7	0.12	4	≤0.008	>16	
	Cefotaxime	61.2	0.5	>64	≤0.015	>64	
	Ceftazidime	67.1	0.5	128	≤0.03	>128	
	Ceftazidime-avibactam	98.0	0.25	0.5	≤0.03	>8	
	Ceftriaxone	64.4	0.5	>4	≤0.015	>4	
	Colistin	NSB	0.25	2	≤0.03	>8	
	Eravacycline (FDA)	89.8	0.25	1	0.06	8	
	Ertapenem	81.3	0.06	1	≤0.008	>8	
	Gentamicin	92.9	0.5	1	≤0.12	>16	
	Levofloxacin	88.6	0.06	1	≤0.004	>4	
	Meropenem	96.3	0.03	0.12	0.0		