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IN VITRO SURVEILLANCE OF ERAVACYCLINE AGAINST GRAM-NEGATIVE PATHOGENS, INCLUDING RESISTANT ISOLATES, COLLECTED WORLDWIDE DURING 2020

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Introduction

Eravacycline is a fully-synthetic, fluorocycline antibiotic approved for the treatment of complicated intra-abdominal infections (cIAI) in patients ≥18 years of age in Europe, Singapore, the US and UK. The purpose of this study was to monitor the *in vitro* activity of eravacycline against Gram-negative isolates, including multidrug-resistant (MDR) isolates, collected in 2020. Eravacycline data were compared with tigecycline and multiple other comparators.

Methods & Materials

Isolates (see Figure 1) were collected from the USA, Europe and Asia/Pacific regions during 2020 from various body sites. Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution (1). Antibiotic susceptibility was determined with EUCAST breakpoints (2). Isolates came from various infections sources including respiratory tract, gastro-intestinal tract, urinary tract and body fluids (Figure 2).

Summary

Summary MIC data for eravacycline and select comparators are shown in Tables 1-4. Susceptibility to eravacycline for Enterobacterales was 93.4%. Against MDR Enterobacterales, susceptibility to eravacycline was 86.1%. ESBL-producing bacteria had similar susceptibility, with the exception of *K. pneumoniae*, where susceptibility of ESBL-positive *K. pneumoniae* were lower than all *K. pneumoniae* grouped. Although there are no clinical breakpoints for *S. maltophilia* or CRAB, eravacycline exhibited promising activity against these species.

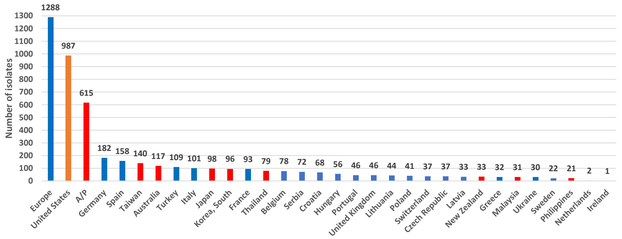
Results

Table 1. Susceptibility of combined Enterobacterales and MDR Enterobacterales Eravacycline and Comparators

Organism (n)	Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Enterobacterales (n= 2,358)	Aztreonam	71.2	0.12	> 16	≤ 0.03	> 16
	Cefepime	79.6	0.06	> 16	≤ 0.008	> 16
	Cefotaxime	72.6	0.12	> 64	≤ 0.015	> 64
	Ceftazidime	72.9	0.25	128	≤ 0.03	> 128
	Ceftazidime-avibactam	98.1	0.12	0.5	≤ 0.03	> 8
	Ceftriaxone	71.7	0.12	> 4	≤ 0.015	> 4
	Colistin	96.7	0.25	0.5	≤ 0.03	> 8
	Eravacycline	**93.4**	**0.25**	**0.5**	**≤ 0.015**	**16**
	Ertapenem	90.9	0.015	0.5	≤ 0.008	> 8
	Gentamicin	88.6	0.5	16	≤ 0.12	> 16
	Levofloxacin	80.7	0.06	> 4	≤ 0.004	> 4
	Meropenem	96.4	0.03	0.06	≤ 0.004	> 16
	Minocycline	NB	2	16	≤ 0.12	> 16
	Piperacillin Tazobactam	74.7	2	> 128	≤ 0.25	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	85.8	0.5	1	0.03	> 8
	Trimethoprim Sulfa	79.4	≤ 0.06	> 4	≤ 0.06	> 4
MDR *Enterobacterales* (n= 645)	Aztreonam	7.8	> 16	> 16	0.06	> 16
	Cefepime	29.0	4	> 16	0.03	> 16
	Cefotaxime	9.3	> 64	> 64	≤ 0.015	> 64
	Ceftazidime	13.2	64	> 128	0.12	> 128
	Ceftazidime-avibactam	93.0	0.5	2	≤ 0.03	> 8
	Ceftriaxone	6.2	> 4	> 4	0.03	> 4
	Colistin	94.1	0.25	0.5	0.12	> 8
	Eravacycline	**86.1**	**0.25**	**1**	**0.03**	**16**
	Ertapenem	67.8	0.25	> 8	≤ 0.008	> 8
	Gentamicin	63.7	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	45.9	1	> 4	0.015	> 4
	Meropenem	86.7	0.06	16	≤ 0.004	> 16
	Minocycline	NB	2	> 16	≤ 0.12	> 16
	Piperacillin Tazobactam	22.5	64	> 128	0.5	> 128
	Tetracycline	NB	4	> 16	≤ 0.25	> 16
	Tigecycline	73.5	0.5	2	0.12	> 8
	Trimethoprim Sulfa	46.7	> 4	> 4	≤ 0.06	> 4

*%S, percent susceptible; MIC_{50} = concentration required to inhibit 50% of the population; MIC_{90} = concentration required to inhibit 90% of the population; NB, no defined breakpoints.

Figure 1. Distribution of All Isolates by Country*



*Total of 2,890 isolates, Asia/Pacific (n=615), Europe (n=1,288) and the USA (n=987); Isolates from USA in orange, Asia-Pacific in red and Europe in blue

Table 2. Susceptibility of individual species of Enterobacterales to Eravacycline and Comparators

Organism (n)	Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Citrobacter freundii (n=347)	Aztreonam	61.7	0.25	> 16	≤ 0.03	> 16
	Cefepime	81.8	0.06	4	0.015	> 16
	Cefotaxime	60.8	0.25	> 64	0.03	> 64
	Ceftazidime	58.2	1	> 128	0.12	> 128
	Ceftazidime-avibactam	96.8	0.25	1	≤ 0.03	> 8
	Ceftriaxone	61.1	0.25	> 4	0.06	> 4
	Colistin	100.0	0.25	0.5	0.06	2
	Eravacycline	**92.2**	**0.25**	**0.5**	**0.06**	**4**
	Ertapenem	91.6	0.015	0.5	≤ 0.008	> 8
	Gentamicin	86.7	0.5	16	≤ 0.12	> 16
	Levofloxacin	80.7	0.12	4	≤ 0.004	> 4
	Meropenem	96.8	0.03	0.12	≤ 0.004	> 16
	Minocycline	NB	2	16	0.5	> 16
	Piperacillin Tazobactam	62.8	4	128	0.5	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	85.6	0.5	1	0.12	4
	Trimethoprim Sulfa	81.8	≤ 0.06	> 4	≤ 0.06	> 4
Enterobacter cloacae (n=456)	Aztreonam	58.3	0.25	> 16	≤ 0.03	> 16
	Cefepime	70.4	0.12	16	0.03	> 16
	Cefotaxime	55.3	0.5	> 64	≤ 0.015	> 64
	Ceftazidime	56.1	0.5	> 128	0.06	> 128
	Ceftazidime-avibactam	96.1	0.25	1	≤ 0.03	> 8
	Ceftriaxone	55.7	0.5	> 4	≤ 0.015	> 4
	Colistin	87.1	0.25	> 8	0.12	> 8
	Eravacycline	**88.6**	**0.25**	**1**	**0.03**	**8**
	Ertapenem	78.7	0.06	2	≤ 0.008	> 8
	Gentamicin	89.7	0.25	4	≤ 0.12	> 16
	Levofloxacin	85.1	0.06	2	0.008	> 4
	Meropenem	96.3	0.03	0.12	≤ 0.004	> 16
	Minocycline	NB	2	8	≤ 0.12	> 16
	Piperacillin Tazobactam	61.8	4	128	0.5	> 128
	Tetracycline	NB	2	16	≤ 0.25	> 16
	Tigecycline	76.1	0.5	1	0.06	> 8
	Trimethoprim Sulfa	80.9	≤ 0.06	> 4	≤ 0.06	> 4
Escherichia coli (n=533)	Aztreonam	76.9	0.12	> 16	≤ 0.03	> 16
	Cefepime	80.7	0.06	> 16	0.015	> 16
	Cefotaxime	78.2	0.06	> 64	≤ 0.015	> 64
	Ceftazidime	78.4	0.25	16	≤ 0.03	> 128
	Ceftazidime-avibactam	100.0	0.12	0.25	≤ 0.03	4
	Ceftriaxone	78.6	0.06	> 4	≤ 0.015	> 4
	Colistin	100.0	0.25	0.25	0.12	1
	Eravacycline	**99.4**	**0.12**	**0.25**	**≤ 0.015**	**16**
	Ertapenem	98.9	0.015	0.06	≤ 0.008	> 8
	Gentamicin	86.7	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	68.7	0.06	> 4	≤ 0.004	> 4
	Meropenem	99.8	0.03	0.03	≤ 0.004	16
	Minocycline	NB	1	8	≤ 0.12	> 16
	Piperacillin Tazobactam	87.6	2	16	≤ 0.25	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	98.7	0.12	0.25	0.06	> 8
	Trimethoprim Sulfa	66.2	≤ 0.06	> 4	≤ 0.06	> 4
Escherichia coli, ESBL (n=106)	Aztreonam	1.9	> 16	> 16	0.5	> 16
	Cefepime	4.7	> 16	> 16	0.5	> 16
	Cefotaxime	1.9	> 64	> 64	≤ 0.015	> 64
	Ceftazidime	7.6	16	128	0.25	> 128
	Ceftazidime-avibactam	100.0	0.12	0.5	≤ 0.03	1
	Ceftriaxone	0.9	> 4	> 4	0.25	> 4
	Colistin	100.0	0.25	0.25	0.12	1
	Eravacycline	**98.1**	**0.12**	**0.25**	**0.06**	**16**
	Ertapenem	97.2	0.06	0.25	≤ 0.008	4
	Gentamicin	69.8	1	> 16	≤ 0.12	> 16
	Levofloxacin	20.8	> 4	> 4	0.015	> 4
	Meropenem	100.0	0.03	0.03	≤ 0.004	0.25
	Minocycline	NB	2	16	0.25	> 16
	Piperacillin Tazobactam	67.9	4	128	1	> 128
	Tetracycline	NB	> 16	> 16	0.5	> 16
	Tigecycline	97.2	0.25	0.5	0.12	> 8
	Trimethoprim Sulfa	34.0	> 4	> 4	≤ 0.06	> 4
Escherichia coli, non ESBL (n=427)	Aztreonam	95.6	0.12	0.25	≤ 0.03	> 16
	Cefepime	99.5	0.06	0.12	0.015	> 16
	Cefotaxime	97.2	0.06	0.25	≤ 0.015	> 64
	Ceftazidime	96.0	0.25	0.5	≤ 0.03	> 128
	Ceftazidime-avibactam	100.0	0.12	0.25	≤ 0.03	4
	Ceftriaxone	97.9	0.06	0.12	≤ 0.015	> 4
	Colistin	100.0	0.25	0.25	0.12	1
	Eravacycline	**99.8**	**0.12**	**0.25**	**≤ 0.015**	**2**
	Ertapenem	99.3	≤ 0.008	0.015	≤ 0.008	> 8
	Gentamicin	90.9	0.5	2	≤ 0.12	> 16
	Levofloxacin	80.6	0.03	> 4	≤ 0.004	> 4
	Meropenem	99.8	0.015	0.03	0.008	16
	Minocycline	NB	1	8	≤ 0.12	> 16
	Piperacillin Tazobactam	92.5	2	16	≤ 0.25	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	99.1	0.12	0.25	0.06	4
	Trimethoprim Sulfa	74.2	≤ 0.06	> 4	≤ 0.06	> 4
Klebsiella oxytoca (n=509)	Aztreonam	80.6	0.25	16	≤ 0.03	> 16
	Cefepime	91.4	0.03	1	0.015	> 16
	Cefotaxime	89.8	0.06	2	≤ 0.015	> 64
	Ceftazidime	92.7	0.12	1	0.06	> 128
	Ceftazidime-avibactam	99.0	0.12	0.25	≤ 0.03	> 8
	Ceftriaxone	84.5	0.12	> 4	≤ 0.015	> 4
	Colistin	99.6	0.25	0.5	≤ 0.03	> 8
	Eravacycline	**97.5**	**0.12**	**0.25**	**0.03**	**2**
	Ertapenem	98.6	0.015	0.03	≤ 0.008	> 8
	Gentamicin	95.7	0.5	1	≤ 0.12	> 16
	Levofloxacin	95.7	0.06	0.25	0.015	> 4
	Meropenem	98.6	0.03	0.03	≤ 0.004	> 16
	Minocycline	NB	1	4	0.25	> 16
	Piperacillin Tazobactam	83.3	2	> 128	≤ 0.25	> 128
	Tetracycline	NB	0.5	2	≤ 0.25	> 16
	Tigecycline	92.1	0.25	0.5	0.03	4
	Trimethoprim Sulfa	93.9	≤ 0.06	0.12	≤ 0.06	> 4
Klebsiella oxytoca, ESBL (n=42)	Aztreonam	0.0	> 16	> 16	2	> 16
	Cefepime	19.1	4	> 16	0.5	> 16
	Cefotaxime	0.0	8	> 64	2	> 64
	Ceftazidime	40.5	4	64	0.25	> 128
	Ceftazidime-avibactam	100.0	0.25	0.5	0.06	4
	Ceftriaxone	0.0	> 4	> 4	> 4	> 4
	Colistin	100.0	0.25	0.5	0.12	1
	Eravacycline	**97.6**	**0.12**	**0.25**	**0.12**	**1**
	Ertapenem	100.0	0.03	0.12	0.015	0.12
	Gentamicin	59.5	1	> 16	≤ 0.12	> 16
	Levofloxacin	76.2	0.25	2	0.03	> 4
	Meropenem	100.0	0.03	0.06	≤ 0.004	0.06
	Minocycline	NB	1	4	0.5	> 16
	Piperacillin Tazobactam	38.1	128	> 128	1	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	88.1	0.25	1	0.12	2
	Trimethoprim Sulfa	61.9	0.12	> 4	≤ 0.06	> 4
Klebsiella oxytoca, non ESBL (n=467)	Aztreonam	87.8	0.25	2	≤ 0.03	> 16
	Cefepime	97.9	0.03	0.12	0.015	> 16
	Cefotaxime	97.9	0.06	0.25	≤ 0.015	> 64
	Ceftazidime	97.4	0.12	0.5	0.06	> 128
	Ceftazidime-avibactam	98.9	0.12	0.25	≤ 0.03	> 8
	Ceftriaxone	92.1	0.12	0.5	≤ 0.015	> 4
	Colistin	99.6	0.25	0.5	≤ 0.03	> 8
	Eravacycline	**97.4**	**0.12**	**0.25**	**0.03**	**2**
	Ertapenem	98.5	0.015	0.015	≤ 0.008	> 8
	Gentamicin	98.9	0.5	0.5	≤ 0.12	> 16
	Levofloxacin	97.4	0.03	0.25	0.015	> 4
	Meropenem	98.5	0.03	0.03	0.015	> 16
	Minocycline	NB	1	4	0.25	> 16
	Piperacillin Tazobactam	87.4	2	32	≤ 0.25	> 128
	Tetracycline	NB	0.5	2	≤ 0.25	> 16
	Tigecycline	92.5	0.25	0.5	0.03	4
	Trimethoprim Sulfa	96.8	≤ 0.06	0.12	≤ 0.06	> 4
Klebsiella pneumoniae (n=513)	Aztreonam	73.9	0.06	> 16	≤ 0.03	> 16
	Cefepime	73.7	0.06	> 16	≤ 0.008	> 16
	Cefotaxime	72.9	0.06	> 64	≤ 0.015	> 64
	Ceftazidime	72.3	0.25	> 128	0.06	> 128
	Ceftazidime-avibactam	97.7	0.12	1	≤ 0.03	> 8
	Ceftriaxone	73.3	0.06	> 4	≤ 0.015	> 4
	Colistin	96.9	0.25	0.5	0.06	> 8
	Eravacycline	**88.1**	**0.25**	**1**	**0.06**	**4**
	Ertapenem	85.4	0.015	8	≤ 0.008	> 8
	Gentamicin	83.8	0.25	> 16	≤ 0.12	> 16
	Levofloxacin	74.3	0.06	> 4	0.008	> 4
	Meropenem	90.3	0.03	2	0.015	> 16
	Minocycline	NB	2	> 16	≤ 0.12	> 16
	Piperacillin Tazobactam	72.1	4	> 128	≤ 0.25	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	75.1	0.5	2	0.12	8
	Trimethoprim Sulfa	75.6	≤ 0.06	> 4	≤ 0.06	> 4
Klebsiella pneumoniae, ESBL (n=95)	Aztreonam	7.4	> 16	> 16	0.25	> 16
	Cefepime	7.4	> 16	> 16	0.25	> 16
	Cefotaxime	5.3	> 64	> 64	0.06	> 64
	Ceftazidime	7.4	32	> 128	0.5	> 128
	Ceftazidime-avibactam	99.0	0.25	1	≤ 0.03	> 8
	Ceftriaxone	5.3	> 4	> 4	0.12	> 4
	Colistin	96.8	0.25	0.5	0.12	> 8
	Eravacycline	**76.8**	**0.25**	**2**	**0.12**	**4**
	Ertapenem	79.0	0.12	4	0.015	> 8
	Gentamicin	46.3	16	> 16	≤ 0.12	> 16
	Levofloxacin	33.7	4	> 4	0.03	> 4
	Meropenem	94.7	0.06	0.25	0.015	> 16
	Minocycline	NB	4	> 16	0.5	> 16
	Piperacillin Tazobactam	37.9	32	> 128	0.5	> 128
	Tetracycline	NB	> 16	> 16	1	> 16
	Tigecycline	55.8	0.5	4	0.25	8
	Trimethoprim Sulfa	24.2	> 4	> 4	≤ 0.06	> 4
Klebsiella pneumoniae, non ESBL (n=418)	Aztreonam	89.0	0.06	> 16	≤ 0.03	> 16
	Cefepime	88.8	0.06	> 16	≤ 0.008	> 16
	Cefotaxime	88.3	0.06	> 64	≤ 0.015	> 64
	Ceftazidime	87.1	0.25	64	0.06	> 128
	Ceftazidime-avibactam	97.4	0.12	1	≤ 0.03	> 8
	Ceftriaxone	88.8	0.06	> 4	≤ 0.015	> 4
	Colistin	96.9	0.25	0.5	0.06	> 8
	Eravacycline	**90.7**	**0.25**	**0.5**	**0.06**	**4**
	Ertapenem	86.8	0.015	> 8	≤ 0.008	> 8
	Gentamicin	92.3	0.25	0.5	≤ 0.12	> 16
	Levofloxacin	83.5	0.06	> 4	0.008	> 4
	Meropenem	89.2	0.03	16	0.015	> 16
	Minocycline	NB	2	> 16	≤ 0.12	> 16
	Piperacillin Tazobactam	79.9	4	> 128	≤ 0.25	> 128
	Tetracycline	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	79.4	0.5	1	0.12	8
	Trimethoprim Sulfa	87.3	≤ 0.06	> 4	≤ 0.06	> 4

*%S, percent susceptible; MIC_{50} = concentration required to inhibit 50% of the population; MIC_{90} = concentration required to inhibit 90% of the population; NB, no defined breakpoints.

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
Acinetobacter baumannii (n=431)	Amikacin	43.2	> 64	> 64	≤ 0.5	> 64
	Ampicillin Sulbactam	NB	32	> 64	≤ 1	> 64
	Aztreonam	NB	64	> 64	2	> 64
	Cefepime	NB	64	> 64	≤ 0.25	> 64
	Ceftazidime	NB	> 64	> 64	1	> 64
	Ceftriaxone	NB	> 64	> 64	2	> 64
	Colistin	95.6	0.5	1	0.25	> 8
	Eravacycline	**NB**	**0.5**	**2**	**≤ 0.015**	**4**
	Gentamicin	41.8	> 16	> 16	0.25	> 16
	Levofloxacin	30.4	8	> 32	≤ 0.12	> 32
	Meropenem	32.3	> 16	> 16	≤ 0.12	> 16
	Minocycline	NB	4	16	≤ 0.12	> 32
	Piperacillin Tazobactam	NB	> 128	> 128	≤ 0.12	> 128
	Tetracycline	NB	> 32	> 32	0.5	> 32
	Tigecycline	NB	2	4	≤ 0.015	> 4
	Trimethoprim Sulfa	47.8	4	> 32	≤ 0.06	> 32
CRAB (n=287)	Amikacin	17.8	> 64	> 64	1	> 64
	Ampicillin Sulbactam	NB	64	> 64	8	> 64
	Aztreonam	NB	> 64	> 64	16	> 64
	Cefepime	NB	> 64	> 64	8	> 64
	Ceftazidime	NB	> 64	> 64	4	> 64
	Ceftriaxone	NB	> 64	> 64	16	> 64
	Colistin	93.7	0.5	1	0.25	> 8
	Eravacycline	**NB**	**1**	**2**	**0.06**	**4**
	Gentamicin	17.1	> 16	> 16	0.25	> 16
	Levofloxacin	1.7	16	> 32	≤ 0.12	> 32
	Meropenem	0.0	> 16	> 16	16	> 16
	Minocycline	NB	8	16	≤ 0.12	> 32
	Piperacillin Tazobactam	NB	> 128	> 128	8	> 128
	Tetracycline	NB	> 32	> 32	1	> 32
	Tigecycline	NB	4	4	0.12	> 4
	Trimethoprim Sulfa	26.5	> 32	> 32	≤ 0.06	> 32

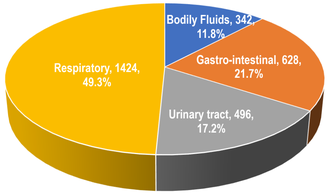
*%S, percent susceptible; MIC_{50} = concentration required to inhibit 50% of the population; MIC_{90} = concentration required to inhibit 90% of the population; NB, no defined breakpoints.

Table 4. Susceptibility of *Stenotrophomonas maltophilia* to Eravacycline and Comparators

Organism (n)	Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Stenotrophomonas maltophilia (101)	Amikacin	NB	> 64	> 64	4	> 64
	Ampicillin Sulbactam	NB	> 64	> 64	8	> 64
	Aztreonam	NB	> 64	> 64	4	> 64
	Cefepime	NB	64	> 64	≤ 0.25	> 64
	Ceftazidime	NB	32	> 64	1	> 64
	Ceftriaxone	NB	> 64	> 64	16	> 64
	Colistin	NB	4	> 8	≤ 0.12	> 8
	Eravacycline	**NB**	**1**	**2**	**0.12**	**8**
	Gentamicin	NB	> 16	> 16	1	> 16
	Levofloxacin	NB	2	4	0.5	32
	Meropenem	NB	> 16	> 16	4	> 16
	Minocycline	NB	0.5	2	≤ 0.12	16
	Piperacillin Tazobactam	NB	> 128	> 128	1	> 128
	Tetracycline	NB	16	32	1	> 32
	Tigecycline	NB	2	4	0.03	> 4
	Trimethoprim Sulfa	0.0	0.25	1	≤ 0.06	16

*%S, percent susceptible; MIC_{50} = concentration required to inhibit 50% of the population; MIC_{90} = concentration required to inhibit 90% of the population; NB, no defined breakpoints.

Figure 2. Number and Percent of Isolates by Infection Source



Conclusion

Eravacycline exhibited sustained high susceptibility against multiple Enterobacterales species, including MDR and ESBL-positive isolates. While EUCAST breakpoints are not defined for *Stenotrophomonas maltophilia* or CRAB, eravacycline demonstrated promising activity against these species. Taken together, these results show that, following several years in clinical use, eravacycline remains highly active against the majority of Gram-negative pathogens studied.

References

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