Poster 1679

SUSCEPTIBILITY OF GRAM-NEGATIVE CLINICAL ISOLATES COLLECTED FROM THE USA IN 2020 TO ERAVACYCLINE AND COMPARATORS

Stephen Hawser[1], Nimmi Kothari[1], Barbara Lemos[1], Federica Monti[1], Tony Hodges[2]

[1]IHMA Europe, Monthey (Valais), Switzerland; [2]La Jolla Pharmaceutical Company, Waltham (MA), USA

Contact: Stephen Hawser
shawser@ihma.com
IHMA Europe,
www.ihma.com

Contact: Sherry Maher Siegert, PharmD
ssiegert@ljpc.com
La Jolla Pharmaceutical Company,
www.lajollapharmaceutical.com

Introduction

Eravacycline (ERV) 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 USA and Great Britain.

The purpose of this study was to monitor the *in vitro* activity of ERV against Gram-negative isolates, including multidrug-resistant (MDR) isolates, collected in 2020 from the USA.

Methods & Materials

Isolates were collected from respiratory (52%), gastro-intestinal (22%), and urinary tract (26%) infections in USA patients during 2020.

Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution (1). Antibiotic susceptibility was determined using CLSI (2) and EUCAST breakpoints (3), except for ERV and tigecycline where FDA breakpoints (4) were used in lieu of CLSI breakpoints due to a lack of CLSI breakpoints for these two drugs. EUCAST breakpoints for ERV against *Escherichia coli* and tigecycline against *E. coli* and *Citrobacter koseri* were used to evaluate all Enterobacterales. MDR was defined as resistance to one or more agents from three or more antimicrobial classes recommended for testing and possessing breakpoints.

Results 1

Summary MIC data for ERV and comparators for isolates from 2020 are shown in Tables 1-3. Susceptibility to ERV against combined Enterobacterales was 93.9% (FDA or EUCAST breakpoints) which has remained unchanged since 2015 (Table 4). Against MDR Enterobacterales, susceptibility to ERV was 82.8% (FDA breakpoint) and 85.5% (EUCAST breakpoint). ERV susceptibility by both FDA and EUCAST breakpoints against extended-spectrum beta-lactamase (ESBL)-positive *E. coli* and *K. oxytoca* was 97.7% and 93.3%, respectively. Susceptibility of ESBL-positive *K. pneumoniae* was 77.4% compared to 87.9% against all *K. pneumoniae* by both FDA and EUCAST breakpoints.

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

Organism	Drug	%S* CLSI	%S EUCAST	MIC 50	MIC 90	MIN MIC	MAX MIC
Enterobacterales (n=1,073)	Aztreonam	79.1	75.7	0.12	> 16	≤ 0.03	> 16
	Cefepime	89.0	85.7	0.06	4	≤ 0.008	> 16
	Cefotaxime	77.3	77.3	0.12	> 64	≤ 0.015	> 64
	Ceftazidime	80.9	77.5	0.25	64	≤ 0.03	> 128
	Ceftazidime-avibactam	99.4	99.4	0.12	0.5	≤ 0.03	> 8
	Ceftriaxone	76.6	76.6	0.12	> 4	≤ 0.015	> 4
	Colistin	0.0	98.0	0.25	0.25	≤ 0.03	> 8
	Eravacycline	**93.9 (FDA)**	**93.9**	**0.25**	**0.5**	**≤ 0.015**	**4**
	Ertapenem	94.1	94.1	0.015	0.5	≤ 0.008	> 8
	Gentamicin	93.3	92.9	0.5	1	≤ 0.12	> 16
	Levofloxacin	87.7	87.7	0.06	1	≤ 0.004	> 4
	Meropenem	98.5	98.7	0.03	0.06	0.008	> 16
	Minocycline	87.8	NB	2	8	≤ 0.12	> 16
	Piperacillin Tazobactam	77.9	77.9	2	64	≤ 0.25	> 128
	Tetracycline	82.6	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	96.8 (FDA)	87.8	0.5	1	0.06	> 8
	Trimethoprim Sulfa	85.4	85.4	≤ 0.06	> 4	≤ 0.06	> 4
MDR (CLSI)** Enterobacterales (n=255)	Aztreonam	16.9	NA	> 16	> 16	0.06	> 16
	Cefepime	56.5	NA	2	> 16	0.03	> 16
	Cefotaxime	14.9	NA	> 64	> 64	0.03	> 64
	Ceftazidime	24.7	NA	64	> 128	0.12	> 128
	Ceftazidime-avibactam	97.7	NA	0.5	1	≤ 0.03	> 8
	Ceftriaxone	11.8	NA	> 4	> 4	0.03	> 4
	Colistin	0.0	NA	0.25	0.25	0.12	> 8
	Eravacycline	**82.8 (FDA)**	**NA**	**0.25**	**1**	**0.03**	**4**
	Ertapenem	75.7	NA	0.25	4	≤ 0.008	> 8
	Gentamicin	76.9	NA	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	59.6	NA	0.5	> 4	0.015	> 4
	Meropenem	93.7	NA	0.06	0.25	0.015	> 16
	Minocycline	70.6	NA	2	> 16	≤ 0.12	> 16
	Piperacillin Tazobactam	25.9	NA	64	> 128	0.5	> 128
	Tetracycline	55.7	NA	4	> 16	0.5	> 16
	Tigecycline	90.6 (FDA)	NA	0.5	2	0.12	> 8
	Trimethoprim Sulfa	57.7	NA	0.25	> 4	≤ 0.06	> 4
MDR (EUCAST)** Enterobacterales (n=234)	Aztreonam	NA	3.9	> 16	> 16	0.12	> 16
	Cefepime	NA	38.9	2	> 16	0.03	> 16
	Cefotaxime	NA	7.3	> 64	> 64	0.06	> 64
	Ceftazidime	NA	11.5	64	> 128	0.25	> 128
	Ceftazidime-avibactam	NA	97.4	0.5	2	≤ 0.03	> 8
	Ceftriaxone	NA	3.0	> 4	> 4	0.06	> 4
	Colistin	NA	96.2	0.25	0.25	0.12	> 8
	Eravacycline	**NA**	**85.5**	**0.25**	**1**	**0.03**	**4**
	Ertapenem	NA	73.1	0.25	4	≤ 0.008	> 8
	Gentamicin	NA	76.9	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	NA	61.5	0.25	> 4	0.015	> 4
	Meropenem	NA	94.0	0.06	0.25	0.015	> 16
	Minocycline	NA	NB	2	16	≤ 0.12	> 16
	Piperacillin Tazobactam	NA	20.5	64	> 128	0.5	> 128
	Tetracycline	NA	NB	2	> 16	≤ 0.25	> 16
	Tigecycline	NA	74.4	0.5	2	0.12	> 8
	Trimethoprim Sulfa	NA	61.1	0.25	> 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; NA, not applicable; NB, no defined breakpoints; **Number of MDR by CLSI or EUCAST vary due to differing breakpoints.

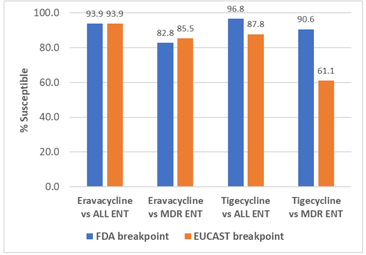

Figure 1. Eravacycline and tigecycline susceptibility against all and MDR Enterobacterales (ENT) by FDA and EUCAST breakpoints.

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

Organism	Drug	%S* CLSI	%S EUCAST	MIC 50	MIC 90	MIN MIC	MAX MIC
Citrobacter freundii (n=94)	Aztreonam	74.5	71.3	0.25	> 16	≤ 0.03	> 16
	Cefepime	91.5	86.2	0.06	2	0.03	> 16
	Cefotaxime	71.3	71.3	0.25	> 64	0.06	> 64
	Ceftazidime	73.4	67.0	0.5	> 128	0.12	> 128
	Ceftazidime-avibactam	100.0	100.0	0.25	0.5	≤ 0.03	2
	Ceftriaxone	72.3	72.3	0.25	> 4	0.06	> 4
	Colistin	0.0	100.0	0.25	0.5	0.06	1
	Eravacycline	**93.6 (FDA)**	**93.6**	**0.25**	**0.5**	**0.06**	**2**
	Ertapenem	95.7	95.7	0.015	0.25	≤ 0.008	> 8
	Gentamicin	86.2	86.2	0.5	16	≤ 0.12	> 16
	Levofloxacin	86.2	86.2	0.12	1	0.015	> 4
	Meropenem	98.9	98.9	0.03	0.06	0.008	> 16
	Minocycline	81.9	NB	2	16	0.5	> 16
	Piperacillin Tazobactam	72.3	72.3	4	128	0.5	> 128
	Tetracycline	77.7	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	100.0 (FDA)	87.2	0.5	1	0.12	2
	Trimethoprim Sulfa	79.8	79.8	≤ 0.06	> 4	≤ 0.06	> 4
Citrobacter koseri (n=72)	Aztreonam	95.8	94.4	0.06	0.25	≤ 0.03	> 16
	Cefepime	98.6	98.6	0.03	0.12	0.015	8
	Cefotaxime	98.6	98.6	0.06	0.5	0.03	> 64
	Ceftazidime	97.2	97.2	0.25	0.5	0.06	32
	Ceftazidime-avibactam	100.0	100.0	0.12	0.25	≤ 0.03	0.5
	Ceftriaxone	95.8	95.8	0.06	0.25	≤ 0.015	> 4
	Colistin	0.0	100.0	0.12	0.25	0.12	0.5
	Eravacycline	**100.0 (FDA)**	**100.0**	**0.12**	**0.25**	**0.12**	**0.5**
	Ertapenem	100.0	100.0	≤ 0.008	0.015	≤ 0.008	0.03
	Gentamicin	95.8	95.8	0.25	0.5	≤ 0.12	> 16
	Levofloxacin	95.8	95.8	0.03	0.25	0.015	1
	Meropenem	100.0	100.0	0.015	0.03	0.015	0.12
	Minocycline	100.0	NB	0.5	2	0.25	4
	Piperacillin Tazobactam	86.1	86.1	2	16	1	64
	Tetracycline	100.0	NB	1	2	0.5	4
	Tigecycline	100.0 (FDA)	100.0	0.25	0.5	0.12	0.5
	Trimethoprim Sulfa	90.3	90.3	≤ 0.06	0.25	≤ 0.06	> 4
Enterobacter cloacae (n=148)	Aztreonam	58.8	55.4	0.25	> 16	≤ 0.03	> 16
	Cefepime	81.8	69.6	0.12	16	0.03	> 16
	Cefotaxime	54.7	54.7	0.5	> 64	0.06	> 64
	Ceftazidime	59.5	55.4	0.5	> 128	0.12	> 128
	Ceftazidime-avibactam	98.0	98.0	0.25	1	0.06	> 8
	Ceftriaxone	56.1	56.1	0.5	> 4	0.06	> 4
	Colistin	0.0	87.2	0.25	> 8	0.12	> 8
	Eravacycline	**84.5 (FDA)**	**84.5**	**0.25**	**1**	**0.03**	**4**
	Ertapenem	74.3	74.3	0.06	2	≤ 0.008	> 8
	Gentamicin	92.6	91.9	0.25	1	≤ 0.12	> 16
	Levofloxacin	85.8	85.8	0.03	2	0.015	> 4
	Meropenem	96.6	97.3	0.03	0.25	0.008	16
	Minocycline	79.1	NB	2	16	≤ 0.12	> 16
	Piperacillin Tazobactam	59.5	59.5	4	> 128	1	> 128
	Tetracycline	81.8	NB	2	16	0.5	> 16
	Tigecycline	91.2 (FDA)	76.4	0.5	2	0.12	> 8
	Trimethoprim Sulfa	81.1	81.1	0.12	> 4	≤ 0.06	> 4
Escherichia coli (n=194)	Aztreonam	82.0	75.8	0.12	> 16	≤ 0.03	> 16
	Cefepime	80.4	79.9	0.06	> 16	0.015	> 16
	Cefotaxime	76.8	76.8	0.12	> 64	≤ 0.015	> 64
	Ceftazidime	83.5	78.4	0.25	32	≤ 0.03	> 128
	Ceftazidime-avibactam	100.0	100.0	0.12	0.25	≤ 0.03	1
	Ceftriaxone	77.8	77.8	0.06	> 4	≤ 0.015	> 4
	Colistin	0.0	100.0	0.25	0.25	0.12	1
	Eravacycline	**99.5 (FDA)**	**99.5**	**0.12**	**0.25**	**≤ 0.015**	**4**
	Ertapenem	99.0	99.0	0.015	0.06	≤ 0.008	4
	Gentamicin	87.6	86.6	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	71.1	71.1	0.03	> 4	≤ 0.004	> 4
	Meropenem	100.0	100.0	0.03	0.03	0.008	0.12
	Minocycline	86.1	NB	1	8	≤ 0.12	> 16
	Piperacillin Tazobactam	90.2	90.2	2	8	≤ 0.25	> 128
	Tetracycline	65.5	NB	1	> 16	≤ 0.25	> 16
	Tigecycline	99.5 (FDA)	97.9	0.12	0.25	0.06	4
	Trimethoprim Sulfa	70.1	70.1	≤ 0.06	> 4	≤ 0.06	> 4
Escherichia coli , ESBL (n=43)	Aztreonam	18.6	2.3	> 16	> 16	0.5	> 16
	Cefepime	11.6	9.3	> 16	> 16	0.5	> 16
	Cefotaxime	2.3	2.3	> 64	> 64	0.12	> 64
	Ceftazidime	25.6	9.3	32	128	1	> 128
	Ceftazidime-avibactam	100.0	100.0	0.25	0.5	≤ 0.03	1
	Ceftriaxone	2.3	2.3	> 4	> 4	0.25	> 4
	Colistin	0.0	100.0	0.25	0.25	0.12	0.5
	Eravacycline	**97.7 (FDA)**	**97.7**	**0.12**	**0.25**	**0.06**	**4**
	Ertapenem	95.4	95.4	0.06	0.25	0.015	4
	Gentamicin	72.1	72.1	1	> 16	0.25	> 16
	Levofloxacin	20.9	20.9	> 4	> 4	0.015	> 4
	Meropenem	100.0	100.0	0.03	0.03	0.015	0.12
	Minocycline	79.1	NB	2	16	0.5	> 16
	Piperacillin Tazobactam	65.1	65.1	4	32	1	> 128
	Tetracycline	34.9	NB	> 16	> 16	1	> 16
	Tigecycline	97.7 (FDA)	95.4	0.25	0.5	0.12	4
	Trimethoprim Sulfa	37.2	37.2	> 4	> 4	≤ 0.06	> 4
Klebsiella aerogenes (n=171)	Aztreonam	73.1	70.8	0.12	> 16	≤ 0.03	> 16
	Cefepime	98.3	95.3	0.06	0.5	0.015	> 16
	Cefotaxime	70.2	70.2	0.12	32	0.03	> 64
	Ceftazidime	71.4	69.0	0.25	64	0.12	> 128
	Ceftazidime-avibactam	100.0	100.0	0.25	0.5	≤ 0.03	1
	Ceftriaxone	70.8	70.8	0.25	> 4	≤ 0.015	> 4
	Colistin	0.0	99.4	0.25	0.25	≤ 0.03	8
	Eravacycline	**95.9 (FDA)**	**95.9**	**0.25**	**0.25**	**0.03**	**2**
	Ertapenem	95.3	95.3	0.06	0.5	≤ 0.008	4
	Gentamicin	99.4	99.4	0.25	0.5	≤ 0.12	> 16
	Levofloxacin	98.3	98.3	0.06	0.12	0.015	2
	Meropenem	100.0	100.0	0.03	0.06	0.008	0.5
	Minocycline	95.3	NB	1	2	≤ 0.12	> 16
	Piperacillin Tazobactam	69.0	69.0	4	64	≤ 0.25	128
	Tetracycline	93.6	NB	1	4	≤ 0.25	> 16
	Tigecycline	97.7 (FDA)	86.0	0.5	1	0.12	4
	Trimethoprim Sulfa	99.4	99.4	≤ 0.06	0.25	≤ 0.06	> 4
Klebsiella oxytoca (n=195)	Aztreonam	85.6	81.5	0.25	> 16	≤ 0.03	> 16
	Cefepime	94.4	92.3	0.03	1	0.015	> 16
	Cefotaxime	90.3	90.3	0.06	1	≤ 0.015	> 64
	Ceftazidime	94.9	93.9	0.12	1	0.06	> 128
	Ceftazidime-avibactam	100.0	100.0	0.12	0.25	≤ 0.03	4
	Ceftriaxone	84.1	84.1	0.12	> 4	≤ 0.015	> 4
	Colistin	0.0	100.0	0.25	0.25	0.12	2
	Eravacycline	**98.0 (FDA)**	**98.0**	**0.12**	**0.25**	**0.12**	**2**
	Ertapenem	98.5	98.5	0.015	0.03	≤ 0.008	> 8
	Gentamicin	95.9	95.9	0.25	0.5	≤ 0.12	> 16
	Levofloxacin	96.4	96.4	0.03	0.25	0.015	> 4
	Meropenem	98.5	98.5	0.03	0.03	0.015	> 16
	Minocycline	95.9	NB	1	4	0.25	16
	Piperacillin Tazobactam	83.6	83.6	2	> 128	≤ 0.25	> 128
	Tetracycline	92.8	NB	0.5	2	≤ 0.25	> 16
	Tigecycline	99.5 (FDA)	93.3	0.25	0.5	0.12	4
	Trimethoprim Sulfa	92.8	92.8	≤ 0.06	0.25	≤ 0.06	> 4
Klebsiella oxytoca , ESBL (n=15)	Aztreonam	6.7	0.0	> 16	> 16	2	> 16
	Cefepime	46.7	26.7	4	> 16	1	> 16
	Cefotaxime	0.0	0.0	8	> 64	2	> 64
	Ceftazidime	60.0	53.3	1	32	0.25	> 128
	Ceftazidime-avibactam	100.0	100.0	0.12	0.5	0.06	4
	Ceftriaxone	0.0	0.0	> 4	> 4	> 4	> 4
	Colistin	0.0	100.0	0.25	0.25	0.12	1
	Eravacycline	**93.3 (FDA)**	**93.3**	**0.12**	**0.25**	**0.12**	**1**
	Ertapenem	100.0	100.0	0.03	0.06	0.015	0.12
	Gentamicin	53.3	53.3	0.5	> 16	≤ 0.12	> 16
	Levofloxacin	93.3	93.3	0.25	0.5	0.03	4
	Meropenem	100.0	100.0	0.03	0.06	0.03	0.06
	Minocycline	93.3	NB	1	4	0.5	8
	Piperacillin Tazobactam	26.7	26.7	128	> 128	1	> 128
	Tetracycline	53.3	NB	1	> 16	0.5	> 16
	Tigecycline	100.0 (FDA)	86.7	0.25	1	0.25	2
	Trimethoprim Sulfa	53.3	53.3	0.12	> 4	≤ 0.06	> 4
Klebsiella pneumoniae (n=199)	Aztreonam	86.4	84.4	0.06	> 16	≤ 0.03	> 16
	Cefepime	84.9	83.9	0.06	> 16	≤ 0.008	> 16
	Cefotaxime	82.9	82.9	0.06	> 64	≤ 0.015	> 64
	Ceftazidime	86.4	82.4	0.25	32	0.06	> 128
	Ceftazidime-avibactam	98.5	98.5	0.12	0.5	≤ 0.03	> 8
	Ceftriaxone	83.4	83.4	0.06	> 4	≤ 0.015	> 4
	Colistin	0.0	99.5	0.25	0.25	0.12	8
	Eravacycline	**87.9 (FDA)**	**87.9**	**0.25**	**1**	**0.12**	**4**
	Ertapenem	96.0	96.0	0.015	0.12	≤ 0.008	> 8
	Gentamicin	94.0	93.5	0.25	0.5	≤ 0.12	> 16
	Levofloxacin	85.4	85.4	0.06	4	0.015	> 4
	Meropenem	96.5	97.0	0.03	0.06	0.015	> 16
	Minocycline	79.9	NB	2	> 16	≤ 0.12	> 16
	Piperacillin Tazobactam	81.4	81.4	4	128	0.5	> 128
	Tetracycline	76.4	NB	1	> 16	0.5	> 16
	Tigecycline	92.5 (FDA)	78.4	0.5	2	0.12	8
	Trimethoprim Sulfa	84.9	84.9	0.12	> 4	≤ 0.06	> 4
Klebsiella pneumoniae , ESBL (n=31)	Aztreonam	25.8	12.9	> 16	> 16	0.25	> 16
	Cefepime	19.4	12.9	> 16	> 16	0.5	> 16
	Cefotaxime	9.7	9.7	> 64	> 64	0.06	> 64
	Ceftazidime	32.3	9.7	32	> 128	0.5	> 128
	Ceftazidime-avibactam	100.0	100.0	0.25	1	≤ 0.03	2
	Ceftriaxone	9.7	9.7	> 4	> 4	0.25	> 4
	Colistin	0.0	96.8	0.25	0.25	0.12	8
	Eravacycline	**77.4 (FDA)**	**77.4**	**0.25**	**2**	**0.12**	**4**
	Ertapenem	90.3	90.3	0.06	0.5	0.015	> 8
	Gentamicin	71.0	67.7	0.25	> 16	0.25	> 16
	Levofloxacin	48.4	48.4	1	> 4	0.03	> 4
	Meropenem	93.6	96.8	0.03	0.12	0.03	> 16
	Minocycline	61.3	NB	2	> 16	0.5	> 16
	Piperacillin Tazobactam	45.2	45.2	16	> 128	1	> 128
	Tetracycline	35.5	NB	> 16	> 16	1	> 16
	Tigecycline	83.9 (FDA)	61.3	0.5	4	0.25	8
	Trimethoprim Sulfa	25.8	25.8	> 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.

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

Organism	Drug	%S* CLSI	%S EUCAST	MIC 50	MIC 90	MIN MIC	MAX MIC
Acinetobacter baumannii (n=122)	Amikacin	65.6	64.8	4	> 64	1	> 64
	Ampicillin Sulbactam	44.3	NB	16	64	≤ 1	> 64
	Aztreonam	NB	NB	64	> 64	2	> 64
	Cefepime	44.3	NB	32	> 64	≤ 0.25	> 64
	Ceftazidime	46.7	NB	16	> 64	1	> 64
	Ceftriaxone	12.3	NB	64	> 64	2	> 64
	Colistin	0.0	99.2	0.5	1	0.25	> 8
	Eravacycline	**NB**	**NB**	**0.5**	**2**	**0.03**	**2**
	Gentamicin	61.5	61.5	2	> 16	0.25	> 16
	Levofloxacin	46.7	45.1	4	32	≤ 0.12	> 32
	Meropenem	50.8	50.8	2	> 16	≤ 0.12	> 16
	Minocycline	65.6	NB	0.5	16	≤ 0.12	32
	Piperacillin Tazobactam	40.2	NB	128	> 128	≤ 0.12	> 128
	Tetracycline	41.0	NB	16	> 32	1	> 32
	Tigecycline	NB	NB	2	> 4	≤ 0.015	> 4
	Trimethoprim Sulfa	65.6	65.6	0.5	> 32	≤ 0.06	> 32
CRAB (CLSI) (n=59)	Amikacin	35.6	NA	> 64	> 64	1	> 64
	Ampicillin Sulbactam	3.4	NA	64	> 64	2	> 64
	Aztreonam	NB	NA	> 64	> 64	32	> 64
	Cefepime	3.4	NA	> 64	> 64	4	> 64
	Ceftazidime	8.5	NA	> 64	> 64	4	> 64
	Ceftriaxone	0.0	NA	> 64	> 64	16	> 64
	Colistin	0.0	NA	0.5	0.5	0.25	> 8
	Eravacycline	**NB**	**NA**	**1**	**2**	**0.25**	**2**
	Gentamicin	37.3	NA	> 16	> 16	0.25	> 16
	Levofloxacin	3.4	NA	16	> 32	≤ 0.12	> 32
	Meropenem	0.0	NA	> 16	> 16	8	> 16
	Minocycline	42.4	NA	8	16	0.25	32
	Piperacillin Tazobactam	1.7	NA	> 128	> 128	8	> 128
	Tetracycline	0.0	NA	> 32	> 32	8	> 32
	Tigecycline	NB	NA	4	> 4	0.5	> 4
	Trimethoprim Sulfa	40.7	NA	32	> 32	≤ 0.06	> 32
CRAB (EUCAST) (n=58)	Amikacin	NA	34.5	> 64	> 64	1	> 64
	Ampicillin Sulbactam	NA	NB	64	> 64	8	> 64
	Aztreonam	NA	NB	> 64	> 64	32	> 64
	Cefepime	NA	NB	> 64	> 64	8	> 64
	Ceftazidime	NA	NB	> 64	> 64	4	> 64
	Ceftriaxone	NA	NB	> 64	> 64	16	> 64
	Colistin	NA	100.0	0.5	0.5	0.25	1
	Eravacycline	**NA**	**NB**	**1**	**2**	**0.25**	**2**
	Gentamicin	NA	36.2	> 16	> 16	0.25	> 16
	Levofloxacin	NA	1.7	16	> 32	0.25	> 32
	Meropenem	NA	0.0	> 16	> 16	> 16	> 16
	Minocycline	NA	NB	8	16	0.25	32
	Piperacillin Tazobactam	NA	NB	> 128	> 128	8	> 128
	Tetracycline	NA	NB	> 32	> 32	8	> 32
	Tigecycline	NA	NB	4	> 4	0.5	> 4
	Trimethoprim Sulfa	NA	39.7	32	> 32	≤ 0.06	> 32
Stenotrophomonas maltophilia (n=35)	Amikacin	NB	NB	64	> 64	4	> 64
	Ampicillin Sulbactam	NB	NB	> 64	> 64	16	> 64
	Aztreonam	NB	NB	> 64	> 64	4	> 64
	Cefepime	NB	NB	32	> 64	2	> 64
	Ceftazidime	31.4	NB	32	> 64	2	> 64
	Ceftriaxone	NB	NB	> 64	> 64	32	> 64
	Colistin	NB	NB	1	4	≤ 0.12	> 8
	Eravacycline	**NB**	**NB**	**0.5**	**4**	**0.25**	**4**
	Gentamicin	NB	NB	16	> 16	1	> 16
	Levofloxacin	71.4	NB	1	16	0.5	32
	Meropenem	NB	NB	> 16	> 16	8	> 16
	Minocycline	100.0	NB	0.5	2	≤ 0.12	4
	Piperacillin Tazobactam	NB	NB	128	> 128	8	> 128
	Tetracycline	NB	NB	16	32	8	> 32
	Tigecycline	NB	NB	1	4	0.03	> 4
	Trimethoprim Sulfa	94.3	0.0	0.25	2	≤ 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; NA, not applicable; NB, no defined breakpoints.

Table 4. Susceptibility of combined Enterobacterales from the USA to Eravacycline by year of collection.

Year	2015	2016	2017	2018	2019	2020
ERV % susceptibility	92.4	94.2	93.9	92.9	92.6	93.9

Results 2

Although there are no clinical breakpoints for *Stenotrophomonas maltophilia* or carbapenem-resistant *A. baumannii*, ERV exhibited promising activity against these species. Unlike ERV, the susceptibility of Enterobacterales to tigecycline was higher using older FDA breakpoints than the up-to-date EUCAST breakpoints, especially against MDR isolates (Fig.1).

Conclusions

ERV exhibited sustained high susceptibility against multiple Enterobacterales species, including MDR and ESBL-positive isolates. While EUCAST breakpoints are not defined for *S. maltophilia* or CRAB, ERV demonstrated promising activity against these species.

Taken together, these results show that, after more than 2 years in clinical use in the USA, ERV remains highly active against the majority of Gram-negative pathogens studied.

These data also highlight that FDA breakpoints for tigecycline against Enterobacterales need urgent review to avoid potential false reporting of tigecycline susceptibility. In contrast, ERV FDA breakpoints are in keeping with those published by EUCAST and can be used to predict the clinical outcome of ERV treatment.

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