Poster #1820

In vitro global surveillance of eravacycline and comparators against *Staphylococcus* spp. and *Enterococcus* spp. over a three-year period (2013-15)

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Abstract

Background: Eravacycline (ERV) is a novel, fully-synthetic fluorocycline antibiotic of the tetracycline class being developed for the treatment of serious infections, including those caused by multidrug-resistant (MDR) pathogens. As methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) have been designated as serious public threats by the CDC, the purpose of this study was to evaluate the activity of ERV and comparators against global isolates of *Staphylococcus* spp. and *Enterococcus* spp. collected from 2013-15.

Materials/methods: Clinical isolates were collected from various body sites in patients in hospitals worldwide from 2013-15. MIC results for ERV and comparators were determined by CLSI broth microdilution.

Results: ERV and comparator MIC results are shown in the table below. MIC_{90} values for the organisms did not vary more than one dilution over the 3-year time range.

Organism	ERV			TGC			VAN		
	N	$MIC_{50/90}$	MIC Range	N	$MIC_{50/90}$	MIC Range	N	$MIC_{50/90}$	MIC Range
Enterococcus faecalis	919	0.06/0.06	0.008-0.5	919	0.12/0.25	≤ 0.015-8	915	1/2	0.12->32
VR *E. faecalis*	35	0.06/0.12	0.03/0.25	35	0.12/0.25	0.06-0.5	35	>32/>32	>16->32
Enterococcus faecium	696	0.03/0.06	0.008-1	696	0.12/0.12	0.03-8	694	1/>32	≤ 0.12->32
VR *E. faecium*	310	0.06/0.06	0.008-1	310	0.12/0.25	0.03-4	310	>32/>32	>16->32
Staphylococcus aureus	1512	0.06/0.12	≤ 0.008-1	1512	0.12/0.25	0.03-1	532	1/1	≤ 0.25-2
MRSA	756	0.06/0.12	0.015-1	756	0.12/0.25	0.03-1	263	1/1	<=0.25-2
Staphylococcus epidermidis	483	0.12/0.5	≤ 0.008-1	483	0.25/0.5	≤ 0.015-1	206	2/2	0.5-2
Staphylococcus haemolyticus	305	0.12/0.5	0.015-2	305	0.25/0.5	0.03-1	148	2/2	0.5-4

$MIC_{50/90}$, minimum inhibitory concentration required to inhibit growth of 50/90% of isolates (mg/L); VR, vancomycin-resistant; TGC, tigecycline; VAN, vancomycin

Conclusion: Eravacycline demonstrated consistent and potent *in vitro* activity against a global collection of *Staphylococcus* spp. and *Enterococcus* spp., including resistant strains, over a recent 3-year time period (2013-2015). The *in vitro* potency for ERV against these organisms was up to 4-fold greater than TGC and a minimum of 8-fold greater than VAN.

Introduction

The Gram-positive organisms *Staphylococcus aureus*, *Enterococcus* spp. and coagulase-negative staphylococci are important pathogens in the hospital setting, accounting for 41% of all pathogens causing healthcare-associated infections.[1] Antibiotic resistance has increased in these organisms, and methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) have been designated as serious public threats by the CDC.[2] Together, MRSA and VRE are leading causes of healthcare-associated infections in the US, resulting in ~12,000 deaths per year.[2,3]

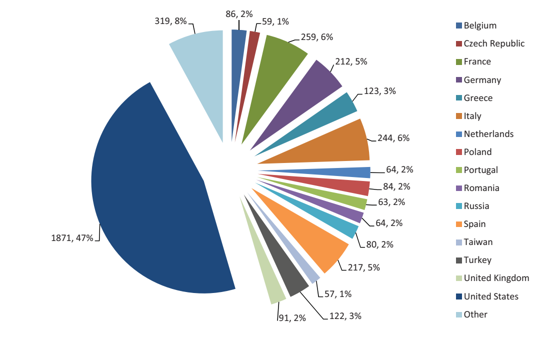
Eravacycline (ERV) is a novel, fully-synthetic fluorocycline antibiotic of the tetracycline class being developed for the treatment of serious infections, including those caused by multidrug-resistant (MDR) pathogens. ERV is in phase 3 clinical development for the treatment of complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI), including pyelonephritis.

The purpose of this study was to evaluate the activity of ERV and comparators against global isolates of *Staphylococcus* spp. and *Enterococcus* spp. collected over a three-year surveillance period (from 2013-2015).

Methods

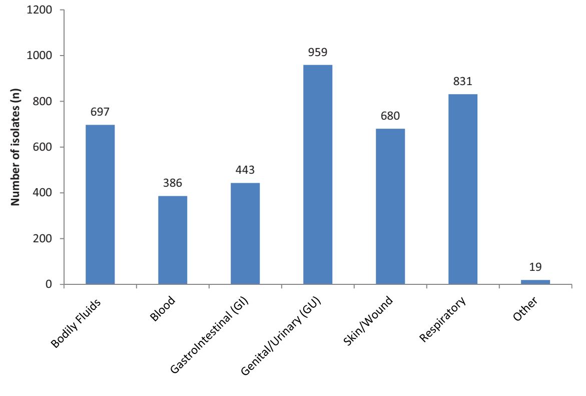
- A total of 4,015 clinical isolates, collected from various body sites from 2013-2015 from 205 hospitals, were tested. Breakdowns by country and site of infection are given in Figures 1 and 2, respectively.
- Minimal inhibitory concentration (MIC) endpoints were determined by broth microdilution according to CLSI guidelines.[4]
- Quality control testing was performed each day of testing as specified by the CLSI using *Enterococcus faecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 29213.
- Antibiotic susceptibility was determined using CLSI 2015 breakpoints[5], with the exception of tigecycline where FDA breakpoints were used.[6]

Figure 1. Isolate counts (n, %) by country of origin for the 4,015 isolates collected from 2013-2015



Countries included as “Other” (Australia, Austria, Croatia, Denmark, Hong Kong, Hungary, Ireland, Japan, S. Korea, Malaysia, Pakistan, Philippines, Singapore, Switzerland, and Thailand) had less than 45 isolates each.

Figure 2. Isolate counts by source of infection for the 4,015 isolates collected from 2013-2015



Other includes HEENT (Head, Eyes, Ears, Nose, and Throat), Instruments (Catheters/Drains/Tubes), Bone and Reproductive Site

Results

- Clinical isolates were from diverse geographic locations, with 47% from countries within North America (specifically, the United States), 47% from within Europe, 5% from within Asia, and 1% from within the South Pacific (Fig. 1).
- Most isolates were collected from GU, respiratory, bodily fluid and skin/wound infection sources followed by GI and blood (Fig. 2).
- Tables 1 and 2 show MIC values for staphylococci and enterococci, respectively.
  - ERV MIC_{90} values for the organisms did not vary more than one dilution over the 3-year time range.
- Cumulative MIC distribution patterns for MRSA and VRE organisms were similar for each of the three years, with some differences observed in the 0.015-0.06 mg/L MIC range.
- The *in vitro* activity (as measured by MIC_{90} values) for ERV against *S. aureus*, including MRSA, was up to 4-fold more potent than tigecycline and primarily 4-fold more potent than minocycline. ERV showed up to 4-fold greater activity than tigecycline, >64-fold greater activity than minocycline, and a minimum of 8-fold greater activity than vancomycin against tested enterococci, including VRE.

Figure 3. MIC distribution (Cumulative %) for ERV against 756 MRSA and 345 VRE (including VR *E. faecium* and VR *E. faecalis*)

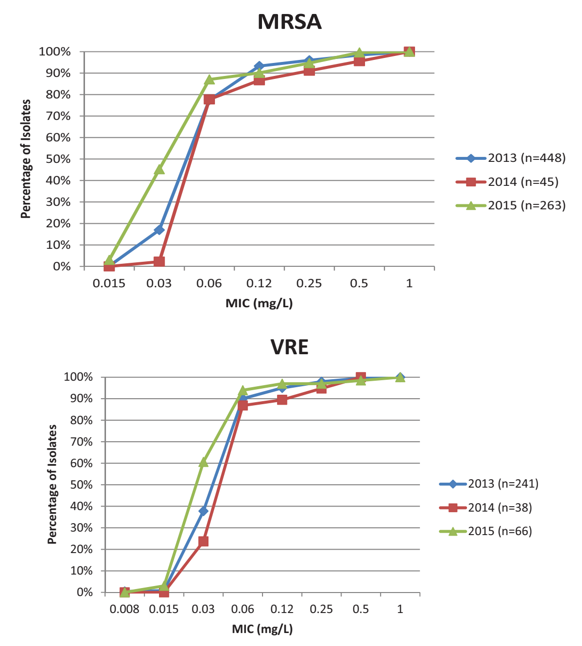


Table 1. Antimicrobial activity of ERV and comparator agents against *Staphylococcus* spp., including resistant isolates, from 2013-2015

Antimicrobial Agent	2013 MIC (mg/L) MIC_{50}	2013 MIC_{90}	2013 Range Min	2013 Range Max	2013 %S	2013 %I	2013 %R	2014 MIC (mg/L) MIC_{50}	2014 MIC_{90}	2014 Range Min	2014 Range Max	2014 %S	2014 %I	2014 %R	2015 MIC (mg/L) MIC_{50}	2015 MIC_{90}	2015 Range Min	2015 Range Max	2015 %S	2015 %I	2015 %R
	S. aureus (871)							*S. aureus* (109)							*S. aureus* (532)						
Amoxicillin Clavulanate	2	16	≤ 0.12	> 16	--	--	--	2	16	0.25	> 16	--	--	--	> 1	> 1	0.25	> 1	--	--	--
Azithromycin	> 8	> 8	0.25	> 8	43.5%	0.3%	56.1%	> 8	> 8	0.5	> 8	43.1%	0%	56.9%	1	> 4	≤ 0.25	> 4	52.6%	0.2%	47.2%
Ceftriaxone	16	> 64	1	> 64	--	--	--	8	> 64	2	> 64	--	--	--							
Daptomycin	0.5	1	0.25	4	99.5%	--	--	0.5	1	0.25	4	99.1%	--	--	0.25	0.5	0.12	2	99.8%	--	--
Eravacycline	0.06	0.12	0.015	1	--	--	--	0.06	0.12	0.03	1	--	--	--	0.06	0.06	≤ 0.008	1	--	--	--
Levofloxacin	0.5	> 8	≤ 0.03	> 8	65.3%	0%	34.7%	0.5	> 8	0.12	> 8	66.1%	0%	33.9%	0.25	> 4	0.06	> 4	57.9%	0.8%	41.4%
Linezolid	2	2	≤ 0.5	2	100%	--	0%	2	2	1	2	100%	--	0%	1	2	≤ 0.5	2	100%	--	0%
Minocycline	0.12	0.25	≤ 0.03	> 8	96.2%	1.7%	2.1%	0.12	0.25	≤ 0.03	8	99.1%	0.9%	0%	0.12	0.25	≤ 0.06	> 8	96.2%	1.9%	1.9%
Penicillin	> 8	> 8	≤ 0.12	> 8	12.6%	--	87.4%	> 8	> 8	≤ 0.12	> 8	7.3%	--	92.7%	> 2	> 2	≤ 0.12	> 2	14.1%	--	85.9%
Tetracycline	0.5	16	≤ 0.06	> 32	89.2%	0.7%	10.1%	0.5	8	0.12	> 32	89.9%	0.9%	9.2%	0.25	16	≤ 0.06	> 16	88.9%	0.4%	10.7%
Tigecycline	0.12	0.25	0.03	1	99.1%	--	0.9%	0.12	0.25	0.06	1	99.1%	--	0.9%	0.12	0.25	0.06	1	99.1%	--	0.9%
	MRSA (448)							MRSA (45)							MRSA (263)						
Amoxicillin Clavulanate	8	16	1	> 16	--	--	--	8	16	1	> 16	--	--	--	> 1	> 1	1	> 1	--	--	--
Azithromycin	> 8	> 8	0.5	> 8	19%	0%	81%	> 8	> 8	0.5	> 8	13.3%	0%	86.7%	> 4	> 4	≤ 0.25	> 4	24.3%	0.4%	75.3%
Ceftriaxone	> 64	> 64	4	> 64	--	--	--	> 64	> 64	4	> 64	--	--	--							
Daptomycin	1	1	0.25	4	99.3%	--	--	0.5	1	0.25	4	97.8%	--	--	0.25	0.5	0.12	2	99.6%	--	--
Eravacycline	0.06	0.12	0.015	1	--	--	--	0.06	0.25	0.03	1	--	--	--	0.06	0.12	0.015	1	--	--	--
Levofloxacin	8	> 8	0.12	> 8	43.8%	0%	56.3%	8	> 8	0.25	> 8	33.3%	0%	66.7%	> 4	> 4	0.06	> 4	22.4%	1.5%	76.1%
Linezolid	2	2	1	2	100%	--	0%	2	2	1	2	100%	--	0%	1	2	≤ 0.5	2	100%	--	0%
Minocycline	0.12	0.25	≤ 0.03	> 8	94.6%	2.7%	2.7%	0.12	0.5	≤ 0.03	8	97.8%	2.2%	0%	0.12	4	≤ 0.06	> 8	92.4%	3.8%	3.8%
Penicillin	> 8	> 8	0.5	> 8	0%	--	100%	> 8	> 8	0.25	> 8	0%	--	100%	> 2	> 2	≤ 0.12	> 2	0.8%	--	99.2%
Tetracycline	0.5	32	0.12	> 32	85.9%	0.2%	13.8%	0.5	32	0.12	> 32	88.9%	0%	11.1%	0.25	> 16	≤ 0.06	> 16	83.7%	0.4%	16.0%
Tigecycline	0.12	0.25	0.03	1	98.2%	--	1.8%	0.12	0.5	0.06	1	97.8%	--	2.2%	0.12	0.25	0.06	1	98.1%	--	1.9%
	S. epidermidis (252)							*S. epidermidis* (25)							*S. epidermidis* (206)						
Amoxicillin Clavulanate	2	16	≤ 0.12	> 16	--	--	--	2	8	0.5	16	--	--	--	> 1	> 1	≤ 0.06	> 1	--	--	--
Azithromycin	> 8	> 8	≤ 0.12	> 8	34.1%	0.4%	65.5%	> 8	> 8	0.25	> 8	28%	0%	72%	> 4	> 4	≤ 0.25	> 4	39.8%	0%	60.2%
Ceftriaxone	16	> 64	≤ 0.5	> 64	--	--	--	16	64	≤ 0.5	> 64	--	--	--							
Daptomycin	1	1	0.25	4	98.0%	--	--	0.5	1	0.5	1	100%	--	--	0.5	0.5	≤ 0.06	1	100%	--	--
Eravacycline	0.25	0.5	0.015	1	--	--	--	0.25	0.5	0.06	0.5	--	--	--	0.12	0.25	≤ 0.008	1	--	--	--
Levofloxacin	4	> 8	0.12	> 8	46.8%	0.8%	52.4%	8	> 8	0.25	> 8	36%	0%	64%	2	> 4	0.12	> 4	42.7%	10.7%	46.6%
Linezolid	1	2	≤ 0.5	> 8	98.8%	--	1.2%	2	2	1	2	100%	--	0%	≤ 0.5	1	≤ 0.5	> 4	99%	--	1%
Minocycline	0.25	0.5	≤ 0.03	1	100%	0%	0%	0.25	0.5	0.06	> 8	96%	0%	4%	0.25	0.5	≤ 0.06	4	100%	0%	0%
Penicillin	4	> 8	≤ 0.12	> 8	11.5%	--	88.5%	4	> 8	≤ 0.12	> 8	8%	--	92%	> 2	> 2	≤ 0.12	> 2	9.7%	--	90.3%
Tetracycline	2	> 32	0.12	> 32	82.1%	1.6%	16.3%	2	8	0.25	> 32	88%	4%	8%	1	16	≤ 0.06	> 16	87.4%	2.4%	10.2%
Tigecycline	0.25	0.5	0.03	1	92.9%	--	7.1%	0.25	0.5	0.06	1	96%	--	4.0%	0.12	0.25	≤ 0.015	0.5	100%	--	0%
	MRSE (166)							MRSE (15)													
Amoxicillin Clavulanate	2	16	≤ 0.12	> 16	--	--	--	2	8	2	8	--	--	--							
Azithromycin	> 8	> 8	≤ 0.12	> 8	24.7%	0.6%	74.7%	> 8	> 8	0.5	> 8	20%	0%	80%							
Ceftriaxone	16	> 64	≤ 0.5	> 64	--	--	--	32	64	8	64	--	--	--							
Daptomycin	0.5	1	0.25	4	97.6%	--	--	0.5	1	0.5	1	100%	--	--							
Eravacycline	0.25	0.5	0.015	1	--	--	--	0.25	0.5	0.06	0.5	--	--	--							
Levofloxacin	8	> 8	0.25	> 8	31.9%	1.2%	66.9%	8	> 8	0.25	> 8	20%	0%	80%							
Linezolid	1	2	≤ 0.5	> 8	98.2%	--	1.8%	2	2	1	2	100%	--	0%							
Minocycline	0.25	0.5	≤ 0.03	1	100%	0%	0%	0.25	0.5	0.06	> 8	93.3%	0%	6.7%							
Penicillin	8	> 8	≤ 0.12	> 8	1.2%	--	98.8%	4	> 8	1	> 8	0%	--	100%							
Tetracycline	2	> 32	0.12	> 32	80.7%	2.4%	16.9%	2	32	0.25	> 32	80%	6.7%	13.3%							
Tigecycline	0.25	0.5	0.03	1	94.0%	--	6.0%	0.5	0.5	0.12	1	93.3%	--	6.7%							
	S. haemolyticus (123)							*S. haemolyticus* (34)							*S. haemolyticus* (148)						
Amoxicillin Clavulanate	16	> 16	≤ 0.12	> 16	--	--	--	8	> 16	1	> 16	--	--	--	> 1	> 1	0.12	> 1	--	--	--
Azithromycin	> 8	> 8	≤ 0.12	> 8	20.3%	0%	79.7%	> 8	> 8	0.25	> 8	23.5%	0%	76.5%	> 4	> 4	≤ 0.25	> 4	18.2%	0%	81.8%
Ceftriaxone	> 64	> 64	1	> 64	--	--	--	> 64	> 64	4	> 64	--	--	--							
Daptomycin	0.5	0.5	0.12	2	99.2%	--	--	0.25	0.5	0.12	1	100%	--	--	0.5	0.5	0.12	1	100%	--	--
Eravacycline	0.25	0.5	0.015	1	--	--	--	0.12	0.25	0.03	0.5	--	--	--	0.12	0.5	0.015	2	--	--	--
Levofloxacin	8	> 8	0.06	> 8	23.6%	0%	76.4%	8	> 8	0.12	> 8	32.4%	0%	67.7%	> 4	> 4	0.06	> 4	21.0%	0.7%	78.4%
Linezolid	2	2	≤ 0.5	> 8	99.2%	--	0.8%	1	2	1	2	100%	--	0%	1	1	≤ 0.5	2	100%	--	0%
Minocycline	0.25	0.5	≤ 0.03	8	99.2%	0.8%	0%	0.25	0.25	0.06	2	100%	0%	0%	0.25	0.25	≤ 0.06	1	100%	0%	0%
Penicillin	> 8	> 8	≤ 0.12	> 8	9.8%	--	90.2%	> 8	> 8	≤ 0.12	> 8	20.6%	--	79.4%	> 2	> 2	≤ 0.12	> 2	14.2%	--	85.8%
Tetracycline	1	> 32	≤ 0.06	> 32	76.4%	0%	23.6%	1	32	0.25	> 32	88.2%	0%	11.8%	1	> 16	0.12	> 16	81.8%	0%	18.2%
Tigecycline	0.25	0.5	0.03	1	92.7%	--	7.3%	0.25	0.5	0.12	1	97.1%	--	2.9%	0.25	0.5	0.06	1	99.3%	--	0.7%
	S. hemolyticus, MR (58)							*S. hemolyticus*, MR (1)													
Amoxicillin Clavulanate	> 16	> 16	0.5	> 16	--	--	--	> 16	> 16	> 16	> 16	--	--	--							
Azithromycin	> 8	> 8	≤ 0.12	> 8	22.4%	0%	77.6%	> 8	> 8	> 8	> 8	0%	0%	100%							
Ceftriaxone	> 64	> 64	4	> 64	--	--	--	> 64	> 64	> 64	> 64	--	--	--							
Daptomycin	0.5	0.5	0.12	1	100%	--	--	0.5	0.5	0.5	0.5	100%	--	--							
Eravacycline	0.12	0.5	0.015	1	--	--	--	0.06	0.06	0.06	0.06	--	--	--							
Levofloxacin	> 8	> 8	0.06	> 8	20.7%	0%	79.3%	0.5	0.5	0.5	0.5	100%	0%	0%							
Linezolid	1	2	≤ 0.5	> 8	98.3%	--	1.7%	2	2	2	2	100%	--	0%							
Minocycline	0.25	0.5	≤ 0.03	0.5	100%	0%	0%	2	2	2	2	100%	0%	0%							
Penicillin	> 8	> 8	≤ 0.12	> 8	3.5%	--	96.6%	0.5	0.5	0.5	0.5	0%	--	100%							
Tetracycline	1	> 32	≤ 0.06	> 32	69%	0%	31%	0.25	0.25	0.25	0.25	100%	0%	0%							
Tigecycline	0.25	0.5	0.03	1	93.1%	--	6.9%	0.25	0.25	0.25	0.25	100%	--	0%							

MR, methicillin-resistant, MRSA, methicillin-resistant *S. aureus*, MRSE, methicillin-resistant *S. epidermidis*, “—”represents lack of an established breakpoint. There were no MRSE nor MR *S. hemolyticus* isolates for 2015.

Table 2. Antimicrobial activity of ERV and comparator agents against *Enterococcus* spp., including resistant strains, from 2013-2015

Antimicrobial Agent	2013 MIC (mg/L) MIC_{50}	2013 MIC_{90}	2013 Range Min	2013 Range Max	2013 %S	2013 %I	2013 %R	2014 MIC (mg/L) MIC_{50}	2014 MIC_{90}	2014 Range Min	2014 Range Max	2014 %S	2014 %I	2014 %R	2015 MIC (mg/L) MIC_{50}	2015 MIC_{90}	2015 Range Min	2015 Range Max	2015 %S	2015 %I	2015 %R
	E. faecalis (433)							*E. faecalis* (68)							*E. faecalis* (418)						
Amoxicillin Clavulanate	1	2	≤ 0.12	> 16	--	--	--	1	1	0.25	2	--	--	--	1	1	≤ 0.12	> 1	--	--	--
Azithromycin	> 8	> 8	≤ 0.12	> 8	--	--	--	> 8	> 8	0.5	> 8	--	--	--							
Ceftriaxone	> 64	> 64	≤ 0.5	> 64	--	--	--	> 64	> 64	2	> 64	--	--	--							
Daptomycin	2	4	≤ 0.06	> 4	99.3%	--	--	2	4	≤ 0.06	4	100%	--	--	1	2	0.06	8	99.8%	--	--
Eravacycline	0.06	0.06	0.008	0.5	--	--	--	0.06	0.12	0.015	0.12	--	--	--	0.06	0.06	0.008	0.5	--	--	--
Levofloxacin	2	> 8	≤ 0.03	> 8	67.9%	0.5%	31.6%	2	> 8	0.5	> 8	55.9%	1.5%	42.7%	1	> 8	0.25	> 8	70.6%	0.2%	29.2%
Linezolid	2	2	≤ 0.5	4	99.3%	0.7%	0%	2	2	1	4	98.5%	1.5%	0%	1	1	0.25	4	99.8%	0.2%	0%
Minocycline	8	> 8	≤ 0.03	> 8	31.9%	18.2%	49.9%	8	> 8	0.06	> 8	27.9%	25%	47.1%	8	> 8	≤ 0.03	> 8	31.1%	39.5%	29.4%
Penicillin	2	4	≤ 0.12	> 8	98.9%	--	1.2%	2	4	0.5	8	100%	--	0%	2	4	0.5	> 8	96.7%	--	3.4%
Tetracycline	> 32	> 32	0.12	> 32	26.6%	0.9%	72.5%	32	> 32	0.25	> 32	17.7%		82.4%	> 32	> 32	≤ 0.06	> 32	21.3%	0.2%	78.5%
Tigecycline	0.12	0.25	≤ 0.015	1	97.5%	--	--	0.12	0.25	≤ 0.015	0.25	100%	--	--	0.12	0.25	0.015	8	99%	--	--
Vancomycin	1	2	0.12	> 32	92.5%	3%	4.4%	1	4	1	> 32	91.2%		8.8%	1	2	0.5	> 16	97.4%	0.2%	2.4%
	E. faecalis, VR (19)							*E. faecalis*, VR (6)							*E. faecalis*, VR (10)						
Amoxicillin Clavulanate	1	2	0.5	> 16	--	--	--	1	1	1	1	--	--	--	1	1	0.5	1	--	--	--
Azithromycin	> 8	> 8	2	> 8	--	--	--	> 8	> 8	4	> 8	--	--	--							
Ceftriaxone	> 64	> 64	4	> 64	--	--	--	> 64	> 64	> 64	> 64	--	--	--							
Daptomycin	2	2	1	4	100%	--	--	2	4	0.5	4	100%	--	--	1	2	1	2	100%	--	--
Eravacycline	0.06	0.12	0.03	0.25	--	--	--	0.06	0.12	0.03	0.12	--	--	--	0.06	0.06	0.03	0.06	--	--	--
Levofloxacin	> 8	> 8	> 8	> 8	0%	0%	100%	> 8	> 8	> 8	> 8	0%	0%	100%	> 8	> 8	0.5	> 8	30%	0%	70%
Linezolid	2	2	1	2	100%	0%	0%	2	2	2	2	100%	0%	0%	1	1	1	1	100%	0%	0%
Minocycline	> 8	> 8	0.06	> 8	26.3%	21.1%	52.6%	> 8	> 8	4	> 8	16.7%	16.7%	66.7%	> 8	> 8	0.06	> 8	20%	20%	60%
Penicillin	4	8	1	> 8	94.7%	--	5.3%	4	8	2	8	100%	--	0%	4	4	2	8	100%	--	0%
Tetracycline	> 32	> 32	0.25	> 32	15.8%	0%	84.2%	32	> 32	32	> 32	0%	0%	100%	> 32	> 32	0.5	> 32	10%	0%	90%
Tigecycline	0.12	0.5	0.06	0.5	--	--	--	0.12	0.25	0.12	0.25	--	--	--	0.12	0.25	0.12	0.25	--	--	--
Vancomycin	> 32	> 32	> 16	> 32	0%	0%	100%	> 32	> 32	> 16	> 32	0%	0%	100%	> 16	> 16	> 16	> 16	0%	0%	100%
	E. faecium (400)							*E. faecium* (59)							*E. faecium* (237)						
Amoxicillin Clavulanate	> 16	> 16	≤ 0.12	> 16	--	--	--	> 16	> 16	≤ 0.12	> 16	--	--	--	> 1	> 1	≤ 0.12	> 1	--	--	--
Azithromycin	> 8	> 8	0.25	> 8	--	--	--	> 8	> 8	0.5	> 8	--	--	--							
Ceftriaxone	> 64	> 64	1	> 64	--	--	--	> 64	> 64	2	> 64	--	--	--							
Daptomycin	4	4	0.12	> 4	91.8%	--	--	4	> 4	1	> 4	72.9%	--	--	2	4	0.12	8	99.6%	--	--
Eravacycline	0.06	0.06	0.008	1	--	--	--	0.06	0.06	0.008	0.5	--	--	--	0.03	0.06	0.015	1	--	--	--
Levofloxacin	> 8	> 8	0.06	> 8	6%	6.5%	87.5%	> 8	> 8	1	> 8	8.5%	8.5%	83.1%	> 8	> 8	0.12	> 8	12.2%	1.3%	86.5%
Linezolid	2	2	≤ 0.5	> 8	98.3%	1%	0.8%	2	2	1	8	94.9%	3.4%	1.7%	1	2	0.5	4	99.6%	0.4%	0%
Minocycline	8	> 8	≤ 0.03	> 8	47%	17.3%	35.8%	8	> 8	≤ 0.03	> 8	37.3%	15.3%	47.5%	0.25	> 8	≤ 0.03	> 8	60.3%	19%	20.7%
Penicillin	> 8	> 8	≤ 0.12	> 8	9%	--	91%	> 8	> 8	≤ 0.12	> 8	11.9%	--	88.1%	> 8	> 8	≤ 0.06	> 8	11%	--	89%
Tetracycline	32	> 32	0.12	> 32	32.3%	0.3%	67.5%	32	> 32	0.12	> 32	30.5%	0%	69.5%	2	> 32	0.12	> 32	50.6%	0%	49.4%
Tigecycline	0.12	0.25	0.03	4	96%	--	--	0.12	0.12	0.03	1	93.2%	--	--	0.06	0.12	0.03	8	98.7%	--	--
Vancomycin	> 16	> 32	≤ 0.12	> 32	43.2%	1%	55.8%	> 32	> 32	0.5	> 32	44.1%	1.7%	54.2%	1	> 16	≤ 0.25	> 16	76.4%	0%	23.6%
	E. faecium, VR (222)							*E. faecium*, VR (32)							*E. faecium*, VR (56)						
Amoxicillin Clavulanate	> 16	> 16	≤ 0.12	> 16	--	--	--	> 16	> 16	2	> 16	--	--	--	> 1	> 1	> 1	> 1	--	--	--
Azithromycin	> 8	> 8	0.25	> 8	--	--	--	> 8	> 8	4	> 8	--	--	--							
Ceftriaxone	> 64	> 64	1	> 64	--	--	--	> 64	> 64	> 64	> 64	--	--	--							
Daptomycin	4	4	0.12	> 4	93.2%	--	--	4	> 4	1	> 4	78.1%	--	--	2	4	0.5	8	98.2%	--	--
Eravacycline	0.06	0.06	0.008	1	--	--	--	0.06	0.25	0.03	0.5	--	--	--	0.03	0.06	0.015	1	--	--	--
Levofloxacin	> 8	> 8	8	> 8	0%	0%	100%	> 8	> 8	> 8	> 8	0%	0%	100%	> 8	> 8	> 8	> 8	0%	0%	100%
Linezolid	2	2	≤ 0.5	> 8	98.7%	0.5%	0.9%	2	2	1	8	96.9%	0%	3.1%	1	1	0.5	2	100%	0%	0%
Minocycline	8	> 8	0.06	> 8	41.9%	17.6%	40.5%	> 8	> 8	0.06	> 8	21.9%	21.9%	56.3%	8	> 8	0.06	> 8	42.8%	35.7%	21.4%
Penicillin	> 8	> 8	> 8	> 8	0%	--	100%	> 8	> 8	> 8	> 8	0%	--	100%	> 8	> 8	2	> 8	3.6%	--	96.4%
Tetracycline	32	> 32	0.12	> 32	18.9%	0.5%	80.6%	> 32	> 32	0.12	> 32	12.5%	0%	87.5%	32	> 32	0.12	> 32	28.6%	0%	71.4%
Tigecycline	0.12	0.25	0.03	4	--	--	--	0.12	0.5	0.06	1	--	--	--	0.12	0.12	0.03	1	--	--	--
Vancomycin	> 32	> 32	> 16	> 32	0%	0%	100%	> 32	> 32	> 32	> 32	0%	0%	100%	> 16	> 16	> 16	> 16	0%	0%	100%

VR, vancomycin-resistant; “—”represents lack of an established breakpoint.

Conclusions

- ERV demonstrated consistent and potent *in vitro* activity against a global collection of *Staphylococcus* spp. and *Enterococcus* spp., including resistant strains, over a recent 3-year time period (2013-2015).
- ERV shows promising activity against globally-isolated Gram-positive organisms, including those with resistant phenotypes.

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