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

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Introduction

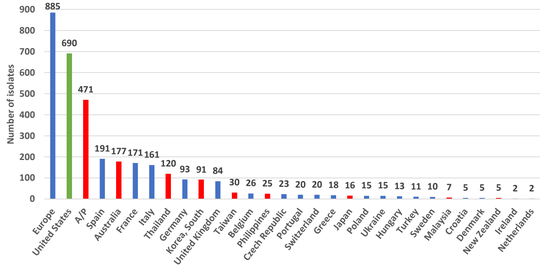
Eravacycline is a fully synthetic, fluorocycline antibiotic approved for the treatment of complicated intra-abdominal infections (cIAI) in patients ≥18 years of age in Europe, Singapore, the US and UK. Previous surveillance studies of eravacycline have demonstrated potent *in vitro* activity against specific Gram-positive pathogens. The purpose of this study was to further monitor the *in vitro* activity of eravacycline against *Staphylococcus aureus* (including methicillin-resistant *S. aureus*, MRSA), *Enterococcus* spp. (including vancomycin-resistant *Enterococcus*, VRE) and *Streptococcus* spp.

Methods & Materials

Clinical isolates were collected from the United States, Europe and Asia/Pacific during 2020 from multiple infection sources, including bodily fluids, gastrointestinal, genitourinary and respiratory (Figures 1 and 2). Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution. Antibiotic susceptibility was determined with EUCAST breakpoints where available.

Results

Figure 1. Distribution of All Isolates (n = 2,046) by Country*



*Total of 2,046 isolates, Asia/Pacific (n=471), Europe (n=885) and the USA (n=690); Isolates from USA in green, Asia-Pacific in red and Europe in blue

Figure 2. Number and Percent of Isolates by Infection Source

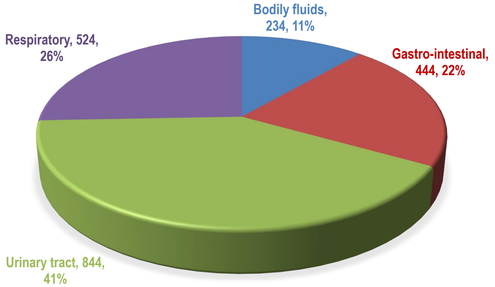


Table 1. Susceptibility of *Enterococcus* spp. to Eravacycline and Comparators

Organism (n)	Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Enterococcus spp. (870)	Amoxicillin Clavulanate	NB	1	> 1	≤ 0.12	> 1
	Ampicillin	62.3	2	> 8	≤ 0.25	> 8
	Daptomycin	NB	1	4	0.06	> 8
	Eravacycline	**99.4**	**0.03**	**0.06**	**0.004**	**2**
	Levofloxacin	53.2	4	> 8	0.12	> 8
	Linezolid	99.5	2	2	≤ 0.12	> 4
	Minocycline	NB	8	> 8	≤ 0.03	> 8
	Penicillin	NB	4	> 8	≤ 0.06	> 8
	Tetracycline	NB	32	> 32	≤ 0.06	> 32
	Tigecycline	99.2	0.06	0.12	≤ 0.008	2
	Vancomycin	87.2	1	> 16	≤ 0.25	> 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.

Table 2. Susceptibility of 473 *E. faecalis* to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	1	1	≤ 0.12	> 1
Ampicillin	99.8	1	2	≤ 0.25	> 8
Daptomycin	NB	1	2	0.06	4
Eravacycline	**99.8**	**0.03**	**0.06**	**0.004**	**0.5**
Levofloxacin	81.0	1	> 8	0.12	> 8
Linezolid	99.6	2	2	≤ 0.12	> 4
Minocycline	NB	8	> 8	≤ 0.03	> 8
Penicillin	NB	2	4	≤ 0.06	> 8
Tetracycline	NB	> 32	> 32	≤ 0.06	> 32
Tigecycline	99.4	0.12	0.12	≤ 0.008	1
Vancomycin	97.3	1	2	≤ 0.25	> 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.

Table 3. Susceptibility of 397 *E. faecium* to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	> 1	> 1	≤ 0.12	> 1
Ampicillin	17.6	> 8	> 8	≤ 0.25	> 8
Daptomycin	NB	2	4	0.06	> 8
Eravacycline	**99.0**	**0.03**	**0.06**	**0.008**	**2**
Levofloxacin	20.2	> 8	> 8	0.5	> 8
Linezolid	99.5	2	2	0.5	> 4
Minocycline	NB	4	> 8	≤ 0.03	> 8
Penicillin	NB	> 8	> 8	0.12	> 8
Tetracycline	NB	32	> 32	≤ 0.06	> 32
Tigecycline	99.0	0.06	0.12	0.015	2
Vancomycin	75.3	1	> 16	≤ 0.25	> 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.

Table 4. Susceptibility of 111 VRE to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	> 1	> 1	0.3	> 1
Ampicillin	10.8	> 8	> 8	0.5	> 8
Daptomycin	NB	2.0	4.0	0.1	> 8
Eravacycline	**99.1**	**0.0**	**0.1**	**0.0**	**2.0**
Levofloxacin	2.7	> 8	> 8	1.0	> 8
Linezolid	99.1	1.0	2.0	0.5	> 4
Minocycline	NB	4.0	> 8	≤ 0.03	> 8
Penicillin	NB	> 8	> 8	2.0	> 8
Tetracycline	NB	32.0	> 32	≤ 0.06	> 32
Tigecycline	98.2	0.1	0.1	0.0	2.0
Vancomycin	0.0	> 16	> 16	8.0	> 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.

Table 5. Susceptibility of 575 *S. aureus* to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	1	> 1	0.12	> 1
Azithromycin	50.6	1	> 4	≤ 0.25	> 4
Clindamycin	85.7	0.12	> 2	≤ 0.03	> 2
Daptomycin	99.8	0.25	0.5	≤ 0.06	2
Eravacycline	**99.3**	**0.03**	**0.06**	**≤ 0.008**	**2**
Levofloxacin	0.0	0.25	> 4	≤ 0.03	> 4
Linezolid	100.0	1	2	≤ 0.5	2
Minocycline	93.7	≤ 0.06	0.12	≤ 0.06	> 8
Oxacillin	54.8	1	> 2	≤ 0.06	> 2
Penicillin	17.2	> 2	> 2	≤ 0.12	> 2
Tetracycline	86.6	0.12	16	≤ 0.06	> 16
Tigecycline	99.3	0.12	0.25	≤ 0.015	1
Trimethoprim Sulfa	97.0	≤ 0.06	≤ 0.06	≤ 0.06	> 4
Vancomycin	100.0	1	1	≤ 0.25	2

*%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 6. Susceptibility of 260 MRSA to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	> 1	> 1	0.25	> 1
Azithromycin	30.0	> 4	> 4	≤ 0.25	> 4
Clindamycin	71.5	0.12	> 2	≤ 0.03	> 2
Daptomycin	99.6	0.25	0.5	0.12	2
Eravacycline	**98.5**	**0.03**	**0.12**	**≤ 0.008**	**2**
Levofloxacin	0.0	> 4	> 4	0.12	> 4
Linezolid	100.0	1	2	≤ 0.5	2
Minocycline	87.3	≤ 0.06	4	≤ 0.06	> 8
Oxacillin	0.0	> 2	> 2	> 2	> 2
Penicillin	0.4	> 2	> 2	≤ 0.12	> 2
Tetracycline	76.2	0.25	> 16	≤ 0.06	> 16
Tigecycline	99.2	0.12	0.5	0.03	1
Trimethoprim Sulfa	93.9	≤ 0.06	0.5	≤ 0.06	> 4
Vancomycin	100.0	1	1	≤ 0.25	2

*%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 7. Susceptibility of 315 MSSA to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	0.5	1	0.12	> 1
Azithromycin	67.6	1	> 4	≤ 0.25	> 4
Clindamycin	97.5	0.12	0.12	≤ 0.03	> 2
Daptomycin	100.0	0.25	0.5	≤ 0.06	1
Eravacycline	**100.0**	**0.03**	**0.06**	**≤ 0.008**	**0.25**
Levofloxacin	0.0	0.25	0.5	≤ 0.03	> 4
Linezolid	100.0	1	2	≤ 0.5	2
Minocycline	99.1	≤ 0.06	≤ 0.06	≤ 0.06	> 8
Oxacillin	100.0	0.25	1	≤ 0.06	2
Penicillin	31.1	2	> 2	≤ 0.12	> 2
Tetracycline	95.2	0.12	0.25	≤ 0.06	> 16
Tigecycline	99.4	0.12	0.25	≤ 0.015	1
Trimethoprim Sulfa	99.7	≤ 0.06	≤ 0.06	≤ 0.06	> 4
Vancomycin	100.0	1	1	0.5	2

*%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 8. Susceptibility of 87 MDR MRSA to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB	> 1	> 1	> 1	> 1
Azithromycin	1.2	> 4	> 4	1	> 4
Clindamycin	21.8	> 2	> 2	0.06	> 2
Daptomycin	98.9	0.25	0.5	0.12	2
Eravacycline	**96.6**	**0.06**	**0.25**	**≤ 0.008**	**2**
Levofloxacin	0.0	> 4	> 4	0.12	> 4
Linezolid	100.0	1	2	≤ 0.5	2
Minocycline	66.7	0.12	> 8	≤ 0.06	> 8
Oxacillin	0.0	> 2	> 2	> 2	> 2
Penicillin	0.0	> 2	> 2	> 2	> 2
Tetracycline	55.2	1	> 16	≤ 0.06	> 16
Tigecycline	100.0	0.12	0.5	0.03	0.5
Trimethoprim Sulfa	85.1	≤ 0.06	> 4	≤ 0.06	> 4
Vancomycin	100.0	1	1	0.5	2

*%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 9. Susceptibility of 35 *S. anginosus* group[a] to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Azithromycin	NB	0.06	> 1	≤ 0.03	> 1
Ceftriaxone	100.0	0.12	0.25	≤ 0.015	0.5
Chloramphenicol	NB	2	4	1	8
Clindamycin	88.6	0.03	> 1	≤ 0.015	> 1
Daptomycin	NB	0.25	0.5	≤ 0.03	1
Eravacycline	**100.0**	**0.015**	**0.03**	**≤ 0.001**	**0.06**
Levofloxacin	NB	0.5	1	≤ 0.25	> 4
Linezolid	NB	1	2	0.5	2
Meropenem	100.0	≤ 0.03	0.06	≤ 0.03	0.12
Minocycline	NB	≤ 0.06	4	≤ 0.06	> 8
Penicillin	100.0	≤ 0.12	≤ 0.12	≤ 0.12	≤ 0.12
Tetracycline	NB	0.25	> 4	≤ 0.03	> 4
Tigecycline	100.0	0.03	0.06	≤ 0.008	0.06
Vancomycin	100.0	0.5	1	≤ 0.06	1

*%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 10. Susceptibility of 54 other *Streptococcus spp.* to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Azithromycin	NB	> 1	> 1	≤ 0.03	> 1
Ceftriaxone	81.5	0.25	2	0.03	> 2
Chloramphenicol	NB	2	4	1	16
Clindamycin	88.9	0.03	> 1	≤ 0.015	> 1
Daptomycin	NB	0.25	1	0.06	> 1
Eravacycline	**98.2**	**0.015**	**0.06**	**0.008**	**0.25**
Levofloxacin	NB	1	4	0.5	> 4
Linezolid	NB	1	2	0.5	2
Meropenem	100.0	0.06	> 0.5	≤ 0.03	> 0.5
Minocycline	NB	0.12	> 8	≤ 0.06	> 8
Penicillin	66.7	≤ 0.12	2	≤ 0.12	> 2
Tetracycline	NB	0.5	> 4	0.12	> 4
Tigecycline	92.6	0.03	0.12	0.015	0.25
Vancomycin	100.0	0.5	0.5	0.25	0.5

*%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.

Results Summary

Summary MIC data for eravacycline and comparators are shown in Tables 1-10. Susceptibility to eravacycline in all Gram-positive pathogens was >95%. Notably, eravavcycline was also very active (>95% susceptible) against VRE, MSSA, MRSA and MDR MRSA.

Conclusion

Eravacycline demonstrated sustained high susceptibility rates against clinically important Gram-positive pathogens, including resistant isolates. These important observations suggest that, following several years in clinical use, eravacycline resistance in Gram-positives remains low.

References

1. CLSI, 2018. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed. CLSI Standard M07. CLSI, Wayne, PA, USA
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