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Global 2018 Surveillance of Eravacycline Against Gram-positive Pathogens, Including Resistant Isolates

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Introduction

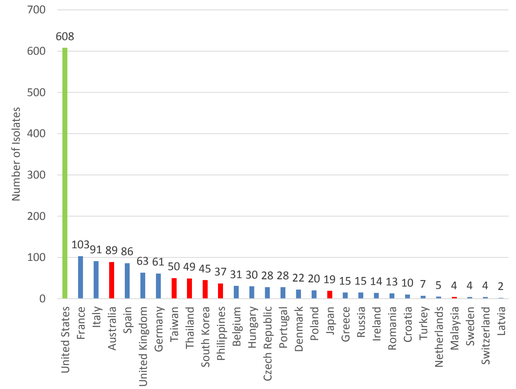
Eravacycline is a novel, fully-synthetic, fluorocycline antibiotic that is approved by the Food and Drug Administration (FDA) for the treatment of complicated intra-abdominal infections (cIAI) caused by susceptible microorganisms including *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii*, *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-positive pathogens collected worldwide as part of an ongoing global surveillance program.

Methods & Materials

Clinical isolates were collected in 2018 from hospitals in 29 countries. In brief, totals of 293, 652 and 608 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). Considering neither agent had CLSI breakpoints but for the majority of species had EUCAST breakpoints, analysis by EUCAST breakpoints (4) was also performed for comparative purposes.

Results

Figure 1. Distribution of All Isolates (n = 1,553) by Country*



*Total of 1,553 isolates, Asia/Pacific (n=293), Europe (n=652) and the USA (n=608); Isolates from USA in green, Asia-Pacific in red and Europe in blue

Figure 2. Number and Percent of Isolates by Infection Source

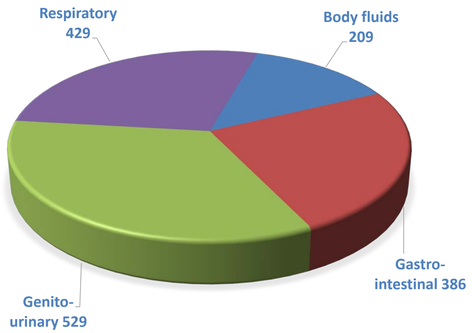


Table 1. Susceptibility of *Enterococcus faecalis* (n=502) to Eravacycline and Comparators

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	98.8	1	2	0.06	4
Eravacycline (FDA)	73.6	0.06	0.12	0.015	0.25
Eravacycline (EUCAST)	99.8				
Levofloxacin	75.7	1	> 8	0.25	> 8
Linezolid	98.4	2	2	≤ 0.12	> 4
Minocycline	31.1	> 8	> 8	≤ 0.03	> 8
Penicillin	97.8	2	4	≤ 0.06	> 8
Tetracycline	25.3	> 32	> 32	0.12	> 32
Tigecycline (FDA)	91.0	0.12	0.25	0.015	2
Tigecycline (EUCAST)	91.0				
Vancomycin	96.4	1	2	≤ 0.25	> 16

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

Table 2. Susceptibility of *Enterococcus faecium* (n=483) to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB**	> 1	> 1	≤ 0.12	> 1
Ampicillin	14.9	> 8	> 8	≤ 0.25	> 8
Daptomycin	81.4	2	4	0.12	8
Eravacycline (FDA)	90.1	0.06	0.06	0.015	1
Eravacycline (EUCAST)	95.2				
Levofloxacin	7.7	> 8	> 8	0.25	> 8
Linezolid	97.9	2	2	0.5	> 4
Minocycline	53.2	4	> 8	≤ 0.03	> 8
Penicillin	13.9	> 8	> 8	≤ 0.06	> 8
Tetracycline	35.6	32	> 32	0.12	> 32
Tigecycline (FDA)	91.5	0.06	0.25	0.03	4
Tigecycline (EUCAST)	91.1				
Vancomycin	64.0	1	> 16	≤ 0.25	> 16

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

Table 3. Susceptibility of Vancomycin-Resistant *Enterococci* (VRE, n=189) to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB**	> 1	> 1	0.25	> 1
Ampicillin	10.1	> 8	> 8	0.5	> 8
Daptomycin	85.7	2	4	0.12	4
Eravacycline (FDA)	80.9	0.06	0.12	0.015	0.5
Eravacycline (EUCAST)	97.6				
Levofloxacin	0.5	> 8	> 8	1	> 8
Linezolid	97.9	1	2	0.5	> 4
Minocycline	47.1	8	> 8	≤ 0.03	> 8
Penicillin	10.1	> 8	> 8	0.25	> 8
Tetracycline	24.3	32	> 32	0.12	> 32
Tigecycline (FDA)	91.0	0.06	0.25	0.03	4
Tigecycline (EUCAST)	91.1				
Vancomycin	0.0	> 16	> 16	> 16	> 16

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

Table 4. Susceptibility of Methicillin-susceptible *Staphylococcus aureus* (MSSA, n=308) to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB**	> 1	> 1	0.5	> 1
Azithromycin	25.9	> 4	> 4	0.5	> 4
Ceftaroline	91.0	1	1	0.12	> 4
Clindamycin	72.6	0.12	> 2	≤ 0.03	> 2
Daptomycin	100.0	0.5	0.5	0.12	1
Eravacycline (FDA)	86.0	0.06	0.25	0.015	1
Eravacycline (EUCAST)	99.7				
Levofloxacin	32.6	4	> 4	0.12	> 4
Linezolid	100.0	2	2	≤ 0.5	2
Minocycline	93.9	0.12	0.5	≤ 0.06	> 8
Oxacillin	NB	> 2	> 2	> 2	> 2
Penicillin	0.0	> 2	> 2	0.25	> 2
Tetracycline	83.5	0.25	> 16	≤ 0.06	> 16
Tigecycline (FDA)	100	0.25	0.5	≤ 0.015	1
Tigecycline (EUCAST)	100				
Vancomycin	100.0	1	1	0.5	2

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

Table 5. Susceptibility of Methicillin-resistant *Staphylococcus aureus* (MRSA, n=212) to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Amoxicillin Clavulanate	NB**	0.5	1	0.12	> 1
Azithromycin	73.1	1	> 4	≤ 0.25	> 4
Ceftaroline	99.7	0.25	0.25	≤ 0.06	2
Clindamycin	95.1	0.12	0.12	≤ 0.03	> 2
Daptomycin	100.0	0.25	0.5	0.12	1
Eravacycline (FDA)	77.4	0.06	0.12	0.015	1
Eravacycline (EUCAST)	95.3				
Levofloxacin	92.5	0.25	0.5	0.06	> 4
Linezolid	100.0	2	2	≤ 0.5	2
Minocycline	99.4	≤ 0.06	0.12	≤ 0.06	8
Oxacillin	100.0	0.5	1	≤ 0.06	2
Penicillin	27.0	2	> 2	≤ 0.12	> 2
Tetracycline	94.5	0.25	0.5	≤ 0.06	> 16
Tigecycline (FDA)	97.6	0.25	0.25	0.03	0.5
Tigecycline (EUCAST)	97.6				
Vancomycin	100.0	1	1	0.5	2

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

Table 6. Susceptibility of *Streptococcus anginosus* groupa (n=48) to Eravacycline and Comparators

Drug	%S*	MIC_{50}	MIC_{90}	MIN MIC	MAX MIC
Azithromycin	81.3	0.06	> 1	≤ 0.03	> 1
Ceftaroline	NB**	0.015	0.03	≤ 0.004	0.06
Ceftriaxone	100.0	0.12	0.25	≤ 0.015	0.5
Clindamycin	81.3	0.03	> 1	≤ 0.015	> 1
Daptomycin	100.0	0.25	0.5	≤ 0.03	0.5
Eravacycline (FDA)	100.0	0.015	0.03	≤ 0.001	0.03
Eravacycline (EUCAST)	100.0				
Levofloxacin	100.0	0.5	0.5	≤ 0.25	1
Linezolid	100.0	1	2	≤ 0.12	2
Meropenem	100.0	≤ 0.03	0.06	≤ 0.03	0.5
Minocycline	NB	≤ 0.06	8	≤ 0.06	> 8
Penicillin	93.8	≤ 0.12	≤ 0.12	≤ 0.12	0.5
Tetracycline	64.6	0.25	> 4	≤ 0.03	> 4
Tigecycline (FDA)***	100	0.03	0.06	≤ 0.008	0.06
Vancomycin	100.0	0.5	1	≤ 0.06	1

*%S, percent susceptible; **NB, no defined breakpoint;***, no EUCAST breakpoint; a, *S. anginosus*, *S. constellatus*, *S. intermedius*; MIC_{50} = concentration required to inhibit 50% of the population; MIC_{90} = concentration required to inhibit 90% of the population

Results Summary

- Eravacycline exhibited good *in vitro* activity against the vast majority of isolates tested in the present study and based on MIC_{90} values it was one of the most active antibiotics of those tested. Against *Enterococci*, including VRE, eravacycline had MIC_{90} of 0.12 mg/L. For S. aureus, MIC_{90} values were 0.25 and 0.12 mg/L for MSSA and MRSA, respectively and against the S. anginosus group MIC_{90} was 0.03 mg/L
- No CLSI breakpoints exist for either eravacycline or tigecycline though for most pathogens FDA and EUCAST breakpoints exist for both antibiotics. Susceptibility to tigecycline was similar when analyzing data by FDA or EUCAST breakpoints. However, susceptibility to eravacycline was significantly higher when analyzing the data using EUCAST breakpoints. With the exception of susceptibility in the *S. anginosus* group, susceptibility to eravacycline in *Enterococci* and *Staphylococci* by EUCAST criteria was >95% for all species though by FDA criteria susceptibility ranged from 73.6% to 90.1%

Conclusion

Eravacycline demonstrated potent *in vitro* activity against Gram-positive pathogens collected worldwide many of which were susceptible to eravacycline. Further surveillance monitoring is warranted and interpretation using different regulatory criteria should continue to be adopted for comparative purposes.

References

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