

# In Vitro Activity of Eravacycline and Comparators against Gram-positive Bacteria Collected from European Hospitals in 2017

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## Introduction

Eravacycline is a novel, fully-synthetic, fluoroquinolone anti-bacterial of the tetracycline class that has recently obtained approval in the US and Europe for the treatment of complicated intra-abdominal infections in adults. Eravacycline has shown activity against a broad range of Gram-negative, Gram-positive and anaerobic organisms. The purpose of this present study was to demonstrate the *in vitro* activity of eravacycline and comparators against Gram-positive bacteria isolated from European patients in 2017.

## Methods & Materials

Non-duplicate, non-consecutive, single-patient clinical isolates causing gastro-intestinal, urinary-tract and respiratory infections were collected in 2017 from hospitals in Europe as part of an ongoing surveillance study of eravacycline activity. MICs were determined by CLSI broth microdilution (1) and susceptibility interpreted using EUCAST clinical breakpoints.

## Results

Figure 1. Distribution of *E. faecalis* Isolates (n = 195) by Country

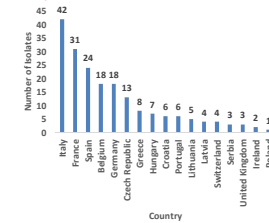


Figure 4. Distribution of MRSA Isolates (n = 114) by Country

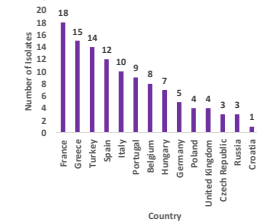


Figure 2. Distribution of *E. faecium* Isolates (n = 191) by Country

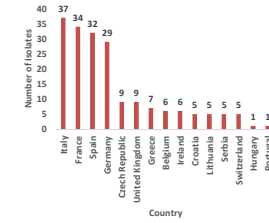


Figure 5. Distribution of MSSA Isolates (n = 103) by Country

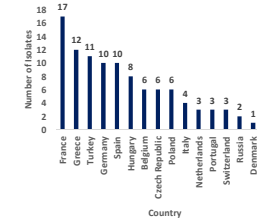


Figure 3. Distribution of Vancomycin-Resistant Enterococci (VRE, n = 48) by Country

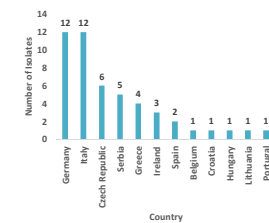


Figure 6. Distribution of Viridans Streptococci (n = 209) by Country

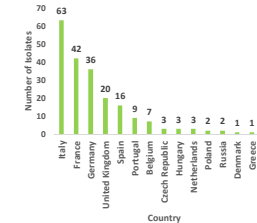


Table 1. Susceptibility of *E. faecalis* (n = 195) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amoxicillin Clavulanate	NB**	-	0.5	> 1	0.25	> 1
Ampicillin	<=4   8   >=16	99.49	1	2	0.5	> 8
Daptomycin	NB	-	1	2	0.25	4
Eravacycline	<=0.12   -   >=0.25	100.00	0.06	0.06	0.008	0.12
Levofloxacin	<=4   -   >=8	71.28	1	> 8	0.5	> 8
Linezolid	<=4   -   >=8	98.97	2	2	1	> 4
Minoscycine	NB	-	> 8	> 8	0.12	> 8
Penicillin	NB	-	2	4	1	> 8
Tetracycline	NB	-	> 32	> 32	0.12	> 32
Tigecycline	<=0.25   -   >=0.5	100.00	0.12	0.12	0.015	0.25
Vancomycin	<=4   -   >=8	99.49	1	2	0.5	> 16

\*%S, percent susceptible. \*\*NB, no defined breakpoint

Table 2. Susceptibility of *E. faecium* (n = 191) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amoxicillin Clavulanate	NB**	-	> 1	> 1	<=0.12	> 1
Ampicillin	<=4   8   >=16	11.52	> 8	> 8	<=0.25	> 8
Daptomycin	NB	-	2	4	<=0.03	8
Eravacycline	<=0.12   -   >=0.25	97.91	0.03	0.06	0.015	0.25
Levofloxacin	<=4   -   >=8	15.71	> 8	> 8	1	> 8
Linezolid	<=4   -   >=8	100.00	2	2	0.5	4
Minoscycine	NB	-	4	> 8	0.12	> 8
Penicillin	NB	-	> 8	> 8	<=0.06	> 8
Tetracycline	NB	-	16	> 32	0.12	> 32
Tigecycline	<=0.25   -   >=0.5	95.81	0.06	0.12	0.03	1
Vancomycin	<=4   -   >=8	74.87	1	> 16	0.5	> 16

\*%S, %NB, no defined breakpoint

Table 3. Susceptibility of Vancomycin-Resistant Enterococci (n = 48) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amoxicillin Clavulanate	NB**	-	> 1	> 1	0.5	> 1
Ampicillin	<=4   8   >=16	2.04	> 8	> 8	1	> 8
Daptomycin	NB	-	2	4	1	8
Eravacycline	<=0.12   -   >=0.25	95.92	0.03	0.06	0.015	0.25
Levofloxacin	<=4   -   >=8	-	> 8	> 8	> 8	> 8
Linezolid	<=4   -   >=8	100.00	1	2	0.5	4
Minoscycine	NB	-	4	> 8	0.12	> 8
Penicillin	NB	-	> 8	> 8	4	> 8
Tetracycline	NB	-	32	> 32	0.25	> 32
Tigecycline	<=0.25   -   >=0.5	95.02	0.06	0.12	0.06	1
Vancomycin	<=4   -   >=8	0.00	> 16	> 16	8	> 16

\*%S, %NB, no defined breakpoint

Table 4. Susceptibility of MRSA (n = 114) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amoxicillin Clavulanate	NB**	-	> 1	> 1	1	> 1
Azithromycin	<=1   2   >=4	41.23	> 4	> 4	<=0.25	> 4
Cefazolin	<=1   2   >=4	84.21	0.5	2	0.12	4
Clinidamycin	<=0.25   0.5   >=1	68.42	0.12	> 2	<=0.03	> 2
Daptomycin	<=1   -   >=2	100.00	0.5	0.5	<=0.06	1
Eravacycline	<=0.25   -   >=0.5	100.00	0.03	0.06	<=0.008	0.25
Levofloxacin	<=1   -   >=2	26.32	> 4	> 4	0.12	> 4
Linezolid	<=4   -   >=8	100.00	1	2	<=0.5	2
Minoscycine	<=0.5   1   >=2	86.84	<=0.06	1	<=0.06	> 8
Oxacillin	<=2   -   >=4	0.00	> 2	> 2	> 2	> 2
Penicillin	<=0.12   -   >=0.25	0.00	> 2	> 2	0.5	> 2
Tetracycline	<=1   2   >=4	74.56	0.25	> 16	<=0.06	> 16
Tigecycline	<=0.5   -   >=1	99.12	0.12	0.25	0.03	1
Vancomycin	<=2   -   >=4	100.00	0.5	1	<=0.25	2

\*%S, %NB, no defined breakpoint

Table 5. Susceptibility of MSSA (n = 103) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amoxicillin Clavulanate	NB**	-	1	1	0.12	> 1
Azithromycin	<=1   2   >=4	81.55	0.5	> 4	<=0.25	> 4
Cefazolin	<=1   2   >=4	100.00	0.25	0.25	<=0.06	0.5
Clinidamycin	<=0.25   0.5   >=1	96.12	0.12	0.12	<=0.03	> 2
Daptomycin	<=1   -   >=2	100.00	0.5	0.5	0.12	1
Eravacycline	<=0.25   -   >=0.5	100.00	0.03	0.06	0.015	0.12
Levofloxacin	<=1   -   >=2	89.32	0.12	4	0.06	> 4
Linezolid	<=4   -   >=8	100.00	2	2	<=0.5	2
Minoscycine	<=0.5   1   >=2	99.03	<=0.06	0.12	<=0.06	8
Oxacillin	<=2   -   >=4	100.00	0.25	0.5	<=0.06	2
Penicillin	<=0.12   -   >=0.25	25.24	> 2	> 2	<=0.12	> 2
Tetracycline	<=1   2   >=4	94.17	0.25	0.25	0.12	> 16
Tigecycline	<=0.5   -   >=1	99.03	0.12	0.25	0.06	1
Vancomycin	<=2   -   >=4	100.00	0.5	1	<=0.25	2

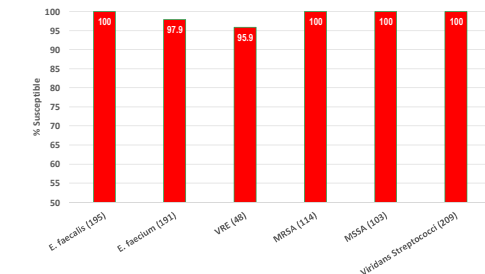
\*%S, percent susceptible. \*\*NB, no defined breakpoint

Table 6. Susceptibility of Viridans Streptococci (n = 209) to Eravacycline and Comparators

Drug	Breakpoints (S/I/R)	%S*	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Azithromycin	NB**	-	0.06	> 1	<=0.03	> 1
Cefazolin	NB	-	0.015	0.06	<=0.004	> 1
Ceftriaxone	<=0.5   -   >=1	91.39	0.12	0.5	<=0.015	> 2
Clinidamycin	<=0.5   -   >=1	88.52	<=0.015	> 1	<=0.015	> 1
Daptomycin	NB	-	0.25	0.5	<=0.03	1
Eravacycline	<=0.12   -   >=0.25	100.00	0.03	0.06	0.004	0.12
Levofloxacin	NB	-	1	2	<=0.25	> 4
Linezolid	NB	-	1	2	0.25	2
Meropenem	<=2   -   >=4	100.00	<=0.03	0.25	<=0.03	> 0.5
Minoscycine	NB	-	0.12	> 8	<=0.06	> 8
Penicillin	<=0.25   0.5   >=1	84.21	<=0.12	0.5	<=0.12	> 2
Tetracycline	NB	-	0.5	> 4	<=0.03	> 4
Tigecycline	<=0.5   -   >=1	-	0.06	0.12	<=0.008	> 1
Vancomycin	<=2   -   >=4	100.00	0.5	1	<=0.06	1

\*%S, percent susceptible. \*\*NB, no defined breakpoint

Figure 7. Summary of Susceptibility Data for Eravacycline Against Gram-Positive Pathogens from 2017



## Results Summary & Conclusion

All species of Gram-positive isolates tested were >95-100% susceptible to eravacycline. Notably, eravacycline was one of the most potent of the antibiotics. The activity of eravacycline was unaffected by VRE or MRSA phenotypes. Further surveillance investigating the susceptibility to eravacycline in European Gram-positive isolates is warranted.

## References

1. CLSI, 2018. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*; Approved Standard - Eleventh Edition M07-A10. Clinical and Laboratory Standards Institute (CLSI), Wayne, PA 19087-1898 USA.
2. The European Committee on Antimicrobial Susceptibility testing, 2019. *Breakpoint tables for interpretation of MICs and zone diameters*. Version 9.0 <http://www.eucast.org>.

## Acknowledgments

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