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In vitro activity of eravacycline and comparators against Staphylococcus aureus and enterococci, including methicillin-resistant and vancomycin-resistant subgroups, collected from European hospitals in 2015

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Background: Eravacycline is a novel, fully-synthetic, fluorocycline antibiotic of the tetracycline class in phase 3 development for the treatment of serious bacterial infections, including those caused by multidrug-resistant pathogens. The purpose of this study was to demonstrate the *in vitro* activity of eravacycline and comparators against *S.aureus* - methicillin-resistant (MRSA) & methicillin-susceptible (MSSA) - and enterococci - vancomycin-resistant (VRE) and vancomycin-susceptible (VSE) -isolated from patients in Europe.

Material/methods: Non-duplicate, non-consecutive, single-patient clinical isolates were collected in 2015 from hospitals in Belgium, Croatia, Czech Republic, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Portugal, Romania, Spain, Switzerland and United Kingdom. MICs for ampicillin (enterococci only), azithromycin (*S. aureus* only), clindamycin (*S. aureus* only), daptomycin, eravacycline, gentamicin (*S. aureus* only), levofloxacin, linezolid, minocycline, oxacillin (*S. aureus* only), penicillin, tetracycline, tigecycline and vancomycin were determined by CLSI broth microdilution. Antibiotic susceptibility was determined with EUCAST version 6.0, 2016 breakpoints, where available.

Results: Summary MIC data for eravacycline and tigecycline are shown in the Table. Eravacycline MIC_s were generally 2 to 4-fold lower than tigecycline MICs, including MRSA and VRE isolates. All *S. aureus*, 99% of VRE and 95% of VSE were tigecycline-susceptible. VSE were 70% susceptible to

ampicillin and 54% susceptible to levofloxacin, whereas susceptibility reduced to 15% and 10% for VRE, respectively. All enterococci were linezolid susceptible. MSSA were ≥90% susceptible to most agents except penicillin (24% susceptible) and MRSA were poorly susceptible to most agents except gentamicin (96% susceptible), tetracyclines (≥95% susceptible), daptomycin (100% susceptible), linezolid (100% susceptible) and vancomycin (100% susceptible).

Organism (N)	Eravacycline MIC (mg/L)				Tigecycline MIC (mg/L)			
	MIC_{50}	**MIC_{90}**	**Min**	**Max**	**MIC_{50}**	**MIC_{90}**	**Min**	**Max**
VSE (434)	0.03	0.06	0.015	0.25	0.12	0.12	0.03	8
VRE (20)	0.03	0.06	0.03	1	0.06	0.25	0.06	1
MRSA (104)	0.06	0.06	0.015	0.25	0.25	0.25	0.06	0.5
MSSA (105)	0.06	0.06	≤ 0.008	0.12	0.12	0.25	0.06	0.25

$MIC_{50/90}$, minimum inhibitory concentration required to inhibit growth of 50/90% of isolates, respectively.

Conclusions: Overall, eravacycline MIC_{90} for *S. aureus* and enterococci isolates was 0.06 mg/L and was unaffected by MRSA or VRE phenotype. ERV shows promising activity, with lower MICs than tigecycline, against *S. aureus* and enterococci, including resistant phenotypes, in patients from Europe.