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In vitro activity of eravacycline and comparators against Acinetobacter baumannii, Stenotrophomonas maltophilia and Enterobacteriaceae, including carbapenem-resistant and ESBL phenotype 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 *A. baumannii, S. maltophilia* and *Enterobacteriaceae*, including extended spectrum beta-lactamase (ESBL) and carbapenem-resistant (CR) phenotypes, 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, Italy, Lithuania, Netherlands, Portugal, Spain, Turkey and United Kingdom. MICs for amikacin, amoxicillin/clavulanic acid (*Enterobacteriaceae* only), ampicillin/sulbactam (not *Enterobacteriaceae*), aztreonam, cefepime, cefotaxime (*Enterobacteriaceae* only), ceftazidime, ceftriaxone, colistin, eravacycline, ertapenem (*Enterobacteriaceae* only), gentamicin, levofloxacin, meropenem, minocycline (not *Enterobacteriaceae*), piperacillin-tazobactam, tetracycline, tigecycline and trimethoprim sulfa were determined by CLSI broth microdilution. ESBL was defined phenotypically according to CLSI guidelines (*Escherichia coli, Klebsiella oxytoca, K. pneumoniae* and *Proteus mirabilis* only). CR was defined as resistant to ertapenem or meropenem. 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 CR and ESBL isolates. Tigecycline susceptibility against all *Enterobacteriaceae* was 68.3%, which reduced to 52.9% against CR isolates. CR isolates were also poorly susceptible (≤52.9% susceptible) to all other antibacterials except amikacin (88.2% susceptible) and colistin (100% susceptible)

Organism (N)	Eravacycline MIC (mg/L)				Tigecycline MIC (mg/L)			
	MIC_{50}	**MIC_{90}**	**Min**	**Max**	**MIC_{50}**	**MIC_{90}**	**Min**	**Max**
A. baumannii (270)	1	2	0.03	8	2	4	0.12	> 16
S. maltophilia (293)	1	2	0.06	8	1	4	0.12	16
CR- *A. baumannii* (193)	1	2	0.12	8	4	8	0.5	> 16
All *Enterobacteriaceae* (1284)	0.5	2	0.06	8	1	4	0.12	16
CR- *Enterobacteriaceae* (17)	0.5	2	0.25	2	1	4	0.5	8
ESBL- *Enterobacteriaceae* (61)	0.25	1	0.06	8	1	4	0.25	16

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

Conclusions: Overall, ERV MIC_{90} values for *Enterobacteriaceae, S. maltophilia* or *A. baumannii* isolates were 2 mg/L and were unaffected by CR or ESBL phenotype. ERV shows promising activity, with lower MICs than tigecycline, against *A. baumannii*, *Stenotrophomonas maltophilia* and *Enterobacteriaceae*, including resistant phenotypes, in patients from Europe.