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Eravacycline, a novel fluorocycline, has antibacterial activity against carbapenem-resistant Enterobacteriaceae (CRE) and Acinetobacter spp, (CRA)

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Background: Carbapenem resistant *Enterobacteriaceae* (CRE) exhibit extremely drug resistant (XDR) and occasionally pan-drug resistant (PDR) phenotypes, compromising successful treatment and clinical outcome for the patient. Colistin is now considered to be the final drug capable of treating infections caused by carbapenem-resistant *Acinetobacter baumannii (*CRA); however, strains are now being isolated that are resistant to this antibiotic as well. The antibiotic 'pipeline' is dry, ergo the pursuit of new antibiotic discovery and/or modification of already existing compounds has never been more pertinent in the battle against these multidrug-resistant infections. Eravacycline (ERV, Tetraphase Pharmaceuticals) is a novel fully-synthetic fluorocycline antibacterial agent that retains activity against the most common acquired tetracycline-specific resistance mechanisms. Herein we evaluate the activity of ERV against 200 CRE and 104 CRA isolates.

Material/methods: A global selection of CRE & CRA were selected. Presence of carbapenemase-producing genes (*bla*$_{NDM}$, *bla*$_{VIM}$ and *bla*$_{OXA-48}$) were confirmed via PCR. MICs for ERV and selected comparator antibiotics (Table1), including cefepime (FEP), ceftazidime (TAZ), cefotaxime (FOT), colistin (COL), gentamicin (GEN), ertapenem (ETP), levofloxacin (LEVO), piperacillin/tazobactam (P/T4), tigecycline (TGC), tetracycline (TET), minocycline (MIN), meropenem (MERO), amikacin (AMI) and trimethoprim-sulfamethoxazole (SXT) were determined using microbroth dilution assays in pre-prepared microtitre plates. Results were interpreted using EUCAST guidelines.

Results: CRE genotypes were: *bla*$_{NDM}$-positive (79%), *bla*$_{OXA-48-}$positive (2%), *bla*$_{VIM}$-positive (2%) and other metallo-b-lactamase (MBL) (17%). CRA genotypes were *bla*$_{NDM}$-positive (59.5%), *bla*$_{OXA-48-}$

positive (26%) and *bla*$_{VIM}$-positive (14.5%). In the case of CRE, ERV recorded MIC_{50} and MIC_{90} of 0.5µg/ml and 2µg/ml respectively; possessing better antibacterial activity than all antibiotics tested (Table 1). For CRA, ERV also was favourable with regard to all antibiotics tested with MIC_{50} and MIC_{90} values of 0.5µg/ml and 4µg/ml, respectively. ERV was more potent than any other tested antibiotics against CRE and CRA.

Conclusions: ERV shows considerable activity against both CRE & CRA, and is more potent *in vitro* than any other antibiotic comparators. ERV has the potential to be a promising empirical treatment option for complicated hospital/health care infections.

Table 1: MIC_{50} & MIC_{90} of CRE (n=200) & CRA (n=104) against Eravacycline and comparator antimicrobials.

Antibiotic	CRE		CRA		Antibiotic	CRE		CRA	
	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}		MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
ERV	0.5	2	0.5	4	**P/T4**	>64	>64	>128	>128
TET	>8	>8	4	>8	**TAZ**	>8	>8	>32	>32
TGC	2	8	4	8	**ERT**	>2	>2	-	-
MIN	-	-	0.5	4	**LEVO**	>2	>2	8	>8
COL	0.5	>2	1	4	**MERO**	-	-	>16	>16
FEP	>8	>8	>16	>16	**AMI**	-	-	32	>32
FOT	>2	>2	-	-	**GEN**	>8	>8	-	-
SXT	-	-	>32/608	>32/608					