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P1149 *In vitro* activity of ceftazidime-avibactam against contemporary carbapenem-resistant/carbapenemase-producing Enterobacteriales and *Pseudomonas aeruginosa* clinical isolates from Argentina

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Background: The global increase in the prevalence of extreme-drug resistant (XDR) pathogens, such as carbapenem resistant /carbapenemase-producing Enterobacteriales (ETB) and *P. aeruginosa* (PA), is a challenge for health systems. Ceftazidime-avibactam (CZA) is a new antimicrobial intended to treat infections caused by these pathogens, including those produce Class A, Class C, and some Class D β-lactamases. **Aim**: to evaluate the *in vitro* activity of CZA in comparison with other antimicrobial agents against isolates submitted to the National Reference Laboratory because of a XDR profile

Materials/methods: We included 701 (518 ETB and 183 PAE) unique and consecutive clinical isolates (219 hospitals), submitted between January 2017 to June 2018. The molecular characterization of β-lactamases genes was performed by PCR/sequencing. MICs of CZA were determined by reference agar dilution/broth microdilution methods while susceptibility to other agents included results either by disk diffusion or MIC methods (CLSI or EUCAST criteria, as appropriate). The bacterial identification was confirmed with MALDI-TOF (Bruker).

Results: Activity of CZA is depicted in Table.

Group (No.)	β lactamase class (No.) and sub-class (No.)	Bacterial species (No.)	CZA			% of susceptible					
			MIC50 (μg/ml)	MIC90 (μg/ml)	Range (μg/ml)	CZA	AMK	COL	FOS	MER	TIG
ETB (518)	Class A carbapenemases (183): KPC-2 (179), KPC-3 (1), GES-3 (2), GES-34 (1)	Cfr (8), Ecl (24), Eco (9), Kae (5), Kpn (110), Kox (7), Kluycrio (1), Mmo (1), Rao (1), Sma (17), Sal (1)	1.0	4.0	0.06 - 16	99	53	68	79	3	86
	Class D carbapenemases (183): OXA-48 (4), OXA-163 (168), OXA-181 (3), OXA-232 (2), OXA-244 (1), OXA-247 (2), OXA-438 (2), OXA-567 (1)	Cfr (4), Ecl (16), Eco (16), Kox (2), Kpn (128), Pst (7), Sma (10)	2.0	8.0	0.12 - 16	98	57	86	74	31	68
	Class B carbapenemases (76): NDM (64), VIM (7), IMP (5)	Cfr (1), Ecl (9), Eco (7), Kluyasc (1), Kox (5), Kpn (29), Pre (17), Pst (7)	512	>512	16 - >512	0	49	66	60	0	45
	Dual carbapenemase producerrs (14):										
	a) KPC-2+OXA-163 (4)	Ecl (2), Eco (1), Kox (1)	NA	NA	0.25 - 8	100	100	75	25	0	100
	b) NDM+IMP (6), KPC+NDM (4)	Kpn (7), Ecl (1), Eco (1), Kox (1)	NA	NA	128 - >512	0	50	75	88	0	70
	CR ETB Non-CP ETB (62): ESBLs (40), AmpC (22)	Ecl (20), Eco (6), Kae (2), Kpn (28), Salm (1), Sma (5)	0.5	2	0.06 - 8	100	73	73	69	46	78
PAE (183)	Class A carbapenemases (40): KPC-2 (38), GES-5 (2)	NA	4	8	2 - 16	95	90	100	NA	0	NA
	Class B carbapenemases (28): IMP (8), VIM (11), NDM (2), SPM (7)	NA	128	>512	4 - >512	0.4	24	96	NA	6	NA
	Dual carbapenemase producers (2): IMP+VIM (1), NDM+IMP (1)	NA	NA	NA	>512	0	0	100	NA	0	NA
	Class A ESBL producers (20): GES-1 (17), PER-2 (1), CTX-M-15 (2)	NA	4	8	0.5 - 32	90	63	90	NA	5	NA
	Class D β lactamase producers (20): OXA-1 (20)	NA	4	8	2 – 16	90	6	98	NA	6	NA
	Non Carbapenemase, Non ESBL (73)	NA	8	32	1 – 32	73	38	99	NA	9	NA

Abbreviations: AMK, amikacin. COL, colistin. FOS, sodium fosfomycin (i.v. use). MER, meropenem. TIG, tigecycline. NA, not available. Cfr, *Citrobacter freundii*. Ecl, *Enterobacter cloacae*. Eco, *Escherichia coli*. Kae, *Klebsiella aerogenes*. Kpn, *K. pneumoniae*. Kox, *K. oxytoca*. Kluyasc, *Kluyvera ascorbata*. Kluycrio, *Kluyvera cryocrescens*. Mmo, *Morganella morganii*. Pre, *Providencia rettgeri*. Pst, *P. stuartii*. Rao, *Raoultella ornithinolytica*. Sma, *Serratia*

marcescens. Sal, *Salmonella*.

Conclusions: Among ETB, a uniform susceptibility to CZA was observed along Class A or/and Class D carbapenemase-producing and those carbapenem-resistant nonproducer ETB. This is the first report describing a potent inhibitory activity of CZA against OXA-163 producers, an OXA-48-like enzyme able to hydrolyze extended-spectrum cephalosporinases, in addition to a weak carbapenemase activity. Only 4 ETB isolates harboring serine enzymes (1 KPC and 3 OXA-163) displayed a resistant MIC (16 mg/L). Among PAE isolates, a potent CZA inhibition was observed for strains with class A carbapenemases or ESBLs and class D cefepimases. Only efflux hyperproducers showed significant acquired CZA resistance. CZA could be a potential alternative for the treatment of infections in patients such as those caused by KPC or OXA producers, which are endemic in Latin-American countries as Argentina.