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P1048 In vitro activity of imipenem-relebactam against KPC and/or OXA-48-producing Klebsiella pneumoniae isolates collected from 2015 to 2016 at Greek hospitals

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Background: Relebactam (REL) (formerly MK-7655) is a beta-lactamase inhibitor of class A and class C carbapenemases. In this study, we evaluated the ability of REL to restore imipenem (IMP) susceptibility against a collection of *K. pneumoniae* isolates from Greek hospitals, collected as part of a national multicenter surveillance study.

Materials/methods: We tested 276 non-MBL carbapenemase-producing *K.pneumoniae* consecutive clinical strains isolated from unique patients at 15 hospitals in Greece, between November 2014 and April 2016. Susceptibility testing for IMP, IMP/REL (fixed concentration of 4 mg/L), meropenem (MEM), doripenem (DOR) and colistin (CST) was performed using the CLSI broth microdilution method. Additionally, MICs of fosfomycin (FM), tigecycline (TIG) and gentamicin (GM) were determined by Etest®. MICs were interpreted per EUCAST breakpoints. IMP/REL MICs were interpreted using the breakpoints proposed for IMP (S, ≤2 mg/L; R, >8 mg/L). Carbapenemase genes were detected using PCR.

Results: IMP/REL inhibited 97.7 % of the KPC-producing isolates at ≤2mg/L ($MIC_{50}/_{90}$, 0.25/2 mg/L) and was considerably more active than IMP ($MIC_{50}/_{90}$, 32/>64 mg/L), MER ($MIC_{50}/_{90}$, 64/>64 mg/L) and DOR ($MIC_{50}/_{90}$, 32/>64 mg/L). Of the comparator agents, gentamicin was the most active against KPC producers (69.8%), followed by colistin (66.0%), while fosfomycin showed enhanced *in vitro* activity against OXA-48 producers (71.4%). The distribution of MIC values is shown on the table. REL provided only weak potentiation of imipenem activity against eight isolates of *K. pneumoniae* with class D OXA-48 enzymes.

Conclusions: REL exhibited strong potential for restoring the *in vitro* activity of IMP against KPC-producing *K.pneumoniae* from Greek hospitals, lowering the imipenem MIC_{50} and MIC_{90} from 32 to 0.25 mg/L, and from >64 to 2 mg/L, respectively. Production of KPC carbapenemase represents the main cause of carbapenem resistance among *K.pneumoniae* in Greek hospitals (66.5%), and this carbapenemase appears to be very well inhibited by REL.

Table. MIC distribution of imipenem/relebactam and comparators of KPC and OXA-48-producing *K.pneumoniae* isolates

Organism / Genotype	Agent	MIC Distribution (mg/L)										MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S
		≤0.25	0.5	1	2	4	8	16	32	64	>64			
KPC-producers	IMP					2	28	66	44	94	28	32	>64	0.0
(n=262)	IMP/REL	145	76	22	13	3	2	1				0,25	2	97.7
	MER				1		22	41	53	42	103	64	>64	0.4
	DOR				3	28	56	29	36	60	50	32	>64	0.0
	CST		25	130	15	6	5	16	32	15	15	1	64	66.0
	FM					1	11	59	79	56	56	32	>64	57.2
	TIG	3	35	98	96	24	4	2				1	4	51.9
	GM		5	46	132	40	2	8	4	5	20	1	>64	69.8
OXA-producers*	IMP					5	6	2			1	8	16	0.0
(n=14)	IMP/REL				2	9	1	1	1			4	16	14.3
	MER						1	7	4	1	1	16	64	0.0
	DOR						7	6			1	16	16	0.0
	CST		3	6	2	1	1				1	32	64	42.9
	FM					1		9		1	3	16	>64	71.4
	TIG		3	6	2	1	1				1	1	8	64.3
	GM			2	2				1		9	>64	>64	28.6

* One isolate harboring also bla_{KPC} is included.

Shaded area indicates susceptible by EUCAST 2017 breakpoint