

Supplementary material. Table 1. Additional β -lactamases present among 75 KPC-producing isolates categorized as isolates carrying multiple β -lactamases.

Additional β -lactamases ^a	Organism	MIC (in $\mu\text{g/ml}$)	
		Meropenem	Meropenem-vaborbactam at fixed 8 $\mu\text{g/ml}$
CTX-M-15-like, OXA-1/30, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	≤ 0.06
CTX-M-15-like, SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
CTX-M-15-like, SHV WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
CTX-M-15-like, SHV WT	<i>Klebsiella pneumoniae</i>	4	≤ 0.06
CTX-M-15-like, SHV WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
CTX-M-15-like, SHV WT	<i>Klebsiella pneumoniae</i>	>64	2
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	2
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	0.12
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.5
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.5
CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
CMY-2-like, CTX-M-15-like, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	1
CMY-2-like, SHV WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
CMY-2-like, TEM WT	<i>Klebsiella pneumoniae</i>	>64	1
de-repressed AmpC, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	≤ 0.06
FOX-like, PSE-like, SHV ESBL	<i>Raoultella planticola</i>	16	≤ 0.06
FOX-like, TEM WT	<i>Klebsiella oxytoca</i>	4	≤ 0.06
OXA-1/30, SHV ESBL, TEM WT	<i>Klebsiella pneumoniae</i>	4	≤ 0.06
OXA-2-like, OXY derepressed	<i>Klebsiella oxytoca</i>	4	≤ 0.06
OXA-2-like, SHV ESBL	<i>Klebsiella oxytoca</i>	16	≤ 0.06
SHV ESBL, SHV WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESBL, SHV WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	4	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	16
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	1
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	0.12
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESBL, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06

Additional β -lactamases ^a	Organism	MIC (in $\mu\text{g/ml}$)	
		Meropenem	Meropenem-vaborbactam at fixed 8 $\mu\text{g/ml}$
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	0.12
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	1
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	1
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	4	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	64	0.5
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	1
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.5
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	8	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.5
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, SHV WT, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.25
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	64	0.25
SHV ESB, TEM WT	<i>Raoultella ornithinolytica</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	>64	0.5
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Enterobacter cloacae</i>	2	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	32	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	16	≤ 0.06
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	64	0.12
SHV ESB, TEM WT	<i>Klebsiella pneumoniae</i>	64	≤ 0.06
SHV ESB, TEM WT	<i>Enterobacter cloacae</i>	8	≤ 0.06

a. WT = wildtype or narrow spectrum enzymes.

Table 2. Expression of efflux pumps and outer membrane protein results for three isolates displaying elevated meropenem-vaborbactam MIC values that did not carry metallo- β -lactamase encoding genes.

Country	Organism	PFGE	Relative expression ^{a,b}			
			<i>acrA</i>	<i>ompK35</i>	<i>ompK36</i>	<i>ompK37</i>
Israel	<i>K. pneumoniae</i>	A	7.80	0.35	4.49	<u>≤ 0.01</u>
USA	<i>K. pneumoniae</i>	B	6.62	0.76	0.19	<u>0.01</u>
USA	<i>K. pneumoniae</i>	C	<u>22.93</u>	0.36	0.46	<u>0.12</u>

a. Expression was normalized with a house-keeping gene (*gyrA*) and compared to the expression of *K. pneumoniae* ATCC 13883.

b. Expression values considered significant are underlined.