Polymyxin triple combinations against polymyxin-resistant, multidrug-resistant KPC-producing *Klebsiella pneumoniae*

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Supplementary data

TABLE S1. Log changes in viable cell counts at 1, 5, 12, 13, 24, 25, 36, 37, and 48h with clinically relevant concentrations of polymyxin B, rifampicin and amikacin as monotherapy and double- and triple-combination therapies against two polymyxin-resistant, MDR *K. pneumoniae* isolates using one-compartment *in vitro* model[a].

Isolate	Time (h)	Log change $[\log_{10}(CFU_t) - \log_{10}(CFU_0)]$							
		Control	PMB	RIF	AMI	PMB + RIF	PMB + AMI	RIF + AMI	PMB + RIF+ AMI
ATH 16	1	0.02	-0.09	-0.88	-0.75	-2.73	-0.17	-0.11	-3.59
	5	1.74	1.74	1.62	1.65	-4.93	-2.57	1.27	-6.59
	12	1.82	1.97	1.95	1.84	-4.93	-2.48	1.67	-6.59
	13	1.86	1.73	1.89	1.64	-4.93	-2.54	2.28	-6.59
	24	1.78	1.77	1.76	1.43	-4.23	1.85	1.69	-6.59
	25	1.67	1.78	1.68	1.60	-2.42	2.03	1.79	-6.59
	36	1.80	1.72	1.76	1.45	-2.93	1.77	1.87	-4.34
	37	1.58	1.75	1.81	1.10	-2.76	1.12	1.68	-4.99
	48	1.52	1.52	1.65	1.49	-1.61	1.74	1.37	-4.45
BD 32	1	0.43	0.43	0.39	0.40	-0.80	0.04	-0.79	-1.37
	5	1.68	1.61	1.77	1.33	-3.24	-0.32	1.12	-3.00
	12	1.84	1.90	1.69	1.61	-2.27	1.70	1.45	-3.32
	13	1.77	1.59	1.74	1.51	-2.99	1.64	1.36	-3.59
	24	1.49	1.82	1.39	1.26	-2.58	1.64	1.22	-3.60
	25	1.70	1.79	1.70	1.41	-2.41	1.75	1.44	-3.26
	36	1.68	2.02	1.67	1.14	-1.48	1.63	1.76	-5.17
	37	1.45	1.42	1.93	1.56	-2.21	1.50	1.68	-4.95
	48	1.44	1.72	1.42	1.19	-0.49	1.40	1.23	-5.35

[a]PMB, polymyxin B (constant concentration of 2 μg/mL); RIF, rifampicin (C_{max}, 5 μg/mL; $t_{1/2}$, 2.5h); AMI, amikacin (C_{max}, 20 μg/mL; $t_{1/2}$, 2.5h). A red background indicates additive against monotherapy; a green background indicates synergistic against monotherapy; black numbers (underlined) in green background indicate synergistic against monotherapy and additive against double combination therapy; red numbers in green background indicate synergistic against both monotherapy and double-combination therapy.

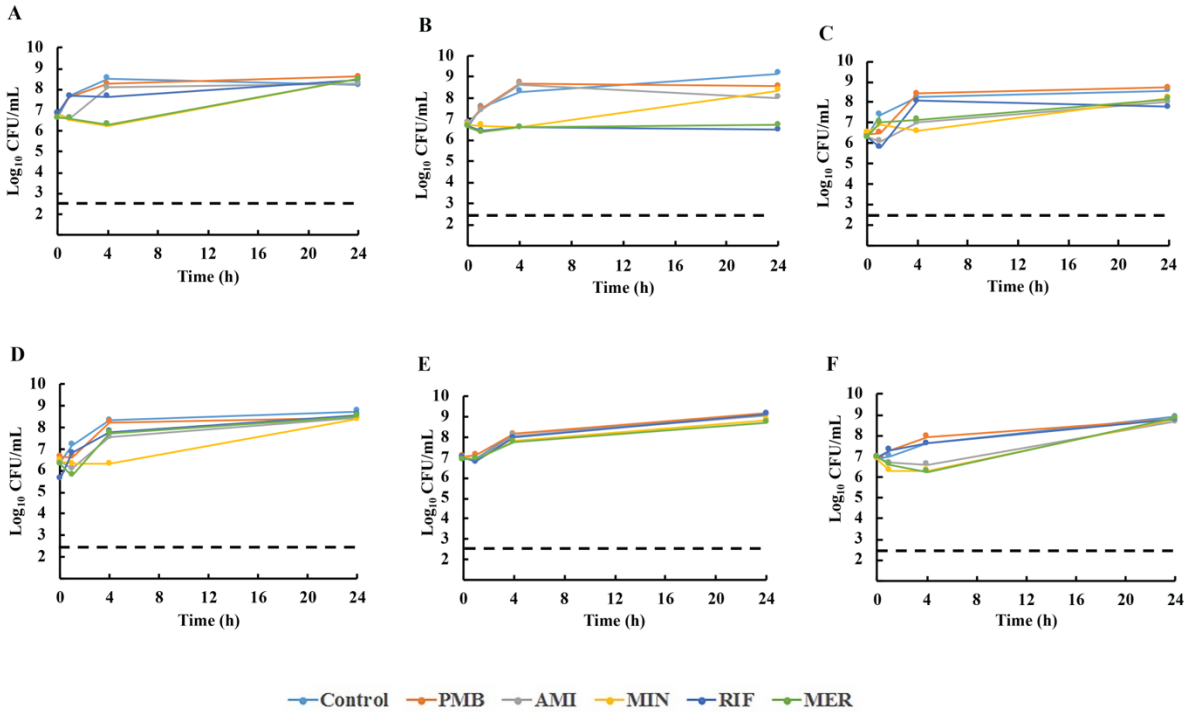

FIG S1. Static time-kill curves with clinically relevant concentrations of polymyxin B (PMB, 2 µg/mL), amikacin (AMI, 20 µg/mL), minocycline (MIN, 4 µg/mL), rifampicin (RIF, 5 µg/mL) and meropenem (MER, 50 µg/mL) as monotherapy with an inoculum of ~10^7 CFU/mL. (**A**) ATH 8; (**B**) ATH 16; (**C**) ATH 18; (**D**) ATH 24; (**E**) BD 32; and (**F**) BD 46. The *y*-axis starts from the limit of detection (~1.3-$\log_{10}$ CFU/mL) and the dashed horizontal line represents the limit of quantification.

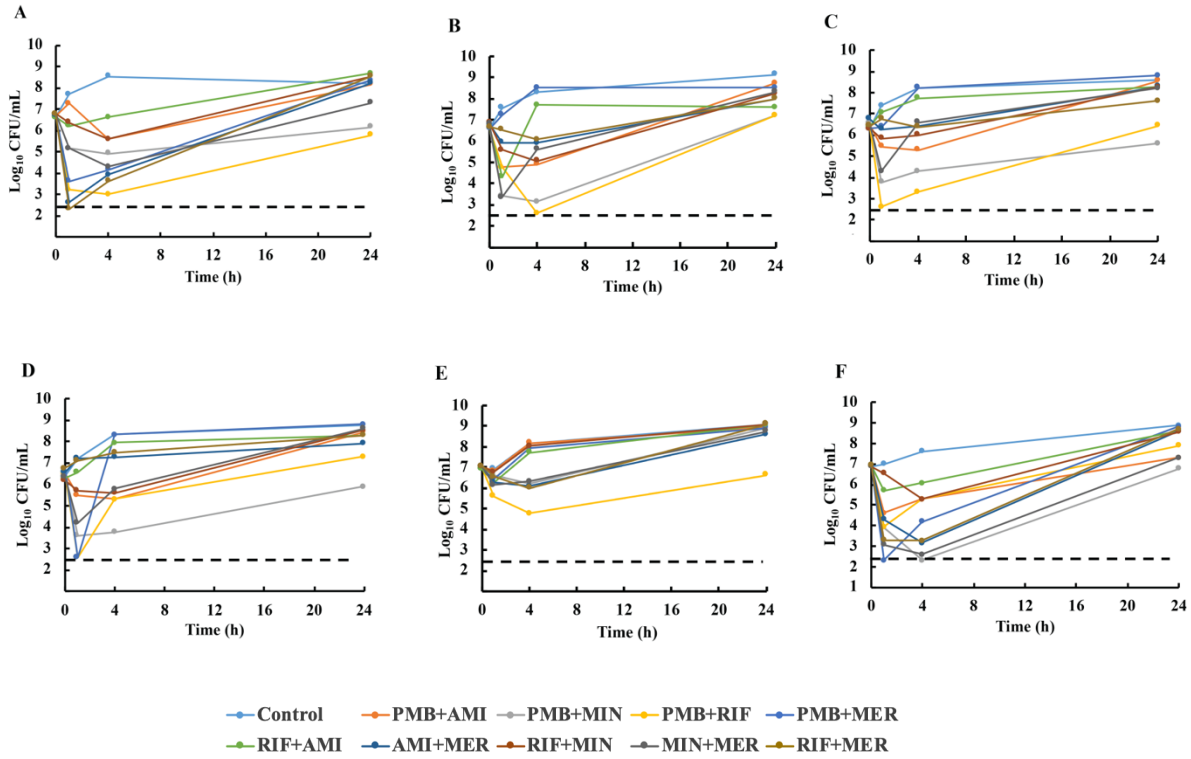

FIG S2. Static time-kill curves with clinically relevant concentrations of polymyxin B (PMB, 2 μg/mL), amikacin (AMI, 20 μg/mL), minocycline (MIN, 4 μg/mL), rifampicin (RIF, 5 μg/mL) and meropenem (MER, 50 μg/mL) as various double combinations with an inoculum of ~10^7 CFU/mL. (**A**) ATH 8; (**B**) ATH 16; (**C**) ATH 18; (**D**) ATH 24; (**E**) BD 32; and (**F**) BD 46. The *y*-axis starts from the limit of detection (~1.3-$\log_{10}$ CFU/mL) and the dashed horizontal line represents the limit of quantification.

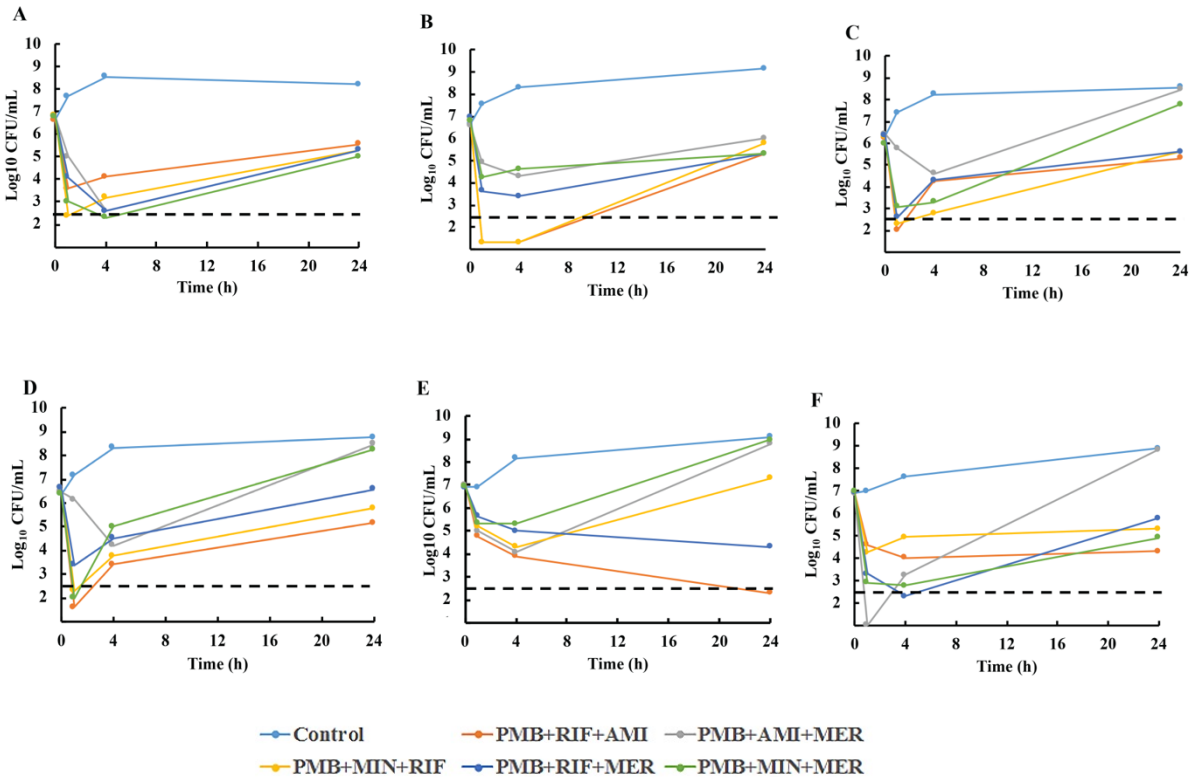

FIG S3. Static time-kill curves with clinically relevant concentrations of polymyxin B (PMB, 2 µg/mL), amikacin (AMI, 20 µg/mL), minocycline (MIN, 4 µg/mL), rifampicin (RIF, 5 µg/mL) and meropenem (MER, 50 µg/mL) as various polymyxin B-based triple combinations with an inoculum of ~10^7 CFU/mL. (**A**) ATH 8; (**B**) ATH 16; (**C**) ATH 18; (**D**) ATH 24; (**E**) BD 32; and (**F**) BD 46. The *y*-axis starts from the limit of detection (~1.3-$\log_{10}$ CFU/mL) and the dashed horizontal line represents the limit of quantification.