

**Table S1.** MIC range of gram-negative pathogens (n=139 from 116 patients) isolated from patients included in the pharmacokinetic/pharmacodynamic analysis.

Pathogen	No. of Isolates	MIC Range (mg/L)
<b>Meropenem</b>		
<i>Klebsiella pneumoniae</i>	17	0.12–16
<i>Pseudomonas aeruginosa</i>	16	0.12–8
<i>Escherichia coli</i>	9	0.12–1
<i>Acinetobacter baumannii</i>	6	0.12–32
<i>Proteus mirabilis</i>	3	0.12
<i>Enterobacter aerogenes</i>	3	0.12–0.25
<i>Enterobacter cloacae</i>	2	0.12
<i>Enterobacter absyriae</i>	1	0.25
<i>Serratia marcescens</i>	1	0.12
<i>Hafnia alvei</i>	1	0.12
<i>Klebsiella variicola</i>	1	0.12
<i>Klebsiella oxytoca</i>	1	0.12
<i>Citrobacter freundii</i>	1	0.12
<i>Morganella morganii</i>	1	0.12
<b>Ceftazidime</b>		
<i>Pseudomonas aeruginosa</i>	2	1–2
<i>Escherichia coli</i>	2	1
<i>Klebsiella pneumoniae</i>	2	1
<i>Klebsiella oxytoca</i>	1	1
<i>Proteus mirabilis</i>	1	1
<i>Enterobacter aerogenes</i>	1	1
<b>Ceftazidime-Avibactam</b>		
<i>Klebsiella pneumoniae</i>	7	2–4
<i>Pseudomonas aeruginosa</i>	3	4–8
<i>Enterobacter aerogenes</i>	1	2
<b>Piperacillin-Tazobactam</b>		
<i>Escherichia coli</i>	16	4–16
<i>Pseudomonas aeruginosa</i>	12	4–16
<i>Klebsiella pneumoniae</i>	9	8–16
<i>Enterobacter aerogenes</i>	5	8–16

<i>Proteus mirabilis</i>	3	8
<i>Klebsiella oxytoca</i>	3	8
<i>Serratia marcescens</i>	2	8–16
<i>Citrobacter koseri</i>	2	8
<i>Enterobacter cloacae</i>	1	8
<i>Klebsiella variicola</i>	1	8
<i>Providencia stuartii</i>	1	8
<i>Prevotella buccae</i>	1	4

MIC: minimum inhibitory concentration.

**Table S2.** Demographics and clinical features of patients with Gram-negative infections showing microbiological failure and/or resistance development.

Case ID	Age/Sex	Antibiotic Therapy/ Dosage	Combination Therapy	Type of Infection	Isolates/MIC (Index Cultures)	C <sub>ss</sub> /MIC	Latency for Microbiological Failure (Days)	Isolates/MIC (Relapse)	Outcome
#1	51/M	Meropenem 500 mg q6h over 6h infusion	No	VAP	<i>Pseudomonas aeruginosa</i> – 8 mg/L	3.84	14	<i>Pseudomonas aeruginosa</i> – 32 mg/L (VAP)	Recovered
#2	66/M	Meropenem 1 g q6h over 6h infusion	Fosfomycin	VAP	<i>Pseudomonas aeruginosa</i> – 8 mg/L	1	8	<i>Pseudomonas aeruginosa</i> – 8 mg/L (BSI)	Died
#3	31/M	Meropenem 1 g q6h over 6h infusion	Fosfomycin + Tigecycline	cIAI	<i>Acinetobacter baumannii</i> – 32 mg/L	1.25	13	<i>Acinetobacter baumannii</i> 32 mg/L (cIAI)	Died
#4	36/F	Meropenem 500 mg q6h over 6h infusion	No	BSI/VAP	<i>Pseudomonas aeruginosa</i> – 1 mg/L	2.5	7	<i>Pseudomonas aeruginosa</i> – 8 mg/L (VAP)	Recovered
#5	55/F	Meropenem 1 g q6h over 6h infusion	Colistin	VAP	<i>Acinetobacter baumannii</i> – 32 mg/L	1.23	9	<i>Acinetobacter baumannii</i> – >32 mg/L (VAP)	Recovered
#6	56/M	Meropenem 1 g q6h over 6h infusion	Colistin	VAP	<i>Acinetobacter baumannii</i> – 32 mg/L	0.44	14	<i>Acinetobacter baumannii</i> – 32 mg/L (VAP)	Died
#7	66/F	Meropenem 500 mg q6h over 6h infusion	No	CR-BSI	ESBL-producing Kp – 1 mg/L	18.9	14	ESBL-producing Kp – 1 mg/L (CR-BSI)	Died
#8	52/M	Meropenem 1 g q6h over 6h infusion	No	VAP	<i>Pseudomonas aeruginosa</i> – 1 mg/L	33.1	12	<i>Pseudomonas aeruginosa</i> – 32 mg/L (VAP)	Recovered
#9	84/M	Meropenem 500 mg q8h over 8h infusion	No	cIAI	<i>Enterobacter aerogenes</i> – 0.25 mg/L	10.8	10	<i>Enterobacter aerogenes</i> – 2 mg/L (cIAI)*	Recovered

#10	74/M	Meropenem 500 mg q6h over 6h infusion	Tigecycline	cIAI	<i>Acinetobacter baumannii</i> – 32 mg/L	0.37	7	<i>Acinetobacter baumannii</i> – >32 mg/L (cIAI)	Died
#11	73/M	Meropenem 250 mg q6h over 6h infusion	No	VAP	<i>Pseudomonas ae- ruginosa</i> – 4 mg/L	3.88	12	<i>Pseudomonas ae- ruginosa</i> – 8 mg/L (VAP)	Died
#12	64/M	Meropenem 1 g q6h over 6h in- fusion	Colistin	BSI/VA P	OXA-48-pro- ducing Kp – 16 mg/L	2.19	25	OXA-48-pro- ducing Kp – 32 mg/L (VAP)	Recov- ered
#13	15/M	Meropenem 1 g q6h over 6h in- fusion	Fosfomycin + Tigecycline	VAP	<i>Pseudomonas ae- ruginosa</i> – 1 mg/L	5	19	<i>Pseudomonas ae- ruginosa</i> – 16 mg/L (VAP)	Recov- ered
#14	77/M	Ceftazidime-avi- bactam 2.5 g q8h over 8h infusion	Tigecycline	cIAI/BSI	KPC-producing Kp – 4 mg/L	2.85	10	<i>Klebsiella pneu- moniae</i> KPC – 64 mg/L (VAP)	Recov- ered
#15	16/M	Ceftazidime-avi- bactam 2.5 g q8h over 8h infusion	No	VAP	KPC-producing Kp – 2 mg/L	3.15	8	<i>Klebsiella pneu- moniae</i> KPC – 4 mg/L (VAP)	Recov- ered
#16	46/M	Ceftazidime-avi- bactam 2.5 g q8h over 8h infusion	No	VAP	KPC/OXA-48- producing Kp – 4 mg/L	1.85	15/31	KPC/OXA-48- producing Kp – >16 mg/L (CR- BSI)	Recov- ered
#17	76/F	Piperacillin-tazo- bactam 18 g/day CI	No	VAP	<i>Enterobacter aer- ogenes</i> – 8 mg/L	14.63	15	ESBL-producing <i>Enterobacter aero- genes</i> – 16 mg/L (BSI)*	Recov- ered
#18	65/M	Piperacillin-tazo- bactam 18 g/day CI	No	VAP	Kp – 8 mg/L	3.5	8	Kp – 8 mg/L (VAP)	Recov- ered
#19	60/M	Piperacillin-tazo- bactam 18 g/day CI	No	VAP	<i>Pseudomonas ae- ruginosa</i> – 8 mg/L	4.63	8	<i>Pseudomonas ae- ruginosa</i> – >16 mg/L (VAP)	Died

#20	16/M	Piperacillin-tazobactam 13.5 g/day CI	No	cIAI/VAP	Kp – 8 mg/L	2.5	7	Kp - >128 mg/L (VAP)	Recovered
#21	37/M	Piperacillin-tazobactam 9 g/day CI	No	VAP	Kp – 16 mg/L	2.02	10	Kp - >16 mg/L (VAP)	Recovered
#22	72/M	Piperacillin-tazobactam 18 g/day CI	No	BSI	<i>Pseudomonas aeruginosa</i> – 8 mg/L	4.46	28	<i>Pseudomonas aeruginosa</i> – >16 mg/L (cUTI)	Recovered
#23	73/M	Piperacillin-tazobactam 18 g/day CI	No	VAP	<i>Pseudomonas aeruginosa</i> – 8 mg/L	36	11	<i>Pseudomonas aeruginosa</i> – >16 mg/L (VAP)	Died
#24	80/M	Piperacillin-tazobactam 18 g/day CI	No	VAP	<i>Pseudomonas aeruginosa</i> – 8 mg/L	4.83	14	<i>Pseudomonas aeruginosa</i> – 8 mg/L (VAP)	Recovered
#25	15/M	Piperacillin-tazobactam 18 g/day CI	Fosfomycin	VAP	<i>Pseudomonas aeruginosa</i> – 8 mg/L	2.16	9	<i>Pseudomonas aeruginosa</i> >16 mg/L (VAP)	Recovered
#26	15/M	Piperacillin-tazobactam 22.5 g/day CI	Fosfomycin + Colistin	VAP	<i>Pseudomonas aeruginosa</i> – 16 mg/L	4.17	20	<i>Pseudomonas aeruginosa</i> >16 mg/L (VAP)	Recovered

\* reduced susceptibility to carbapenems; BSI: bloodstream infection; cIAI; complicated intrabdominal infection; CI: continuous infusion; CR-BSI: catheter-related bloodstream infection; Css: concentration at steady state; cUTI: complicated urinary tract infection; ESBL: extended-spectrum beta-lactamase; ICU: intensive care unit; KPC: Klebsiella pneumoniae carbapenemase; Kp: Klebsiella pneumoniae; MIC: minimum inhibitory concentration; VAP: ventilator-associated pneumonia.