

Supplementary Materials: Parametric and Nonparametric Population Pharmacokinetic Models to Assess Probability of Target Attainment of Imipenem Concentrations in Critically Ill Patients

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Table S1. Population parameter estimates. V_c : central distribution volume, K_{cp} : rate constant from central to peripheral compartment, K_{pc} : rate constant from peripheral to central compartment, K_e : elimination rate constant, K_{ecov} : covariate effect on K_e , CV: coefficient of variation.

Parameter	NONMEM		Pmetrics	
	Parameter estimate	CV (%)	Mean parameter estimate	CV (%)
V_c (L)	29.6	-	31.1	42.6
K_{cp} (h^{-1})	0.166	-	0.374	81.2
K_{pc} (h^{-1})	0.195	-	0.495	72.0
K_e (h^{-1})	0.637	19.0	0.681	34.0
K_{ecov}	0.655	-	0.658	55.2
Parametric model (NONMEM): exponential error (mg/L)	0.348	-	N/A	-
Nonparametric model (Pmetrics): gamma (error model)	N/A	-	3.40	-

Table S2. Probabilities of target attainment (PTA) for targets of 50% and 100% $fT_{>MIC}$ attained by several imipenem dosing regimens and eGFR values (measured by the CKD-EPI equation unadjusted for BSA) of 150, 120 and 90 mL/min. The PTAs were calculated by Monte Carlo simulations ($n = 5000$) using parametric (a) and nonparametric (b) popPK models. The grey shaded cells indicate the highest MIC for which the PTA is higher than 97.5%.

Table S2a. PTA simulations using the parametric model.

eGFR (mL/min)	Dose regimen	Target $fT_{>MIC}$	PTA (%) at specified MIC (mg/L)													
			0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	
150	500mg q6h	100%	100	100	100	99	81	22	0	0	0	0	0	0	0	
	1000mg q8h	100%	100	100	100	100	95	47	4	0	0	0	0	0	0	
	1000mg q6h	100%	100	100	100	100	99	84	27	1	0	0	0	0	0	
	500mg q6h	50%	100	100	100	100	100	100	84	15	0	0	0	0	0	
	1000mg q8h	50%	100	100	100	100	100	100	91	40	1	0	0	0	0	
	1000mg q6h	50%	100	100	100	100	100	100	100	94	32	0	0	0	0	
120	500mg q6h	100%	100	100	100	100	94	50	3	0	0	0	0	0	0	
	1000mg q8h	100%	100	100	100	100	99	76	15	0	0	0	0	0	0	
	1000mg q6h	100%	100	100	100	100	100	96	58	5	0	0	0	0	0	
	500mg q6h	50%	100	100	100	100	100	100	96	39	0	0	0	0	0	
	1000mg q8h	50%	100	100	100	100	100	100	98	71	6	0	0	0	0	
	1000mg q6h	50%	100	100	100	100	100	100	100	99	63	0	0	0	0	
90	500mg q6h	100%	100	100	100	100	100	84	21	0	0	0	0	0	0	
	1000mg q8h	100%	100	100	100	100	100	96	50	2	0	0	0	0	0	
	1000mg q6h	100%	100	100	100	100	100	100	88	26	0	0	0	0	0	
	500mg q6h	50%	100	100	100	100	100	100	100	77	1	0	0	0	0	
	1000mg q8h	50%	100	100	100	100	100	100	100	93	28	0	0	0	0	

1000mg q6h	50%	100	100	100	100	100	100	100	100	100	90	4	0	0	0
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Table S2b. PTA simulations using the nonparametric model.

eGFR (mL/min)	Dose regimen	Target $fT_{>MIC}$	PTA (%) at specified MIC (mg/L)												
			0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64
150	500mg q6h	100%	100	99	98	92	78	47	13	2	1	0	0	0	0
	1000mg q8h	100%	99	99	96	90	79	56	24	4	1	0	0	0	0
	1000mg q6h	100%	100	100	100	98	94	81	39	6	1	0	0	0	0
	500mg q6h	50%	100	100	100	100	100	96	74	25	5	1	0	0	0
	1000mg q8h	50%	100	100	100	100	100	98	87	49	13	2	0	0	0
	1000mg q6h	50%	100	100	100	100	100	100	98	81	31	5	1	0	0
120	500mg q6h	100%	100	100	100	98	91	64	20	3	1	0	0	0	0
	1000mg q8h	100%	100	100	99	97	90	72	35	6	1	0	0	0	0
	1000mg q6h	100%	100	100	100	100	99	93	52	10	2	1	0	0	0
	500mg q6h	50%	100	100	100	100	100	99	88	39	7	2	1	0	0
	1000mg q8h	50%	100	100	100	100	100	100	96	67	20	3	1	0	0
	1000mg q6h	50%	100	100	100	100	100	100	99	91	44	8	1	1	0
90	500mg q6h	100%	100	100	100	100	98	87	36	6	2	1	0	0	0
	1000mg q8h	100%	100	100	100	100	99	91	57	11	2	1	0	0	0
	1000mg q6h	100%	100	100	100	100	100	99	67	15	4	1	0	0	0
	500mg q6h	50%	100	100	100	100	100	100	95	59	13	3	1	0	0
	1000mg q8h	50%	100	100	100	100	100	100	98	85	36	6	1	0	0
	1000mg q6h	50%	100	100	100	100	100	100	100	97	63	15	3	1	0