TABLE S1 Summary of univariable and multivariable population PK model building process

Univariable analysis for each parameter	Type of variables	Population model		OFV	ΔOFV
		Vc	CL		
Base model (BW on Vc and CL)		$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1608.55	-
eGFR on CL	Continuous	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (eGFR/38.2)^{\theta CL\text{-}eGFR}$	1533.21	−75.34
SIRS score on CL	Categorical	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (1 + \theta_{CL\text{-}SIRS})^{SIRS}$	1555.02	−53.53
Daily urine excretion on CL	Continuous	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (UE/480)^{\theta CL\text{-}UE}$	1610.21	+1.66
Daily ascites excretion on CL	Continuous	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (AE/105)^{\theta CL\text{-}AE}$	1608.45	−0.10
CRRT on CL	Categorical	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (1 + \theta_{CL\text{-}CRRT})^{CRRT}$	1612.58	+4.03
Liver transplantation on CL	Categorical	$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (1 + \theta_{CL\text{-}LT})^{LT}$	1588.54	−20.01
eGFR on Vc	Continuous	$Vc = \theta_V \times (BW)^{1.0} \times (eGFR / 38.2)^{\theta V-eGFR}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1561.46	−47.09
SIRS score on Vc	Categorical	$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}SIRS})^{SIRS}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1533.22	−75.33
Daily urine excretion on Vc	Continuous	$Vc = \theta_V \times (BW)^{1.0} \times (UE/480)^{\theta V\text{-}UE}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1613.71	+5.16
Daily ascites excretion on Vc	Continuous	$Vc = \theta_V \times (BW)^{1.0} \times (AE/105)^{\theta V\text{-}AE}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1613.65	+5.10
CRRT on Vc	Categorical	$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}CRRT})^{CRRT}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1583.59	−24.96
Liver transplantation on Vc	Categorical	$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}LT})^{LT}$	$CL = \theta_{CL} \times (BW)^{1.0}$	1606.57	−1.98
Multivariable Model					
Full model		$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}CRRT})^{CRRT}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (eGFR/38.2)^{\theta CL\text{-}eGFR} \times (1 + \theta_{CL\text{-}SIRS})^{SIRS} \times (1 + \theta_{CL\text{-}LT})^{LT}$	1512.41	-
Final model (- LT on CL)		$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}CRRT})^{CRRT}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (eGFR/38.2)^{\theta CL\text{-}eGFR} \times (1 + \theta_{CL\text{-}SIRS})^{SIRS}$	1514.70	+2.29
(- eGFR on CL)		$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}CRRT})^{CRRT}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (1 + \theta_{CL\text{-}SIRS})^{SIRS}$	1545.02	+32.61
(- CRRT on Vc)		$Vc = \theta_V \times (BW)^{1.0}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (eGFR/38.2)^{\theta CL\text{-}eGFR} \times (1 + \theta_{CL\text{-}SIRS})^{SIRS}$	1538.01	+25.6
(- SIRS score on CL)		$Vc = \theta_V \times (BW)^{1.0} \times (1 + \theta_{V\text{-}CRRT})^{CRRT}$	$CL = \theta_{CL} \times (BW)^{1.0} \times (eGFR/38.2)^{\theta CL\text{-}eGFR}$	1525.14	+12.73

Vc, central volume of distribution; CL, clearance; OFV, objective function value; ΔOFV, change in OFV from base model or full model; BW, body weight (kg);eGFR, estimated glomerular filtration rate (ml/min); SIRS, systemic inflammatory response syndrome; UE, daily urine excretion; AE, daily ascites excretion CRRT, continuous renal replacement therapy; LT, liver transplantation.

TABLE S2 The probability of target attainment at levels of 40% and 100% time during unbound concentration exceeds the MIC in each of the four meropenem dosing regimens

Target MIC	Infusion rate	%f_uT>MIC	SIRS status	CRRT status	SCr-based eGFR, ml/min														
					10				25				50				100		
					10 mg/kg q8h	20 mg/kg q8h	40 mg/kg q8h	80 mg/kg q8h	10 mg/kg q8h	20 mg/kg q8h	40 mg/kg q8h	80 mg/kg q8h	10 mg/kg q8h	20 mg/kg q8h	40 mg/kg q8h	80 mg/kg q8h	10 mg/kg q8h	20 mg/kg q8h	40 mg/kg q8h
MIC = 1	0.5 h	40	−	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			−	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			+	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	82.6	100.0	100.0
			+	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
		100	−	−	68.3	100.0	100.0	100.0	14.4	69.9	100.0	100.0	2.0	27.3	80.0	100.0	0.2	7.3	44.5
			−	+	100.0	100.0	100.0	100.0	79.7	100.0	100.0	100.0	34.1	97.2	100.0	100.0	9.4	61.5	100.0
			+	−	22.7	81.0	100.0	100.0	2.0	24.1	77.7	100.0	0.0	4.0	35.2	85.1	0.0	0.7	11.3
			+	+	89.9	100.0	100.0	100.0	31.0	94.4	100.0	100.0	6.2	49.8	100.0	100.0	0.7	18.6	70.4
	3 h	40	−	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			−	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			+	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			+	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
		100	−	−	94.8	100.0	100.0	100.0	37.8	96.7	100.0	100.0	8.4	54.1	100.0	100.0	1.3	21.2	74.3
			−	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	66.0	100.0	100.0	100.0	27.3	92.9	100.0
			+	−	49.6	100.0	100.0	100.0	7.2	52.0	100.0	100.0	0.6	14.8	63.5	100.0	0.0	2.8	28.9
			+	+	100.0	100.0	100.0	100.0	61.3	100.0	100.0	100.0	20.6	85.2	100.0	100.0	4.0	45.5	99.6
MIC = 2	0.5 h	40	−	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	84.7	100.0	100.0	100.0	47.3	100.0	100.0
			−	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	95.7	100.0	100.0
			+	−	100.0	100.0	100.0	100.0	61.6	100.0	100.0	100.0	11.9	86.5	100.0	100.0	2.2	47.3	100.0
			+	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	52.8	100.0	100.0	100.0	18.5	100.0	100.0
		100	−	−	10.6	67.4	100.0	100.0	1.1	25.6	84.5	100.0	0.0	2.3	26.7	79.8	0.0	0.2	7.3
			−	+	60.1	100.0	100.0	100.0	19.5	92.8	100.0	100.0	1.4	33.1	97.1	100.0	0.1	9.4	62.2
			+	−	0.3	14.9	100.0	100.0	0.0	1.3	31.5	100.0	0.0	0.0	1.7	32.9	0.0	0.0	0.1
			+	+	3.8	55.4	100.0	100.0	0.3	16.6	77.3	100.0	0.0	0.9	20.0	71.9	0.0	0.0	4.5
	3 h	40	−	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			−	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
			+	−	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	98.6	100.0	100.0	100.0	62.4	100.0	100.0

			+	+	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	97.0	100.0	100.0	100.0	59.1	100.0	100.0
		100	−	−	26.0	95.3	100.0	100.0	4.7	52.8	100.0	100.0	0.1	8.6	55.3	100.0	0.0	1.0	21.2
			−	+	86.7	100.0	100.0	100.0	41.9	100.0	100.0	100.0	5.1	65.4	100.0	100.0	0.7	27.1	93.8
			+	−	1.3	47.1	100.0	100.0	0.0	6.2	81.5	100.0	0.0	1.5	9.5	77.2	0.0	0.0	1.0
			+	+	12.5	86.1	100.0	100.0	1.5	39.9	100.0	100.0	0.0	4.9	47.5	100.0	0.0	0.6	17.1
		40	−	−	81.8	100.0	100.0	100.0	24.4	100.0	100.0	100.0	3.4	84.3	100.0	100.0	0.3	46.5	100.0
			−	+	99.6	100.0	100.0	100.0	43.7	100.0	100.0	100.0	9.4	100.0	100.0	100.0	1.4	95.6	100.0
			+	−	32.7	100.0	100.0	100.0	2.9	84.6	100.0	100.0	0.2	36.6	100.0	100.0	0.0	10.5	81.8
	0.5 h		+	+	54.1	100.0	100.0	100.0	8.8	100.0	100.0	100.0	0.9	89.4	100.0	100.0	0.0	49.2	100.0
		100	−	−	0.1	9.8	67.4	100.0	0.0	0.5	15.9	70.5	0.0	0.0	2.1	26.5	0.0	0.0	0.4
			−	+	2.2	60.3	100.0	100.0	0.0	11.4	80.2	100.0	0.0	1.1	34.3	96.2	0.0	0.0	9.3
			+	−	0.0	1.0	21.8	80.7	0.0	0.0	2.1	24.8	0.0	0.0	0.1	4.3	0.0	0.0	0.0
MIC = 4			+	+	0.1	17.0	90.0	100.0	0.0	1.0	32.8	95.0	0.0	0.0	6.4	50.9	0.0	0.0	0.7
		40	−	−	100.0	100.0	100.0	100.0	64.2	100.0	100.0	100.0	20.0	100.0	100.0	100.0	3.5	100.0	100.0
			-	+	100.0	100.0	100.0	100.0	53.5	100.0	100.0	100.0	14.3	100.0	100.0	100.0	2.8	100.0	100.0
			+	−	76.0	100.0	100.0	100.0	19.3	100.0	100.0	100.0	2.3	100.0	100.0	100.0	0.1	95.0	100.0
	3 h		+	+	64.6	100.0	100.0	100.0	13.7	100.0	100.0	100.0	1.4	100.0	100.0	100.0	0.1	94.1	100.0
		100	−	−	0.5	26.2	96.2	100.0	0.0	2.1	39.0	98.0	0.0	0.1	8.5	55.3	0.0	0.0	1.4
			−	+	6.5	87.6	100.0	100.0	0.1	29.3	100.0	100.0	0.0	5.4	63.8	100.0	0.0	0.6	26.7
			+	−	0.0	4.1	48.9	100.0	0.0	0.1	7.9	53.3	0.0	0.0	0.6	14.7	0.0	0.0	0.0
			+	+	0.4	38.9	100.0	100.0	0.0	4.4	63.2	100.0	0.0	0.2	20.6	84.3	0.0	0.0	4.0
		40	−	−	0.4	82.2	100.0	100.0	0.0	23.7	100.0	100.0	0.0	3.6	85.8	100.0	0.0	0.4	47.6
			−	+	0.5	100.0	100.0	100.0	0.0	41.0	100.0	100.0	0.0	9.7	100.0	100.0	0.0	1.7	96.3
			+	−	0.0	34.5	100.0	100.0	0.0	3.4	82.8	100.0	0.0	0.3	36.2	100.0	0.0	0.0	10.8
	0.5 h		+	+	0.0	56.6	100.0	100.0	0.0	8.3	100.0	100.0	0.0	0.8	87.5	100.0	0.0	0.0	49.4
		100	−	−	0.0	0.1	11.3	68.0	0.0	0.0	0.4	16.1	0.0	0.0	1.1	34.8	0.0	0.0	0.0
			-	+	0.0	2.3	62.9	100.0	0.0	0.0	11.2	80.1	0.0	0.0	0.0	0.1	0.0	0.0	0.1
			+	−	0.0	0.0	1.0	23.5	0.0	0.0	0.0	1.8	0.0	0.0	0.0	2.3	0.0	0.0	0.0
MIC = 8			+	+	0.0	0.1	18.9	91.2	0.0	0.0	1.2	31.9	0.0	0.0	0.0	6.0	0.0	0.0	0.0
		40	−	−	0.9	100.0	100.0	100.0	0.0	62.4	100.0	100.0	0.0	19.7	100.0	100.0	0.0	4.6	100.0
			−	+	0.4	100.0	100.0	100.0	0.0	51.5	100.0	100.0	0.0	13.9	100.0	100.0	0.0	2.7	100.0
			+	−	0.0	75.9	100.0	100.0	0.0	18.6	100.0	100.0	0.0	2.7	100.0	100.0	0.0	0.2	96.0
	3 h		+	+	0.0	66.8	100.0	100.0	0.0	12.1	100.0	100.0	0.0	1.4	100.0	100.0	0.0	0.1	94.8
		100	−	−	0.0	0.3	27.6	96.9	0.0	0.0	2.1	38.5	0.0	0.0	0.1	8.3	0.0	0.0	0.0
			−	+	0.0	7.2	89.5	100.0	0.0	0.2	28.2	100.0	0.0	0.0	5.0	64.8	0.0	0.0	0.7

+	−	0.0	0.0	4.5	50.7	0.0	0.0	0.1	7.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0
+	+	0.0	0.4	40.7	100.0	0.0	0.0	4.3	62.3	0.0	0.0	0.3	19.7	0.0	0.0	0.0

SCr, serum creatinine; eGFR, estimated glomerular filtration rate; SIRS, systemic inflammatory response syndrome; CRRT, continuous renal replacement therapy. Shaded blocks indicate probability target attainment >90%.