

Table 1 Meropenem 1g q8h intermittent 0.5hr-pump infusion in ICU septic patients

Number of subjects	Parameters PK data analysis			Software	Blood sampling	PTA %f Δ T>MIC		
	$t_{(1/2)\beta}$ (h)	CL _T (L/h)	Vd ^{ss} (L)			MIC 1 mg/L	MIC 2 mg/L	MIC 4 mg/L
Reference data Healthy volunteers				Noncompartmental data analysis	Number samples			
[21] Nilsson-Ehle (1991) N=8 1g q8h	1.0/0.1 (0.9-1.1)	11.3/1.9 (9.4-13.1)	12.5/1.5 (11.0-14.0)	Two compartments	15	NAP	NAP	NAP
ICU Critically ill septic patients-preserved/augmented CLcr								
[23] Kupa (2019) G1 N=12 1g q8h	2.0 (1.8-2.1)	5.3 (5.2-5.4)	15.4 (14.1-16.2)	One compartment	5	12/12 100% f Δ T>MIC C	12/12 100% f Δ T>MIC	3/12 100% f Δ T>MIC IC
[24] Gonçalves- Pereira (2014) N=15 1g q8h	2.3 (1.8-3.1)	4.4 (2.7-7.2)	15.7 (12.7-19.4)	Two compartments	10	15/15 100% f Δ T>MIC C	14/15 100% f Δ T>MIC	9/15 100% f Δ T>MIC IC
[27] Silva Jr (2017a) G1 N=10 1g q8h	1.9 (1.7-2.3)	3.4 (3.3-3.5)	9.1 (8.5-10.4)	One compartment	5	10/10 60% f Δ T>MIC	10/10 60% f Δ T>MIC	10/10 60% f Δ T>MIC C
[29] Adnan (2013) N=5 1g q8h	3.2 (3.1-4.7)	5.7 (5.1-10.5)	29.9 (25.5-40.9)	Two compartments	7	5/5 40% f Δ T>MIC	5/5 40% f Δ T>MIC	ND
[30] Cheatham (2008) 0.5g q6h N=7 1g q8h	2.5 /0.9 (1.6-3.4)	10.7/2.6 (8.2-13.2)	29.3/8.7 (21.0-37.6)	One compartment	10	7/7 40% f Δ T>MIC	7/7 40% f Δ T>MIC	7/7 40% f Δ T>MIC C
[31] Novelli (2005) N=10 1g q8h	1.7 /0.5 (1.2-2.2)	13.0/2.0 (11.1-14.9)	25.4 /4.9 (20.7-30.1)	Two compartments	10	10/10 40% f Δ T>MIC	10/10 (100%) 40% f Δ T>MIC	10/10 40% f Δ T>MIC C
[32] Kitzes-Cohen (2002) N=8 1g q8h	2.5 /1.2 (1.4-3.6)	9.4/2.5 (7.0-11.7)	21.7/5.7 (16.3-27.1)	Two compartments	8	7/7 40% f Δ T>MIC	7/7 40% f Δ T>MIC	7/7 (40% f Δ T>MIC C

Abbreviations and symbols–[21-32]: reference bibliography number related to Author (year); G1, group; ICU, intensive care unit; $t_{(1/2)\beta}$, biological half-life; CL_T, total body clearance; Vd^{ss}, volume of distribution at steady state; PTA, probability of target attained; med (IQ25-75), medians (quartiles); 95% CI, confidence interval of means/standard deviation; NAP, not applicable; ND, not determined

Table 2 Meropenem 1g q8h extended 3hrs.-pump infusion in ICU septic patients

Number of subjects	Parameters PK data analysis			Software	Blood sampling	PTA %fΔT>MIC		
Reference data Healthy volunteers	$t_{(1/2)\beta}$ (h)	CL _T (L/h)	Vd ^{ss} (L)	Noncompartmental data analysis	Reference data H.V.	MIC 1 mg/L	MIC 2 mg/L	MIC 4 mg/L
[22] Jaruratanasirikul (2003) N=12	0.64/0.02 (0.6-0.7)	13.0 /0.2 (12.8-13.2)	11.9/0.4 (11.5-12.3)	One compartment	13	NAP	NAP	NAP
ICU Critically ill septic patients-preserved/augmented CLcr								
[33] Camargo (2022) G1 N=10/20 1g q8h	3.5 (3.2-4.2)	8.4 (7.2-9.0)	42 (34-58)	One compartment	4	10/10 100%fΔT>MI C	10/10 100%fΔT>MI C	10/10 100%fΔT>MI C
[33] Camargo (2022) G2 N=10/20 1g q8h	2.7 (2.5-3.2)	6.3 (5.8-8.3)	23 (22-37)	One compartment	4	10/10 100%fΔT>MI C	10/10 100%fΔT>MI C	10/10 100%fΔT>MI C
[34] Messiano (2022) N=15 Set 1 2nd day	3.4 (2.3-4.5)	7.1 (5.8-8.4)	34 (24-44)	One compartment	5	15/15 100%fΔT>MI C	15/15 100%fΔT>MI C	15/15 100%fΔT>MI C
[34] Messiano (2022) N=15 Set 2 14th day	1.4 (1.3-1.5)	7 (6.6-7.2)	12.7 (13-14)	One compartment	5	15/15 100%fΔT>MI C	12/15 100%fΔT>MI C	2/15 100%fΔT>MI C
[23] Kupa (2019) G2 N=13 1g q8h	3.6 (3.3-4.4)	8.4 (8.2-8.9)	42 (40-45)	One compartment	5	13/13 100%fΔT>MI C	13/13 100%fΔT>MI C	13/13 100%fΔT>MI C
[27] Silva Jr (2017) G2 N=10 1g q8h	3.2 (2.9-3.6)	5.2 (4.8-5.3)	24 (23-26)	One compartment	5	10/10 60%fΔT>MIC	10/10 60%fΔT>MIC	10/10 60%fΔT>MIC
[36] Kothekar (2020) N=23 1g q8h	0.6/0.2 (0.4-0.8)	22.9/3.8 (19.3-26.5)	19.8/6.1 (13-25)	One compartment	12	ND	23/23 40%fΔT>MIC	14/23 40%fΔT>MIC
[37] Mattioli (2016) N=8 1g q8h	2.2 (0.8-3.7)	9.4/4.5 (5.1-13.6)	26.2/14.6 (12-40)	NONMEM One compartment	6	8/8 40%fΔT>MIC	4/8 40%fΔT>MIC	0/8 40%fΔT>MIC
[38] De Waale (2014) N=15 1g q8h	1.2 (1.-1.5)	15,9 (12.8 - 23.8)	35.1 (28-37)	One compartment	9	5/5 50%fDT>MIC	5/5 50%fDT>MIC	ND

Abbreviations and symbols—[22,33-38]: reference bibliography number related to Author (year); G1, group; G2, group; ICU, intensive care unit; $t_{(1/2)\beta}$, biological half-life; CL_T, total body clearance; Vd^{ss}, volume of distribution at steady state; PTA, probability of target attained; med (IQ25-75), medians (quartiles); 95%CI, confidence interval of means/standard deviation; NAP, not applicable; ND, not determined

Table 3 Piperacilin-Tazobactam 4.5g q8h or q6h intermittent 0.5hr-pump infusion in ICU septic patients

Number of subjects	Parameters PK data analysis			Software	Blood sampling	PTA %fΔT>MIC		
	$t_{(1/2)\beta}$ (h)	CL _T (L/h)	Vd ^{ss} (L)			MIC 4 mg/L	MIC 8 mg/L	MIC 16 mg/L
Reference data Healthy volunteers				Noncompartmental data analysis	Number samples			
[39]Ochipinti (1997) N=12	0.8 (0.7-0.9)	10.9 (9.7-12.1)	11.9 (10.3-13.6)	Two compartments	15	NAP	NAP	NAP
ICU Critically ill septic patients-preserved/augmented CLcr								
[41] Souza (2021) G1 N=22 4.5g q6h	1.2 (1.1-1.3)	8.9 (8.7 – 9.1)	15 (14-16)	One compartment	5	18/22 100%fΔT>MIC	1/22 100%fΔT>MIC	0/22 100%fΔT>MIC
[42] Udy (2015) N=47 4.5 q6h	ND	16.3 (14.0-18.9)	18.8 (11-32)	NONMEM Two compartments	5	32/47 100%fΔT>MIC	23/47 100%fΔT>MIC	16/47 100%fΔT>MIC
[43] Silva Jr (2017b) G1 N=22/35 4.5g q8h	1.5 (1.0-2.5)	6.8 (5.7-9.3)	25 (20-29)	One compartment	5	23/26 70%fΔT>MIC	14/26 70%fΔT>MIC	0/26 70%fΔT>MIC
[43] Silva Jr (2017b) G2 N=9 4.5g q6h	1.5 (1.0 – 2.5)	6.8 (5.7 – 9.3)	25 (20-29)	One compartment	5	9/9 70%fΔT>MIC	9/9 70%fΔT>MIC	9/9 70%fΔT>MIC
[44] Bourget (1996) N=10 4.5g q6h	1.5 (1.2-1.8)	7.4 (6.3-8.5)	15.8 (14-17)	Two compartments	9	10/10 70%fΔT>MIC	ND	ND
[45] Jeon (2014) N=50 4.5 q8h	2.9 (1.0-4.8)	16.2 (14.8-17.7)	ND	NONMEM Two compartments	5	50/50 50%fΔT>MIC	50/50 50%fΔT>MIC	45/50 50%fΔT>4xMIC
[46] Taccone (2010) N=27 4.5 q8h	2.6 (1.5-3.8)	9.1 (6.0-19.2)	28.5 (22-32)	One compartment	5	27/27 50%fΔT>4xMIC	27/27 50%fΔT>4xMIC	12/27 50%fΔT>4xMIC
[47] Li (2005) N=132 3.375g q6h	1.2 (0.6-1.8)	13.7 (9.6-17.8)	22.4 (17-28)	One compartment	4	132//132 50%fΔT>4xMIC	ND	ND

Abbreviations and symbols–[39,41,43-47]: reference bibliography number related to Author (year); G1, group; G2, group; ICU, intensive care unit; $t_{(1/2)\beta}$, biological half-life; CL_T, total body clearance; Vd^{ss}, volume of distribution at steady state; PTA, probability of target attained; med (IQ25-75), medians (quartiles); 95%CI, confidence interval of means/standard deviation; NAP, not applicable; ND, not determined

Table 4 Piperacilin-Tazobactam 4.5g q8h or q6h extended 3hrs.-pump infusion in ICU septic patients

Number of subjects	Parameters PK data analysis			Software	Blood sampling	PTA %fΔT>MIC		
	$t_{(1/2)\beta}$ (h)	CL _T (L/h)	Vd ^{ss} (L)			MIC 4 mg/L	MIC 8 mg/L	MIC 16 mg/L
Reference data Healthy volunteers				Noncompartmental data analysis	Number samples			
Ochipinti (1997) N=12	0.8 (0.7-0.9)	10.9 (9.7-12.1)	11.9 (10.3-13.6)	Two compartments	15	NAP	NAP	NAP
ICU Critically ill septic patients-preserved/augmented CLcr								
[41] Souza (2021) G2 N=9 4.5g q6h 2hrs.infusion	1.2 (1.1 - 1.3)	9.5 (8.9 - 11.3)	17 (16 - 20)	One compartment	5	9/9 100% fΔT>MIC	7/9 100% fΔT>MIC	1/9 100% fΔT>MIC
[41] Souza (2021) G3 N=9 4.5g q6h 3hrs.infusion	1.7 (1.5 - 1.9)	10.8 (8.5 - 11.6)	29 (18 - 31)	One compartment	5	9/9 100% fΔT>MIC	9/9 100% fΔT>MIC	9/9 100% fΔT>MIC
[48] Sime (2015) N=16 4.5g q6h	ND	5.2 (4.0-7.4)	ND	One compartment	2	ND	ND	11/16 100% fΔT>MIC
[38] De Waele (2014) N=15 4.5 q6h	1.2 (0.8-1.9)	13.2 (10.2-22.7)	26 (20-28)	One compartment	7	15/15 100% fΔT>4xMIC	15/15 100% fΔT>4xMIC	7/15 100% fΔT>4xMIC
[49] Chung (2015) N=11 4.5g q8h	2.1 (1.0 – 3.2)	9.8 (6.9-2.7)	25 (17-38)	NONMEM One compartment	8	11/11 90% fΔT>MIC	11/11 90% fΔT>MIC	11/11 90% fΔT>MIC

Abbreviations and symbols–[38,39,41,48,49]: reference bibliography number related to Author (year); G1, group; G2, group; ICU, intensive care unit; $t_{(1/2)\beta}$, biological half-life; CL_T, total body clearance; Vd^{ss}, volume of distribution at steady state; PTA, probability of target attained; med (IQ25-75), medians (quartiles); 95%CI, confidence interval of means/standard deviation; NAP, not applicable; ND, not determined