

Supplementary material-Table S1

Supplementary Table S1a. Dosing of novel antibiotics for nosocomial pneumonia.

Antibiotic	Infusion time	Standard dose [~]	Dose in ARC [*] and renal impairment
Ceftolozane-tazobactam^{&1}	1 hour (h)	3g every 8 h	ARC [*] : 3g every 8 h ² 30≤GFR [*] <50 1.5 g every 8 h 15≤GFR [*] <30 0.75g every 8 h 15<GFR [*] 0.450g every 8 h IHD [*] a single initial dose of 2.25 g should be followed by 0.450 g every 8 h
Ceftazidime-avibactam³	2 hours	2g/0.5g every 8 h	ARC [*] 2g/0.5g every 8 h ⁴ 30≤GFR [*] <50 1g/0.25g every 8 h 15≤GFR [*] <30 0.750g/0.1875g every 12 h 6≤GFR [*] <15 0.750g/0.1875g every 24 h GFR [*] <6 or IHD [*] every 48 h or after dialysis session
Meropenem-vaborbactam⁵	3 hours	2g/2g every 8 h	ARC [*] : insufficient data regarding dosing-continuous infusion may be required. 20≤GFR [*] <40 1g/1g every 8 10≤GFR [*] <20 1g/1g every 12 h GFR [*] <10 or IHD [*] 0.5g/0.5g every 12 h
Imipenem-cilastatin-relebactam⁶	30 minutes	500/500/250 mg every 6 h	ARC [*] 500/500 /250 mg every 6 h ⁷ 60≤GFR [*] <90 400/400/200 mg every 6 h 30≤GFR [*] <60 300/300/150 mg every 6 h 15≤GFR [*] <30 or IHD [*] 200/200/100 mg every 6 h <i>For patients with GFR<15 imipenem-cilastatin-relebactam is not recommended unless IHD is commenced within 48 h from drug initiation.</i>
Cefiderocol⁸	3 hours	2g every 8 h	GFR≥120 2g every 6 h 30≤GFR [*] <60 1.5 g every 8 h 15≤GFR [*] <30 1g every 8 h GFR [*] <15 or IHD [*] 0.75g every 12 h

Sulbactam - durlobactam⁹	3hours	1g/1g every 6 hours	GFR [*] ≥130 1g/1g every 4 h 30≤GFR [*] <45 1g/1g every 8 h 15≤GFR [*] <30 1g/1g every 12 h GFR [*] <15 or IHD [*] 1g/1g at 0 12 and 24 hours and then every 24 h
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[&]Dose provided is for HAP/VAP- the dose for complicated intraabdominal and urinary infections is 50% of the above mentioned doses; ^{*}ARC, augmented renal clearance; GFR: Glomerular filtration rate, measured in ml/min; h: hour(s); IHD, intermitted hemodialysis, dose must be administrated after dialysis session is completed; [~]For the first 24 to 48 hours, physicians should consider prescribing this dose, irrespective of patients' renal function. Renal impairment dose refers to the dose prescribed after the first 24-48 hours and is based on the calculated GFR in patients with stable renal function. In patients with Acute Kidney Injury, estimated GFR is a poor marker to assess renal function and dosing should be guided by monitoring antibiotic levels; [#] limited available data.

The tables are indicative- for prescribing, we refer the reader to the national and/or local guidelines.

Supplementary Table S1b. Dosing of novel antibiotics for nosocomial pneumonia during Continuous Renal Replacement Therapy (CRRT).

Drug	Loading dose	Maintenance dose			
		Effluent rate			
		<2 L/h	2L/h	3-4 L/h	>4L
Ceftolazone-tazobactam^{4,10,11}	3 g	0.750 g every 8 h (h)	1.5g every 8 h	3g every 8 h	3g every 8 h
Ceftazidime-avibactam^{~12,13}	2.5g	1.25-2.5 g every 8 h	2.5g every 8 h	IE [*]	IE [*]
Cefiderocol¹⁴	2g	1.5 g every 12 h	2g every 12 h	1.5 g every 8 h	2g every 8 h
Imipenem-cilastatin-relebactam^{+4,15}	200 mg/100 mg every 6 hours (based on ex-vivo models)				
Meropenem-vaborbactam^{\$4,16}	1000 mg/1000 mg every 8 hours (data available from 1 case report only)				
Sulbactam-durlobactam	No available data				

[~]Evidence is limited and based on effluent rates of 2.5 L/h. The 2.5 g dose is recommended if resistant strain or difficult to treat infection; ^{*}IE: insufficient evidence

⁺No published PK data in critically ill patients with AKI or receiving CRRT. In ex vivo continuous hemofiltration (CH) and continuous haemodialysis (CHD) models, imipenem-cilastatin-relebactam (I-C-T) clearance was assessed and was shown that I-C-R was not removed by adsorption, but crossed effectively the hemodiafiltration membrane and a dose of 200 mg/100 mg every 6 hours was sufficient to achieve the

PK/PD targets. Note: although a warning regarding insufficient drug concentrations risk in cases of creatinine clearance >150 mL/min is found on I-C-T product specification, no dose adjustments are provided.

[%]Data only from a case report that PK characteristics of meropenem–vaborbactam (M-V) were assessed on an anuric patient on CRRT: 1000/1000 mg or even lower doses given as 3-hour infusion, achieved the PK/PD target for the isolated strain.

The tables are indicative- for prescribing, we refer the reader to the national and/or local guidelines.

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