Milano, 14–15 Ottobre 2022

Quali indicazioni per Meropenem-varbobactam nelle infezioni da MDR

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REVIEW

Meropenem-vaborbactam: a carbapenem and beta-lactamase inhibitor with activity against carbapenem-resistant *Enterobacteriaceae*

Young R. Lee[1] · Nathaniel T. Baker[1]

Meropenem–vaborbactam: a new weapon in the war against infections due to resistant Gram-negative bacteria

Twisha S Patel[1], Jason M Pogue*[,2], John P Mills[3] & Keith S Kaye[3]

PHARMACOTHERAPY
accp
REVIEW OF THERAPEUTICS

Meropenem and Vaborbactam: Stepping up the Battle against Carbapenem-resistant Enterobacteriaceae

In 2017, following priority review, the FDA approved meropenem–vaborbactam for complicated UTIs caused by susceptible enterobacteria.

Infect Dis Ther
https://doi.org/10.1007/s40121-018-0214-1

CrossMark

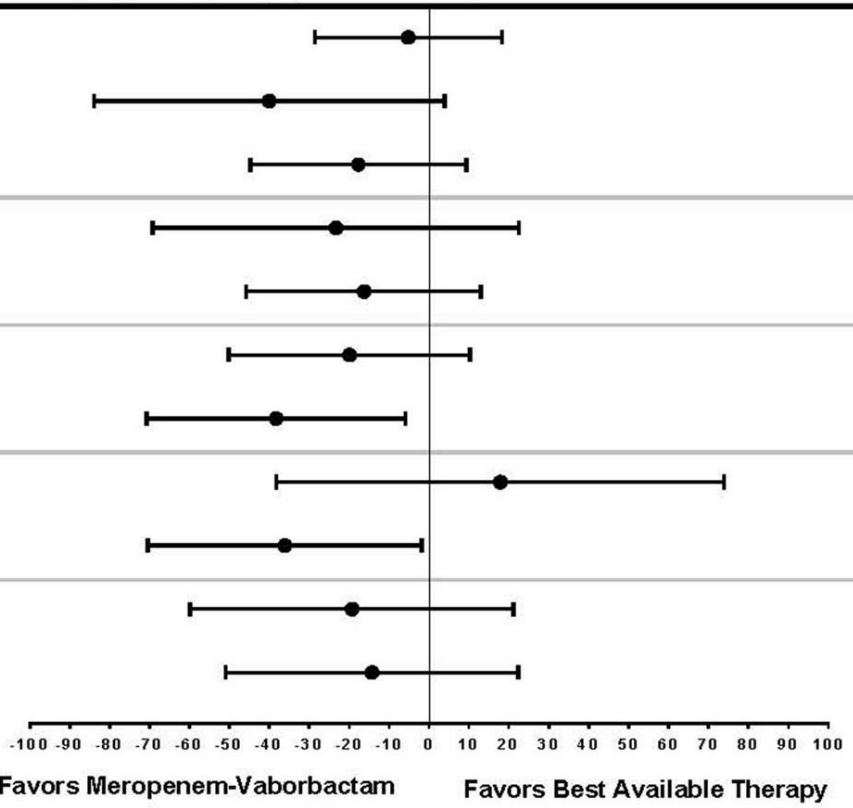
ORIGINAL RESEARCH

M–V (n = 32)
BAT (n = 15)
Total (N = 47)

Effect and Safety of Meropenem–Vaborbactam versus Best-Available Therapy in Patients with Carbapenem-Resistant Enterobacteriaceae Infections: The TANGO II Randomized Clinical Trial

Published online: 01 October 2018

B Day 28 all-cause mortality by subgroup (mCRE-MITT)



		Meropenem-Vaborbactam	Best Available Therapy	Difference (95% CI)
Age	<65 years	1/17 (5.9%)	1/9 (11.1%)	-5.2 (-28.6, 18.2)
	≥65 years	4/15 (26.7%)	4/6 (66.7%)	-40.0 (-83.9, 3.9)
	All	5/32 (15.6%)	5/15 (33.3%)	-17.7 (-44.7, 9.3)
SIRS Status	Yes	4/15 (26.7%)	3/6 (50.0%)	-23.3 (-69.2, 22.5)
	No	1/17 (5.9%)	2/9 (22.2%)	-16.3 (-45.7, 13.0)
Charlson Comorbidity Score Category	≥4	5/27 (18.5%)	5/13 (38.5%)	-19.9 (-50.2, 10.3)
	≥6	1/14 (7.1%)	5/11 (45.5%)	-38.3 (-70.7, -5.9)
Creatinine Clearance	<50 mL/min	3/7 (42.9%)	1/4 (25.0%)	17.9 (-38.2, 73.9)
	≥50 mL/min	2/24 (8.3%)	4/9 (44.4%)	-36.1 (-70.4, -1.8)
Immuno-compromised	Yes	2/11 (18.2%)	3/8 (37.5%)	-19.3 (-59.9, 21.2)
	No	3/21 (14.3%)	2/7 (28.6%)	-14.3 (-50.9, 22.4)

Monotherapy with M-V for CRE infection was associated with increased clinical cure, decreased mortality, and reduced nephrotoxicity compared with BAT.

Wunderink IDT 2018

EXPERT REVIEW OF ANTI-INFECTIVE THERAPY
https://doi.org/10.1080/14787210.2020.1756775

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REVIEW

Meropenem/vaborbactam: a next generation β-lactam β-lactamase inhibitor combination

Table 1. Activity of Meropenem/Vaborbactam *vs*. various difficult-to-treat Gram-negative pathogens.

Pathogens and relevant resistance mechanisms (no. isolates)	Sources (years)	% susceptibility (CLSI)	% susceptibility (EUCAST)	References
Enterobacterales KPC+ (294)[a]	Global (2000–2013)	94.6	97.3	[69]
Enterobacterales KPC+ (135)[b]	Global (2014)	99.3	100	[25]
Enterobacterales KPC+ (991)[c]	Global (2014–2015)	99	99.6	[49]
Enterobacterales KPC+ (206)	Global (2015)	99.5	99.5	[33]
Enterobacterales KPC+ (124)	USA (2016–2018)	99.2	100	[23]
Enterobacterales KPC+ (128)[d]	China (2004–2014)	81.3	97.7	[24]
Achromobacter spp. (100)[e]	USA-Canada (2013–2018)	86	≥90	[30]
Burkholderia cepacia complex (150)[f]	USA-Canada (2013–2018)	97	≥97	[30]
Burkholderia gladioli [48]	USA-Canada (2013–2018)	100	100	[30]

[a]Including *Klebsiella pneumoniae, Klebsiella oxytoca, Escherichia coli, Enterobacter cloacae, Citrobacter freundii.*
[b]Including *K. pneumoniae, K. oxytoca, E. coli, E. cloacae, C. freundii, Serratia marcescens.*
[c]Including *K. pneumoniae, K. oxytoca, E. coli, Enterobacter* spp., *Citrobacter* spp., *Serratia marcescens.*
[d]Including 94 *K. pneumoniae* and 22 *E. coli.*
[e]Including *A. dolens, A. ruhlandii*, and *A. xylosoxydans.*
[f]Including *B. cenocepacia, B. cenocepacia, B. contaminans, B. multivorans, B. vietnamiensis.*

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doi:10.1093/jac/dkab252 Advance Access publication 23 July 2021

Journal of Antimicrobial Chemotherapy

Activity of meropenem/vaborbactam and comparators against Gram-negative isolates from Eastern and Western European patients hospitalized with pneumonia including ventilator-associated pneumonia (2014–19)

Dee Shortridge[1]*, Cecilia Carvalhaes [1], Lalitagauri Deshpande[1] and Mariana Castanheira[1]

The most common Gram-negative pathogens isolated from PHP were P. aeruginosa (n = 3567), K. pneumoniae (n = 1877) and Escherichia coli (n = 1646).

Overall, 98.0% of Enterobacterales and 82.1% of P. aeruginosa were susceptible to meropenem/vaborbactam.

KPC was the most common carbapenemase in WE, while OXA-48-like was the most common carbapenemase in EE.

Meropenem/vaborbactam susceptibility was 63.0% for all CRE (92.2% in WE and 51.5% in EE).

Meropenem/vaborbactam inhibited 99.1% of KPC-producing isolates and 40.5% of OXA-48-like-producing isolates.

JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlac097

JAC-Antimicrobial Resistance

Activity of meropenem/vaborbactam and comparators against non-carbapenemase-producing carbapenem-resistant Enterobacterales isolates from Europe

Dee Shortridge *, Lalitagauri M. Deshpande, Jennifer M. Streit and Mariana Castanheira

- 978 CREs were identified with MICs >2 mg/L to meropenem
- Whole-genome sequencing was performed on each CRE isolate.
- 125 isolates were negative for carbapenemase genes, including *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{IMP}$, *bla*$_{VIM}$ and *bla*$_{OXA-48-like}$
- Susceptibility to meropenem/vaborbactam was 96.0/97.6% (CLSI/EUCAST)
- Meropenem/vaborbactam had potent in vitro activity against CRE isolates that lacked known carbapenemases

Epidemiology of Meropenem/Vaborbactam Resistance in KPC-Producing *Klebsiella pneumoniae* Causing Bloodstream Infections in Northern Italy, 2018

62 KPC-Kp bloodstream isolates collected from hospitalized patients

Paolo Gaibani [1,*], Donatella Lombardo [1], Linda Bussini [2], Federica Bovo [1], Beatrice Munari [1], Maddalena Giannella [2], Michele Bartoletti [2], Pierluigi Viale [2], Tiziana Lazzarotto [1] and Simone Ambretti [1]

Isolate	Patient	MIC (mg/L)				ST	Genetic Determinants				*Porins*		Plasmid_Replicons (InC)
		MEM	CAZ/AVI	MEM/VAB	CST		Beta-lactams	Aminoglycoside	Fluoroquinolone	Sulfonamide	*OmpK35*	*OmpK36*	
KpBO3	1	256	32	256	0.25	512	bla_{KPC-3}, bla_{SHV-11}	*aac(6′)-Ib*	*oqxA, oqxB, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (K), IncFIB(pKPHS1), IncX3, ColRNAI
KpBO6	2	256	16	256	0.5	258	bla_{KPC-3}, bla_{SHV-12}	*aadA2, aph(3′)-Ia, aac(6′)Ib-cr*	*oqxA, oqxB, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIIK, IncFIB(K), IncX3, ColRNAI
KpBO7	3	256	≥256	256	0.5	1519	bla_{KPC-3}, bla_{TEM-1A}, bla_{OXA-9}, bla_{SHV-11}	*aadA2, aph(3′)-Ia, aac(6′)Ib-cr*	*oqxA, oqxB, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (pQIL), IncFIB (pKPSH1), IncFIB(K), IncFII(K), IncX3, ColRNAI, Col(BS512)
KpBO8	4	32	8	48	0.5	512	bla_{KPC-3}, bla_{SHV182}, bla_{TEM-1A}, bla_{OXA-9}	*aadA2, aph(3′)-Ia, aac(6′)-Ib*	*oqxA, oqxB, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (pQIL), IncFIB (pKPSH1), IncFIB(K), IncFII(K), ColRNAI
KpBO11	5	256	8	256	0.25	512	bla_{KPC-3}, bla_{SHV182}	*aadA2, aph(3′)-Ia, aac(6′)-Ib*	*oqxA, oqxB, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (pKPSH1), IncFIB(K), IncFII(K), ColRNAI, IncX3
KpBO12	6	256	8	256	0.5	512	bla_{KPC-3}, bla_{SHV182}	*aadA2, aph(3′)-Ia, aac(6′)-Ib*	*oqxB, oqxA, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (pKPSH1), IncFIB(K), IncFII(K), ColRNAI, IncX3
KpBO13	7	32	8	256	0.5	1519	bla_{KPC-3}, bla_{SHV182}, bla_{OXA-9}	*aadA2, aac(6′)-Ib*	*oqxB, oqxA, aac(6′)Ib-cr*	*sul1*	truncated	GD134–135	IncFIB (pQIL), IncFIB (pKPSH1), IncFIB(K), IncFII(K), ColRNAI, IncX3, Col(BS512)
KpBO14	8	256	8	256	0.25	512	bla_{KPC-3}, bla_{SHV182}	*aac(6′)-Ib*	*oqxA, oqxB, aac(6′)Ib-cr*	-	truncated	GD134–135	IncFIB (pKPSH1), IncFIB(K), ColRNAI, IncX3

Meropenem/vaborbactam-resistance was found in 8% (n = 5) KPC-Kp, while 5% (n = 3) strains exhibited cross-resistance to ceftazidime/avibactam.

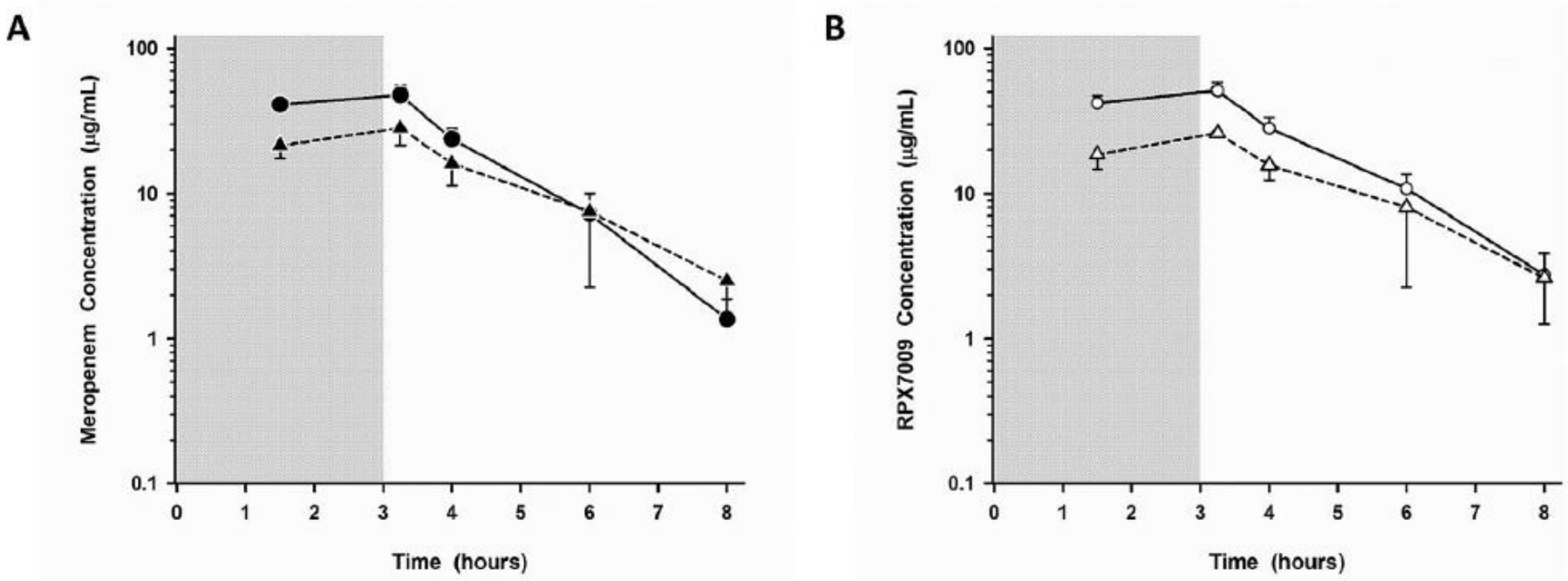
Resistance to meropenem/vaborbactam was due to porins mutations and is associated with reduced susceptibility to both ceftazidime/avibactam and carbapenems.

Infect Dis Ther (2020) 9:769–784
https://doi.org/10.1007/s40121-020-00344-z

REVIEW

An Appraisal of the Pharmacokinetic and Pharmacodynamic Properties of Meropenem-Vaborbactam

Eric Wenzler · Patrick J. Scoble



Mean (± SD) plasma (filled and open circles; solid line) and epithelial lining fluid (ELF) (filled and open triangles; dashed lines) concentration-versus-time profiles of meropenem (a) and vaborbactam (b) after the third dose of meropenem 2 g / vaborbactam 2 g administered as a 3-h intravenous infusion

Clinical Infectious Diseases

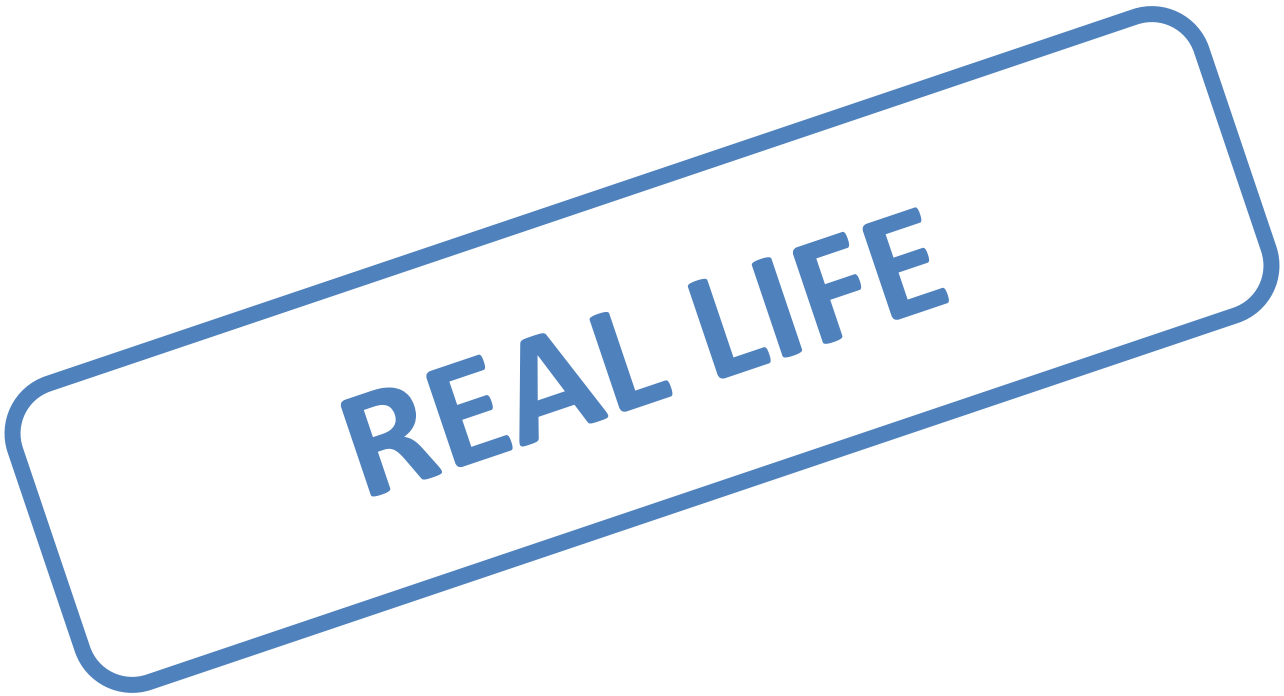
INVITED ARTICLE

REVIEWS OF ANTI-INFECTIVE AGENTS: Louis D. Saravolatz, Section Editor

Ceftazidime/Avibactam, Meropenem/Vaborbactam, or Both? Clinical and Formulary Considerations

Jason M. Pogue,[1,2] Robert A. Bonomo,[3,4,5] and Keith S. Kaye[6]

- Both ceftazidime/avibactam and meropenem/vaborbactam are “game-changing” therapies for the management of CRE infections
- CAZ/AVI and M/V represent an effective treatment option for KPC producers. However, issues pertaining to the emergence of resistance are concerning.
- Encouragingly, data suggest that cross-resistance currently remains infrequent.
- CAZ/AVI is the preferred agent for treatment of OXA-48–producing CRE.
- Avibactam’s broad inhibitory profile also makes it an ideal agent to combine with aztreonam for the management of MBLs.
- Local CRE epidemiology will drive decisions regarding the preferred agent, based on the most frequent mechanism of carbapenem resistance (KPC vs OXA-48 vs MBL) within an institution. Furthermore, because resistance mechanisms are complex and often multifactorial, we recommend that all CRE pathogens be routinely tested against both CAZ/AVI and M/V.


REAL LIFE

Meropenem-Vaborbactam as Salvage Therapy for Ceftazidime-Avibactam-Resistant *Klebsiella pneumoniae* Bacteremia and Abscess in a Liver Transplant Recipient

The isolate carried a gene encoding a mutated KPC-2, in addition to TEM-1, SHV-11, and SHV-12, and disruptions in OmpK35, OmpK36, and OmpK37.

TABLE 1 Antibiotic susceptibility of the patient's multidrug-resistant *K. pneumoniae* blood isolates

Antibiotic	MIC, μg/ml (interpretation)[a]			
	Day 5	Day 54	Day 62	Day 68
Ampicillin-sulbactam	≥32 (R)	≥32 (R)	≥32 (R)	≥32 (R)
Cefazolin	≥64 (R)	≥64 (R)	≥64 (R)	≥64 (R)
Ceftriaxone	≥64 (R)	≥64 (R)	≥64 (R)	≥64 (R)
Cefepime	≥64 (R)	≥64 (R)	≥64 (R)	≥64 (R)
Ceftazidime-avibactam	4 (S)	4 (S)	128 (R)	>256 (R)[b]
Piperacillin-tazobactam	≥128 (R)	≥128 (R)	128 (R)	16 (S)
Ertapenem	≥8 (R)	≥8 (R)	>8 (R)	≥8 (R)
Meropenem	≥16 (R)	≥16 (R)	2 (I)	4 (R)[c]
Ciprofloxacin	≥4 (R)	≥4 (R)	≥4 (R)	≥4 (R)
Gentamicin	≤1 (S)	≤1 (S)	≤1 (S)	≤1 (S)
Polymyxin B[d]	>4 (NI)	2 (NI)	1 (NI)	1 (NI)
Tigecycline	≤1 (S)	0.5 (S)	≤1 (S)	≤1 (S)
TMP-SMX[e]	≥4/76 (R)	≥4/76 (R)	≥4/76 (R)	≥4/76 (R)
Meropenem-vaborbactam	NP	NP	NP	2 (S)[b]

blaKPC mutants conferring ceftazidime-avibactam resistance function as extended-spectrum β-lactamases with reduced carbapenem hydrolytic activity. However, the mechanism and stability of enhanced carbapenem susceptibility have not been fully elucidated

no single KPC mutation has been shown to confer resistance to meropenem-vaborbactam, suggesting a higher overall barrier to resistance compared to ceftazidime-avibactam

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January 2019 Volume 63 Issue 1 e01551-18

Clinical Infectious Diseases

BRIEF REPORT

Early Experience With Meropenem-Vaborbactam for Treatment of Carbapenem-resistant Enterobacteriaceae Infections

Ryan K. Shields,[1,2,3] Erin K. McCreary,[3] Rachel V. Marini,[3] Ellen G. Kline,[1] Chelsea E. Jones,[1] Binghua Hao,[1,2] Liang Chen,[4] Barry N. Kreiswirth,[4] Yohei Doi,[1] Cornelius J. Clancy,[1,2,5] and M. Hong Nguyen[1,2,3]

CRE infection types included bacteremia (n=8), pneumonia (n=6; 83% [5/6] ventilator-associated), tracheobronchitis (n=2; 50% [1/2] ventilator-associated), skin/soft tissue (n=2), pyelonephritis (n=1), and peritonitis with intra-abdominal abscess (n=1).

Twenty patients with carbapenem-resistant Enterobacteriaceae infections were treated with meropenem-vaborbactam. (80% monotherapy).

Thirty day clinical success and survival rates were 65% (13/20) and 90% (18/20), respectively.

Thirty-five percent of patients had microbiologic failures within 90 days. One patient developed a recurrent infection due to meropenem-vaborbactam–nonsusceptible, *ompK36* porin mutant *Klebsiella pneumoniae*.

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CLINICAL THERAPEUTICS

Meropenem-Vaborbactam versus Ceftazidime-Avibactam for Treatment of Carbapenem-Resistant *Enterobacteriaceae* Infections

Renee Ackley,[a] Danya Roshdy,[a] Jacqueline Meredith,[a] Sarah Minor,[b] William E. Anderson,[c] Gerald A. Capraro,[d] Christopher Polk[e]

131 patients
105 ceftazidime-avibactam
26 meropenem-vaborbactam
40% had bacteremia.

TABLE 4 Clinical outcomes[a]

	Ceftazidime-avibactam group (n = 105)	Meropenem-vaborbactam group (n = 26)	P value
No. of clinical successes[b] (%)	65 (61.9)	18 (69.2)	0.49
No. of failures to resolve signs and symptoms of infection (%)	4 (3.8)	1 (3.8)	1.0
Failure to sterilize blood cultures within 7 days of treatment initiation [no. of failures/no. of bacteremias (%)]	1/44 (2.3)	1/9 (11.1)	0.31
No. of 30-day mortalities (%)	20 (19.1)	3 (11.5)	0.57
No. of 90-day mortalities (%)	30 (28.6)	7 (26.9)	0.48
Median length of hospital stay[c] (days) (IQR)	15.3 (9.3–28.5)	15.6 (9.5–33.1)	0.99
Median length of ICU stay (days) (IQR)	15.0 (5.0–32.0)	12.0 (5.0–22.0)	0.53
No. of recurrences of CRE infection (%)	15 (14.3)	3 (11.5)	1.0
No. of increases in study drug MIC in mg/liter (%)	6 (40.0)	0	0.51
No. of emergences of study drug resistance (%)	3 (20.0)	0	1.0

Patients in the ceftazidime-avibactam arm received combination therapy more often than patients in the meropenem-vaborbactam arm (61% versus 15%).

No significant difference in clinical success was observed between groups (62% versus 69%)

No difference in 30- and 90-day mortality resulted, and rates of AE were similar between groups.

Open Forum Infectious Diseases
MAJOR ARTICLE

Real-world, Multicenter Experience With Meropenem-Vaborbactam for Gram-Negative Bacterial Infections Including Carbapenem-Resistant *Enterobacterales* and *Pseudomonas aeruginosa*

Sara Alosaimy,[1] Abdalhamid M. Lagnf,[1] Taylor Morrisette,[1] Marco R. Scipione,[2] Jing J. Zhao,[2] Sarah C. J. Jorgensen,[1,3] Ryan Mynatt,[1,4] Travis J. Carlson,[5,6] Jinhee Jo,[5] Kevin W. Garey,[5] David Allen,[7] Kailynn DeRonde,[8] Ana D. Vega,[8] Lilian M. Abbo,[8] Veena Venugopalan,[9] Vasilios Athans,[10] Stephen Saw,[10] Kimberly C. Claeys,[11] Mathew Miller,[12] Kyle C. Molina,[12] Michael Veve,[1,13,14] Wesley D. Kufel,[15,16] Lee Amaya,[17,18] Christine Yost,[17] Jessica Ortwine,[19] Susan L. Davis,[1,20] and Michael J. Rybak[1,2,21]

The most common infection sources were respiratory tract (38.1%) and intra-abdominal (19.0%) origin, while the most common isolated pathogens were CRE (78.6%).
53 K. Pneumoniae, 25 E. coli, 24 Enterobacter

Only 34.1% of MEV patients were on combination therapy

Thirty-day mortality and recurrence occurred in 18.3% and 11.9%, respectively

Outcome[a]	Total Study (n = 126)	PsA Spp. (n = 8)	Non-PsA (n = 118)	CRE Spp. (n = 99)
Efficacy				
30-d mortality	23 (18.3)	0 (0)	23 (19.5)	19 (19.2)
90-d mortality	39 (33.1)	1 (12.5)	40 (31.7)	34 (34.3)
In-hospital mortality	30 (23.8)	1 (12.5)	29 (24.6)	25 (25.3)
30-d recurrence	15 (11.9)	2 (25.0)	13 (11.0)	13 (13.1)
30-d readmission	23 (18.3)	0 (0)	23 (19.5)	21 (21.2)
Worsen or failure to improve while on MEV	30 (23.8)	2 (25.0)	28 (23.7)	25 (25.3)
Development of MEV resistance (n = 25)	0 (0)	0 (0)	0 (0)	0 (0)
Length of hospital stay, d	34.5 (17.8–62.3)	37.0 (14.5–95.5)	34.5 (18.0–62.3)	40.0 (18.0–64.0)

Table 4. Independent Predictors of Negative Clinical Outcomes

Variable	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Timely MEV[a]	0.387 (0.098–1.522)	.174	0.277 (0.081–0.941)	.040
APACHE II score	1.083 (1.012–1.159)	.021	1.095 (1.029–1.166)	.004
Nosocomial infection[b]	2.298 (0.583–9.055)	.234	4.041 (1.132–14.426)	.031
Heart failure	5.313 (1.188–23.763)	.029	4.216 (1.129–15.733)	.032
Intra-abdominal infection	0.162 (0.022–1.206)	.076	0.151 (0.027–0.835)	.030

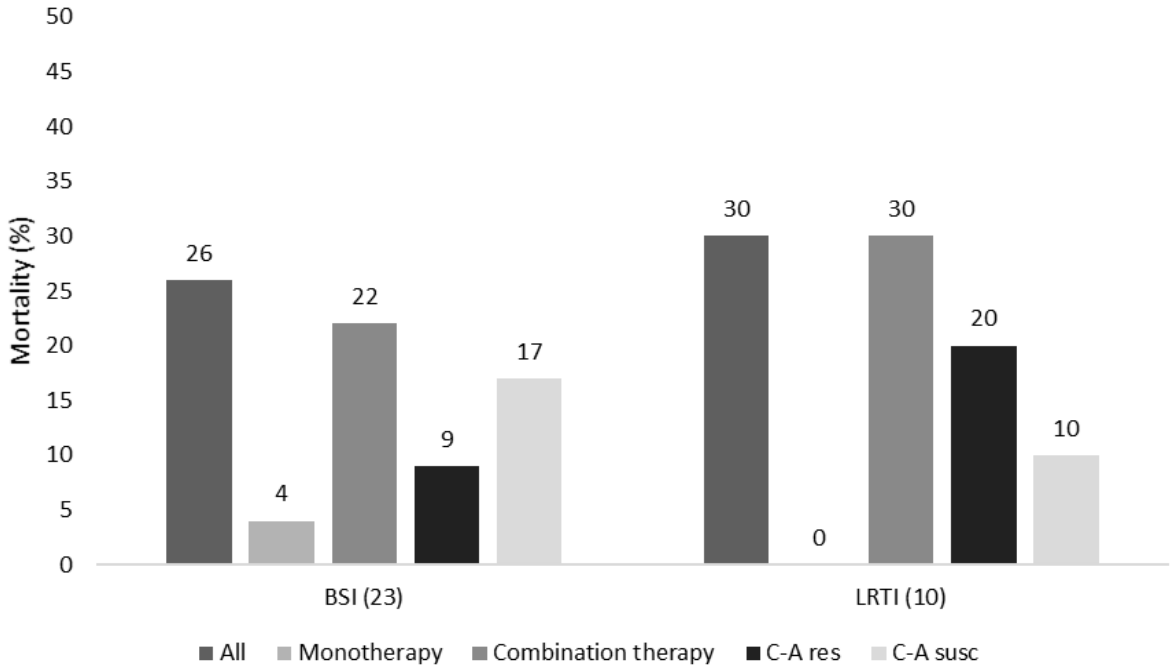
Compassionate use of meropenem/vaborbactam for infections caused by KPC-producing *Klebsiella pneumoniae*: a multicentre study

Mario Tumbarello[1,2*], Francesca Raffaelli[3], Antonio Cascio[4], Marco Falcone[5], Liana Signorini[6], Cristina Mussini[7], Francesco Giuseppe De Rosa[8], Angela Raffaella Losito[3], Gennaro De Pascale[9,10], Renato Pascale[11], Daniele Roberto Giacobbe[12,13], Alessandra Oliva[14], Alberto Farese[15], Paola Morelli[16,17], Giusy Tiseo[5], Marianna Meschiari[7], Paola Del Giacomo[3], Francesca Montagnani[1,2], Massimiliano Fabbiani[2], Joel Vargas[10], Teresa Spanu[3,10], Matteo Bassetti[12,13], Mario Venditti[14] and Pierluigi Viale[11]

37 KPC-Kp infections
BSIs, *n*=23
LRTIs, *n*=10
CZA res. n=22
Combination regimens 62%

Clinical cure was achieved in 28 (75.6%) cases. Nine patients (24.3%) died in hospital with persistent signs of infection. Most were aged over 60 years, with high comorbidity burdens and INCREMENT scores ≥8.

Outcomes were unrelated to the isolate's ceftazidime/avibactam susceptibility status.



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International Journal of Infectious Diseases 122 (2022) 1041–1043

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journal homepage: www.elsevier.com/locate/ijid

Case Report

A Post-Neurosurgical Infection due to KPC-Producing Klebsiella pneumoniae Treated with Meropenem-Vaborbactam: A Case Report

Seohyun Choi[1], Marianna Fedorenko[2,**], Janet Lin-Torre[3], Nirav Mistry[3], Steven Smoke[4,*]

Le Infezioni in Medicina, n. 2, 277-284, 2022
doi: 10.53854/liim-3002-14

CASE REPORT

Thoracic aorta graft infection by avibactam-resistant KPC-producing *K. pneumoniae* treated with meropenem/vaborbactam: a case report and literature review

Alessandra Belati[1], Roberta Novara[1], Davide Fiore Bavaro[1], Andrea Procopio[1], Cecilia Fico[1], Lucia Diella[1], Federica Romanelli[2], Stefania Stolfa[2], Adriana Mosca[2], Francesco Di Gennaro[1], Annalisa Saracino[1]

MBL

AAC Accepted Manuscript Posted Online 30 September 2019
Antimicrob. Agents Chemother. doi:10.1128/AAC.01426-19

1 **Searching for the Optimal Treatment for Metallo- and Serine-β-Lactamase Producing**
2 **Enterobacteriaceae: Aztreonam in Combination with Ceftazidime-avibactam or**
3 **Meropenem-vaborbactam**
4
5 Biagi M[1], Wu T[1], Lee M[1], Patel S[1], Butler D[1], Wenzler E[1]
6 [1]College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA

- 8 clinical Enterobacteriaceae strains (4 *Escherichia coli* and 4 *Klebsiella pneumoniae*) co-producing NDM and at least one serine β-lactamase were used for all experiments.
- All strains were resistant to ceftazidime-avibactam and meropenem-vaborbactam and 7/8 (87.5%) strains were resistant to aztreonam.
- Aztreonam combined with ceftazidime-avibactam was synergistic against all 7 aztreonam-resistant strains.
- Aztreonam combined with meropenem-vaborbactam was synergistic against all aztreonam-resistant strains with the exception of an OXA-232-69 producing *K. pneumoniae* strain.

antibiotics

MDPI

Case Report

Meropenem/Vaborbactam Plus Aztreonam as a Possible Treatment Strategy for Bloodstream Infections Caused by Ceftazidime/Avibactam-Resistant *Klebsiella pneumoniae*: A Retrospective Case Series and Literature Review

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Table 1. Antimicrobial susceptibility test of three *Klebsiella pneumoniae* strains resistant to avibactam.

	Strain 1 (KPC-*Kp*)	Strain 2 (MBL-*Kp*)	Strain 3 (MBL-*Kp*)
Antimicrobial	**MIC**	**MIC**	**MIC**
Amikacin	≤1 **	4 **	NA
Amoxicillin/Clavulanate	>16	>16	>16
Cefepime	>16	>16	>16
Cefotaxime	>32	>32	>32
Ceftazidime	>32	>32	>32
Ceftazidime/Avibactam	>8	>8	>8
Ceftolozane/Tazobactam	>8	>8	>8
Ciprofloxacin	>2	>2	>2
Colistin *	2	>2	>2
Gentamycin	2	8	8
Imipenem	>8	>8	>8
Meropenem	>8	>8	>8
Piperacilline/Tazobactam	>64	>64	>64
Tobramycin	8	8	8
Trimetropim/Sulphametoxazole	>160	>160	>160
Meropenem/Vaborbactam *	0.25 **	128	128

Three patients with CAZ/AVI-R-Kp sepsis were treated with M/V plus ATM not knowing the carbapenemase gene. Two had an NDM-Kp infection for which, upon obtaining the result of sensitivity to M/V, combination therapy was maintained. The third had KPC-Kp infection for which ATM was discontinued, after the acquisition of an antibiogram reporting full sensitivity to M/V.

Meropenem-vaborbactam has a strong activity against KPC-producing Enterobacterales.

PK / PD characteristics suggests that meropenem/vaborbactam may be an important treatment option for both ICU and non-ICU HP, including VAP, caused by Enterobacterales in regions with a high prevalence of KPCs.

The activity of meropenem–vaborbactam would not be expected to differ from that of meropenem alone in the presence of MBL and/or oxacillinase producers.

The activity of meropenem-vaborbactam against nonfermenting Gram-negative bacilli such as P. aeruginosa and Acinetobacter spp. appears to be similar to that of meropenem alone.