SITA
Società Italiana di Terapia Antinfettiva
Antibatterica Antivirale Antifungina

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BL/BLI

Mario Tumbarello

UNIVERSITÀ DI SIENA 1240

Azienda ospedaliero-universitaria Senese

Ceftolozane–tazobactam versus meropenem for treatment of nosocomial pneumonia (ASPECT-NP): a randomised, controlled, double-blind, phase 3, non-inferiority trial

Marin H Kollef, Martin Nováček, Ülo Kivistik, Álvaro Réa-Neto, Nobuaki Shime, Ignacio Martin-Loeches, Jean-François Timsit, Richard G Wunderink, Christopher J Bruno, Jennifer A Huntington, Gina Lin, Brian Yu, Joan R Butterton, Elizabeth G Rhee

www.thelancet.com/infection Published online September 25, 2019 https://doi.org/10.1016/S1473-3099(19)30403-7

- **Patients received either 3 g ceftolozane–tazobactam or 1 g meropenem as 1-h intravenous infusions every 8 h for 8–14 days.**

	Ceftolozane–tazobactam group	Meropenem group	% difference (95% CI)*
Gram-negative pathogens	157/259 (60·6%)	137/240 (57·1%)	3·5 (–5·1 to 12·1)
Enterobacteriaceae	120/195 (61·5%)	105/185 (56·8%)	4·8 (–5·1 to 14·5)
ESBL-producing Enterobacteriaceae	48/84 (57·1%)	45/73 (61·6%)	–4·5 (–19·3 to 10·7)
Pseudomonas aeruginosa	36/63 (57·1%)	39/65 (60·0%)	–2·9 (–19·4 to 13·8)
Multidrug-resistant *P aeruginosa*	13/24 (54·2%)	6/11 (54·5%)	–0·4 (–31·2 to 31·7)
Extensively drug-resistant *P aeruginosa*	4/10 (40·0%)	2/5 (40·0%)	0·0 (–43·6 to 40·3)

Data are n/N (%). *Unstratified Newcombe CIs; inferences drawn from these intervals might therefore not be reproducible.

Table 3: Per-pathogen clinical cure at test-of-cure visit in the microbiological intention-to-treat population

- **High-dose ceftolozane–tazobactam is an efficacious and well tolerated treatment for Gram-negative nosocomial pneumonia in mechanically ventilated patients, a high-risk, critically ill population.**

Open Forum Infectious Diseases
MAJOR ARTICLE March 2021.

A Multicenter Evaluation of Ceftolozane/Tazobactam Treatment Outcomes in Immunocompromised Patients With Multidrug-Resistant *Pseudomonas aeruginosa* Infections

Delaney E. Hart,[1] Jason C. Gallagher,[2] Laura A. Puzniak,[3] and Elizabeth B. Hirsch[1]; for the C/T Alliance to deliver Real-world Evidence (CARE)

69 immunocompromised patients treated with C/T for MDR *P. aeruginosa*, clinical cure was achieved in 68% and mortality was 19%,

Table 2. Clinical Outcomes

Outcome	
Clinical cure, all infection sources (n = 69), No. (%)	47 (68)
Pneumonia, receiving pneumonia dosing (n = 28)	21 (75)
Pneumonia, receiving nonpneumonia dosing (n = 10)	3 (30)
30-d all-cause mortality, all infection sources (n = 69), No. (%)	13 (19)
Pneumonia, receiving pneumonia dosing (n = 28)	5 (18)
Pneumonia, receiving nonpneumonia dosing (n = 10)	3 (30)
Length of C/T therapy, mean ± SD, d	13 ± 11
Length of hospital stay, median (IQR), d	38 (54)

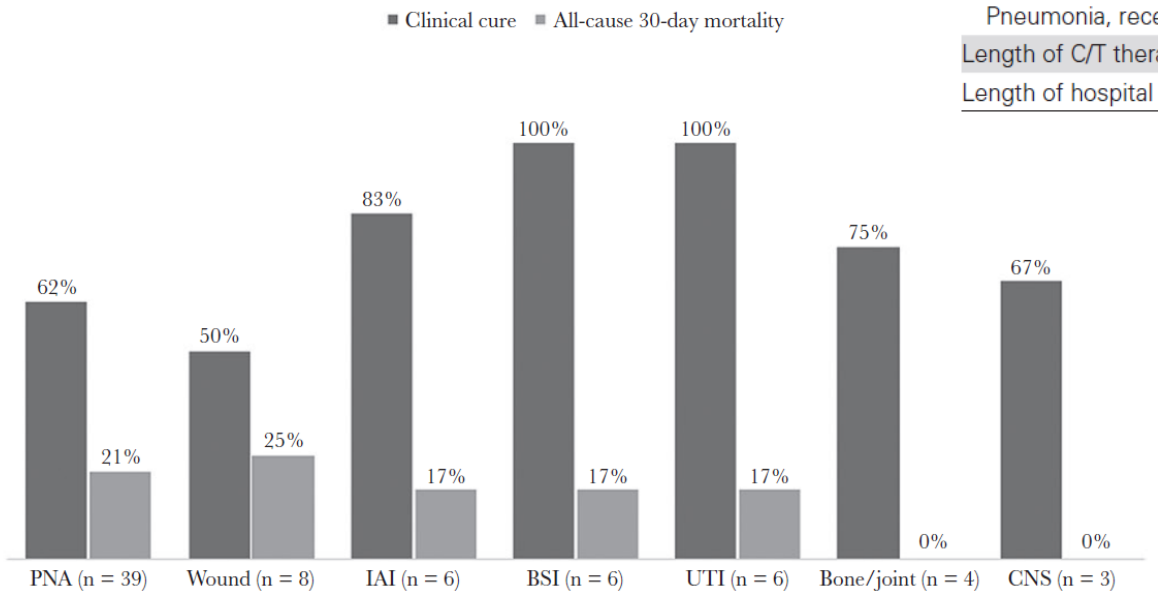


Figure 1. Clinical outcomes by source of infection. Abbreviations: BSI, primary bloodstream infection; CNS, central nervous system; IAI, intra-abdominal infection; PNA, pneumonia; UTI, urinary tract infection.

European Journal of Clinical Microbiology & Infectious Diseases (2019) 38:1457–1461
https://doi.org/10.1007/s10096-019-03573-4

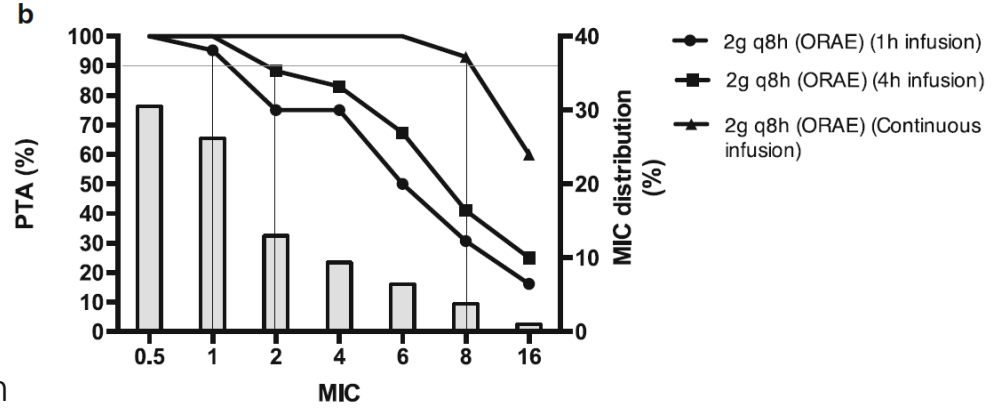
ORIGINAL ARTICLE

Continuous infusion of ceftolozane/tazobactam is associated with a higher probability of target attainment in patients infected with *Pseudomonas aeruginosa*

Benoît Pilmis[1,2] · Grégoire Petitjean[3,2] · Philippe Lesprit[4] · Matthieu Lafaurie[5] · Najoua El Helali[3,6] · Alban Le Monnier[3,2,6] · on behalf the ATB PK/PD study group

- 72 patients were enrolled, 79% were hospitalized in ICU, 51.4% were immunosuppressed
- The major site of infection was the respiratory tract (66.7%).
- In-hospital mortality rate was 15.2%.
- The PK/PD objectives (100% ƒT>4 MIC) were achieved for all patients infected with strains with CTZ/TZ MICs < 4 mg/L, regardless of the mode of administration.
- In contrast, intermittent bolus administration and prolonged infusion did not achieve the PK/PD objectives when the CTZ/TZ MICs were ≥ 4 mg/L.
- However, the PK/PD objectives (100% ƒT>4 MIC) were achieved for strains with MICs up to 8 mg/L in patients receiving continuous infusion of CTZ/TZ.

Prospective multicenter cohort study to compare prolonged or continuous infusion versus intermittent administration of CTZ/TZ for the treatment of MDR P. aeruginosa infections



A dosing regimen of 2 g/1 g CTZ/TZ administered every 8 h as a 1-h intravenous infusion, as currently recommended, did not provided adequate coverage to achieve a sufficient probability of target attainment for P. aeruginosa strains with MICs ≥4 mg/L.

Clinical Infectious Diseases

MAJOR ARTICLE

Clinical Infectious Diseases® 2020;

Modifiable Risk Factors for the Emergence of Ceftolozane-tazobactam Resistance

Pranita D. Tamma,[1] Stephan Beisken,[2] Yehudit Bergman,[3] Andreas E. Posch,[4] Edina Avdic,[5] Sima L. Sharara,[6] Sara E. Cosgrove,[7] and Patricia J. Simner[8]

Table 2. Comparison of 28 Patients with MDR *Pseudomonas aeruginosa* Treated with at Least 72 Hours of Ceftolozane-tazobactam (TOL-TAZ) with at Least a 4-Fold Increase in TOL-TAZ MICs on Subsequent *P. aeruginosa* Isolates Compared to Patients Who Did Not Have at Least a 4-Fold Increase in TOL-TAZ MICs on Subsequent *P. aeruginosa* Isolates

Variable	Increase in TOL-TAZ MIC (mcg/mL) (n = 14, 50%)	No Increase in TOL-TAZ MIC (mcg/mL) (n = 14, 50%)	*P*-value
Demographics			
Age in years (median, IQR)	56 (40–65)	56 (48–60)	.95
Female	5 (36%)	3 (21%)	.40
Weight in kilograms (median, IQR)	62 (56–79)	63 (56–76)	.87
Renal replacement therapy	4 (29%)	1 (7%)	.14
Underlying medical condition			
Cystic fibrosis	2 (14%)	1 (7%)	.54
Chronic ventilator dependence	3 (21%)	4 (29%)	.66
Burn	1 (7%)	1 (7%)	.99
Active immunosuppressive therapy	8 (57%)	5 (36%)	.26
Complex cardiovascular disease with foreign material[a]	3 (21%)	1 (7%)	.28
Site of infection			
Pneumonia	9 (64%)	10 (71%)	.69
Bacteremia	4 (29%)	1 (7%)	.14
Intra-abdominal infection	1 (7%)	3 (21%)	.28
Treatment data			
3 grams IV every 8 hours of TOL-TAZ	12 (86%)	14 (100%)	.14
1.5 grams IV every 8 hours of TOL-TAZ	2 (14%)	0	.14
1-hour TOL-TAZ infusion	14 (100%)	10 (71%)	.04
3-hour TOL-TAZ infusion	0	4 (29%)	.04
Duration of TOL-TAZ therapy	15 (8–22)	8.5 (6–14)	.32
Combination therapy for > 48 hours	6 (43%)	4 (29%)	.43
No source control[a]	4 (29%)	0	.04

Extending TOL-TAZ infusions may be protective for emergence of TOL-TAZ resistance during therapy

Time to clinical response among patients treated with Ceftazidime-Avibactam versus Ceftolozane-Tazobactam for multidrug-resistant *Pseudomonas aeruginosa* infections in the United States (CACTUS)

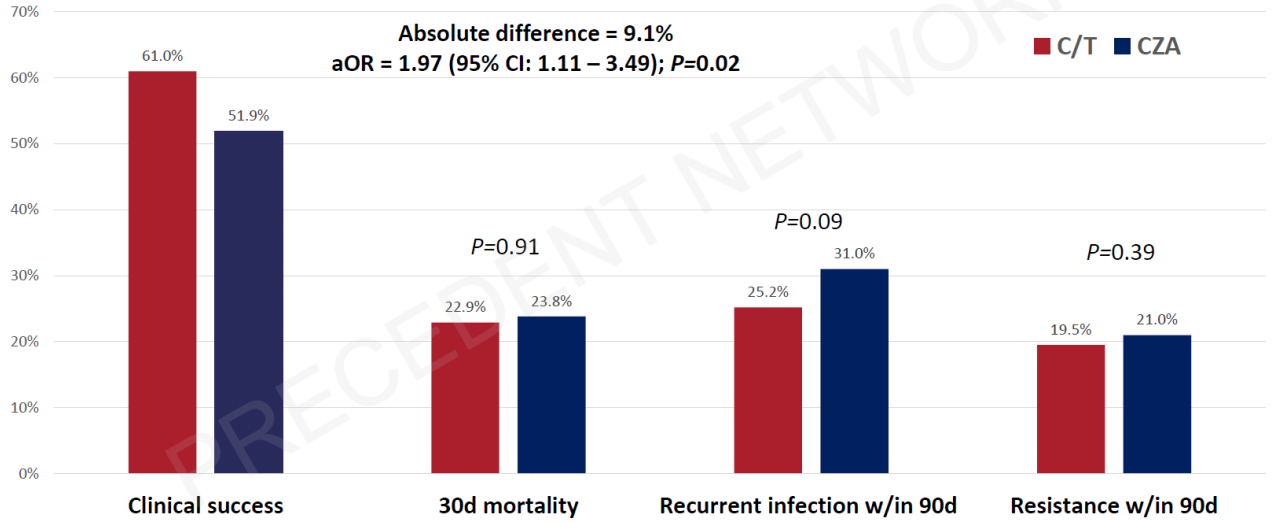
Abstract 02272

Authors: Shields RK, Abbo LM, Ackley R, Aitken SL, Albrecht B, Babiker A, Cifuentes R, Claeys KC, DeSear K, Gallagher JG, Gregory E, Heil EL, Hickey C, Klatt M, Kline EG, Kubat RC, Kufel WD, Lee JH, Lim A, Lingg T, MacDougall C, Mathers A, McCreary EK, Moore WJ, Olson S, Oxer J, Pearson J, Pham C, Polk C, Satlin MJ, Satola SW, Shah S, Solanki YB, Tamma PD, Vega A, Venugopalan V, Veve M, Wangchinda W, Witt LS, Wu J, Pogue JM

- Study Co-PI's:
  - Ryan K. Shields, University of Pittsburgh
  - Jason M. Pogue, University of Michigan

PRECEDENT NETWORK

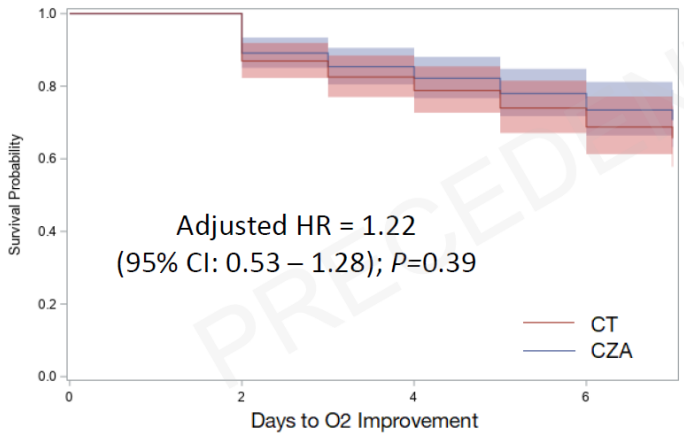
Clinical outcomes



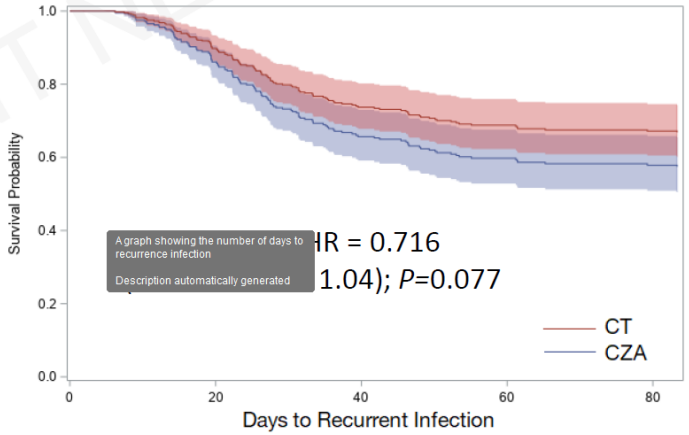
Secondary clinical outcomes (All patients)

- No difference in time to hemodynamic stability, defervescence, or normalization of leukocytosis

Time to improved oxygenation



Time to recurrent infection



- **Objective:** To compare the clinical efficacy of C/T vs. CZA for the treatment of MDR P. aeruginosa **pneumonia and bloodstream infections**
- **Study design:** Retrospective, matched cohort study
  - Patients matched by study site, severity of illness, infection site, and time to initiation of treatment
  - Conditional logistic regression analyses
- **Targeted sample size:** 420 patients (210 pairs)

Clinical Infectious Diseases
MAJOR ARTICLE 2018

Efficacy of Ceftazidime-Avibactam Salvage Therapy in Patients With Infections Caused by *Klebsiella pneumoniae* Carbapenemase–producing *K. pneumoniae*

Mario Tumbarello,[1,a] Enrico Maria Trecarichi,[1,a] Alberto Corona,[2] Francesco Giuseppe De Rosa,[3] Matteo Bassetti,[4] Cristina Mussini,[5] Francesco Menichetti,[6] Claudio Viscoli,[7] Caterina Campoli,[8] Mario Venditti,[9] Andrea De Gasperi,[10] Alessandra Mularoni,[11] Carlo Tascini,[12] Giustino Parruti,[13] Carlo Pallotto,[14] Simona Sica,[15] Ercole Concia,[16] Rosario Cultrera,[17] Gennaro De Pascale,[18] Alessandro Capone,[19] Spinello Antinori,[20] Silvia Corcione,[3] Elda Righi,[4] Angela Raffaella Losito,[1] Margherita Digaetano,[5] Francesco Amadori,[6] Daniele Roberto Giacobbe,[7] Giancarlo Ceccarelli,[9] Ernestina Mazza,[10] Francesca Raffaelli,[1] Teresa Spanu,[21] Roberto Cauda,[1] and Pierluigi Viale[8]

- 138 patients treated with CAZ-AVI salvage therapy after a first-line treatment with other antimicrobials.
- CAZ-AVI was administered with at least 1 other active antibiotic in 78.9% cases.
- Thirty days after infection onset **34.1% of the 138 patients had died**.
- Thirty-day mortality among the 104 patients with bacteremic KPC-Kp infections was significantly lower than that of a matched cohort whose KPC-Kp bacteremia had been treated with drugs other than CAZ-AVI (36.5% vs 55.8%, $P = .005$).

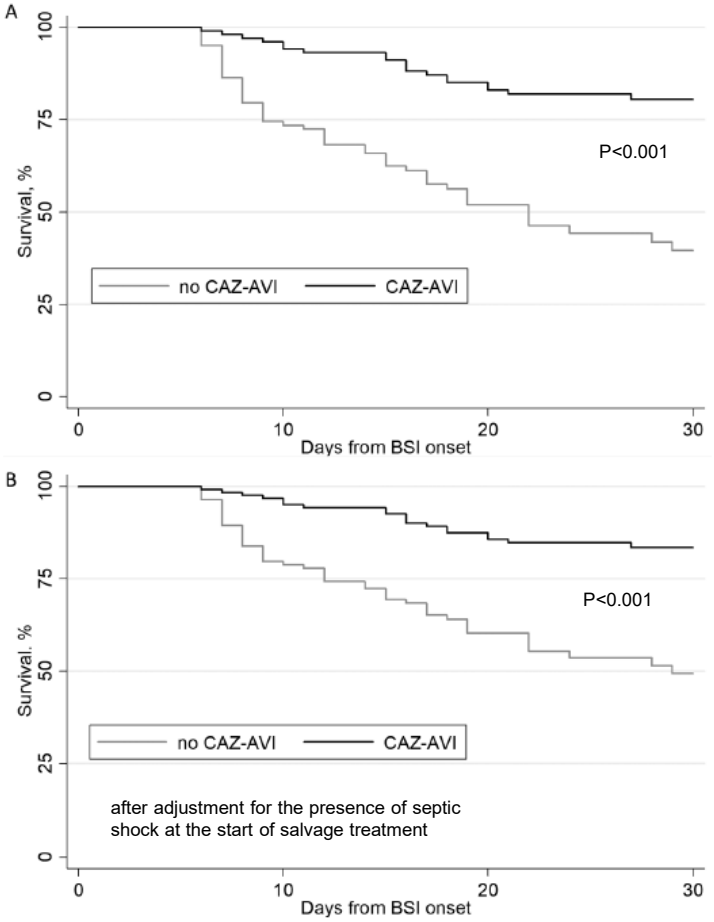


Table 4. Multivariate Analysis of Factors Associated With 30-Day Mortality in the 208 Patients With *Klebsiella pneumoniae* Carbapenemase–producing *K. pneumoniae* Bacteremia

	Without Propensity Score Adjustment		Adjusted for the Propensity Score for Therapy With CAZ-AVI	
Variable	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)
Mechanical ventilation	<.001	4.25 (1.99–9.09)	<.001	4.31 (1.99–9.33)
Charlson comorbidity index ≥3	.001	3.31 (1.61–6.77)	.001	3.30 (1.61–6.77)
Neutropenia	.01	3.22 (1.25–8.29)	.03	3.36 (1.25–8.75)
Septic shock	.002	2.95 (1.46–5.94)	.003	2.94 (1.46–5.92)
Any regimen that included CAZ-AVI	<.001	0.25 (.13–.51)	.001	0.27 (.13–.57)

Infect Dis Ther
https://doi.org/10.1007/s40121-023-00762-9

ORIGINAL RESEARCH

The Use and Effectiveness of Ceftazidime–Avibactam in Real-World Clinical Practice: EZTEAM Study

Alex Soriano · Philippe Montravers · Matteo Bassetti · Galina Klyasova · George Daikos · Paurus Irani · Gregory Stone · Richard Chambers · Pascale Peeters · Mitesh Shah · Claire Hulin · Natalia Albuquerque · Efim Basin · Benjamin Gaborit · Irene Kourbeti · Francesco Menichetti · María Teresa Perez-Rodriguez · Mathias W. Pletz · Marisa Sanchez · Ivan Trompa · Anita Verma · Maria Lavinea N. de Figueiredo · Claudie Charbonneau

Table 4 Ceftazidime–avibactam usage by indication

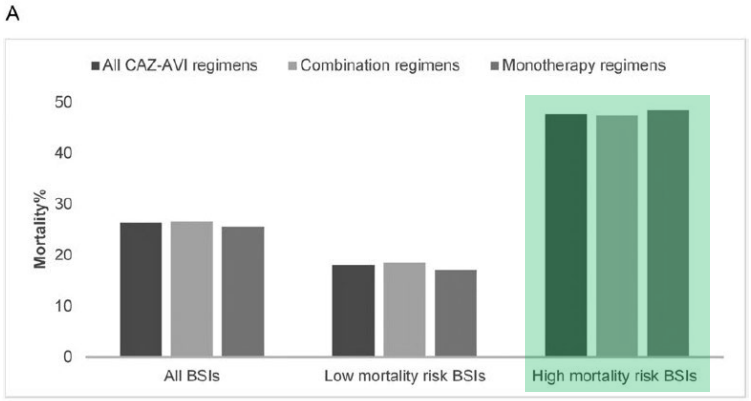
Characteristic	cIAI (n = 90)	cUTI (n = 103)	HAP/VAP (n = 114)	Other (n = 209)[a]	Total (n = 516)
Use of ceftazidime–avibactam overall, n (%)					
Monotherapy	26 (28.9)	68 (66.0)	25 (21.9)	39 (18.7)	158 (30.6)
Combination therapy	64 (71.1)	35 (34.0)	89 (78.1)	170 (81.3)	358 (69.4)
Gram-negative coverage	22 (24.4)	17 (16.5)	43 (37.7)	94 (45.0)	176 (34.1)
Other coverage[b]	17 (18.9)	8 (7.8)	19 (16.7)	20 (9.6)	64 (12.4)
Gram-negative and other coverage	25 (27.8)	10 (9.7)	27 (23.7)	56 (26.8)	118 (22.9)
Total duration of administration of ceftazidime–avibactam (days), n (%)					
Mean (SD)	13.6 (12.5)	9.3 (5.7)	10.3 (6.6)	13.3 (14.3)	11.9 (11.4)

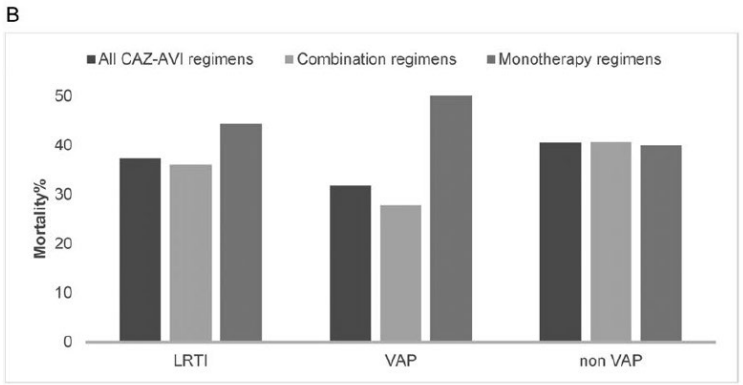
- 516 patients were treated for at least 72 h (354 patients from Europe and 162 patients from LATAM);
- Infection sources were intra-abdominal, urinary, respiratory, bloodstream infections, and other infections (approximately 20% each).
- K. pneumoniae was the most common microorganism identified (59.3%).
- The common MDR mechanisms for K. pneumoniae were KPC carbapenemase (33.9%), oxacillinase 48 (25.2%), ESBL (21.5%), or MBL (14.2%) production.
- Without prior patient exposure, 17 isolates (mostly K. pneumoniae) were resistant to ceftazidime–avibactam.
- Treatment success was achieved in 77.3% of patients overall.
- In-hospital mortality rate was 23.1%.
- Adverse events were reported for six of the 569 patients enrolled.

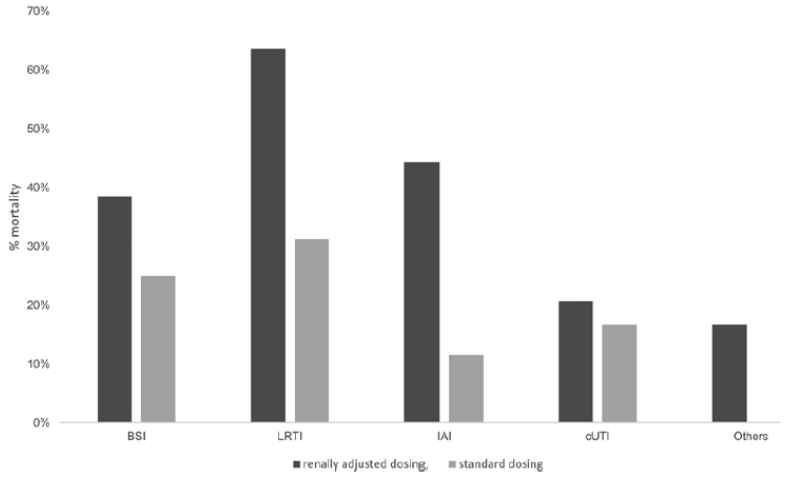
Clinical Infectious Diseases
MAJOR ARTICLE

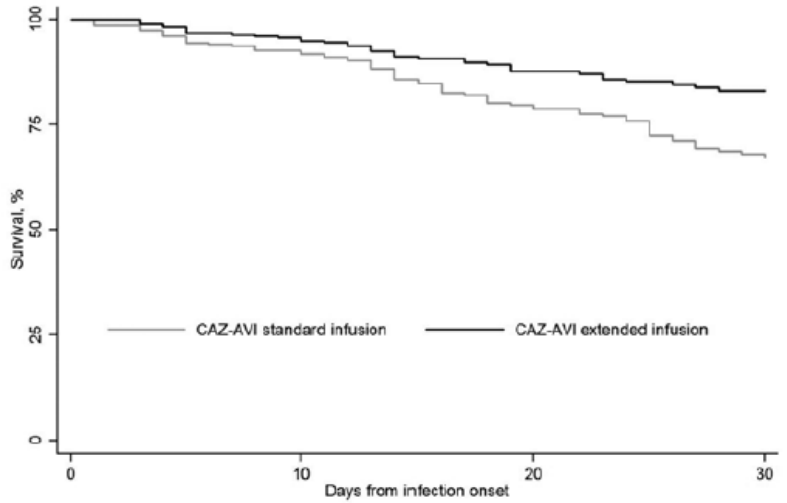
Ceftazidime-Avibactam Use for Klebsiella pneumoniae Carbapenemase–Producing *K. pneumoniae* Infections: A Retrospective Observational Multicenter Study

- 577 adults with bloodstream infections (391) or nonbacteremic infections involving mainly the urinary tract, lower respiratory tract, and intra-abdominal structures.
- All received treatment with CAZ-AVI alone (165) or with ≥1 other active antimicrobials (412).
- The all-cause mortality rate 30 days after infection onset was 25%







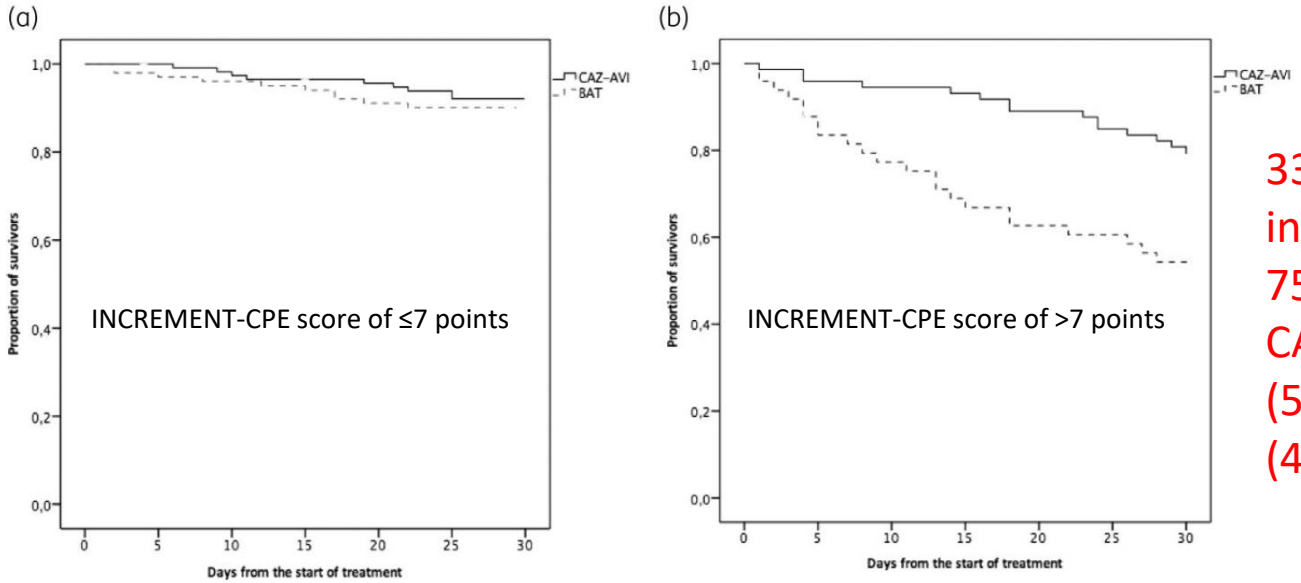


Impact of ceftazidime/avibactam versus best available therapy on mortality from infections caused by carbapenemase-producing Enterobacterales (CAVICOR study)

Journal of Antimicrobial Chemotherapy

OXA-48

Juan José Castón[1,2,3,4]*, Angela Cano[1,2,3,4], Inés Pérez-Camacho[5], Jose M. Aguado[4,6,7], Jordi Carratalá[4,8,9], Fernando Ramasco[10], Alex Soriano[4,11], Vicente Pintado[12], Laura Castelo-Corral[13], Adrian Sousa[14], María Carmen Fariñas[4,15,16], Patricia Muñoz[4,17,18,19,20], Vicente Abril López De Medrano[21], Óscar Sanz-Peláez[22], Ibai Los-Arcos[4,23,24], Irene Gracia-Ahufinger[3,25], Elena Pérez-Nadales[1,2,3], Elisa Vidal[1,2,3,4], Antonio Doblas[1], Clara Natera[1,2], Luis Martínez-Martínez[3,4,25,26] and Julian Torre-Cisneros[1,2,3,4]



339 patients with CPE infections.
75% OXA-48.
CAZ-AVI was used in 189 (55.8%) patients and 150 (44.2%) received BAT

Table 3. Multivariate analysis of factors associated with 30 day mortality in the 339 patients with infections caused by CPE

	Without propensity score adjustment			Adjusted for the propensity score for therapy with CAZ-AZI		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
CAZ-AVI-containing therapy	0.42	0.22–0.80	0.008	0.41	0.20–0.80	0.01
SOFA score at diagnosis of infection	1.22	1.10–1.35	<0.001	1.20	1.08–1.34	0.001
INCREMENT-CPE score >7 points	2.13	1.01–4.46	0.04	2.57	1.18–5.58	0.01

Clinical Infectious Diseases
MAJOR ARTICLE

Clinical Features and Outcomes of Infections Caused by Metallo-β-Lactamase–Producing Enterobacterales: A 3-Year Prospective Study From an Endemic Area

Marco Falcone,[1] Cesira Giordano,[2] Alessandro Leonildi,[2] Valentina Galfo,[1] Aurelio Lepore,[1] Lorenzo Roberto Suardi,[1] Niccolò Riccardi,[1] Simona Barnini,[2] and Giusy Tiseo[1]

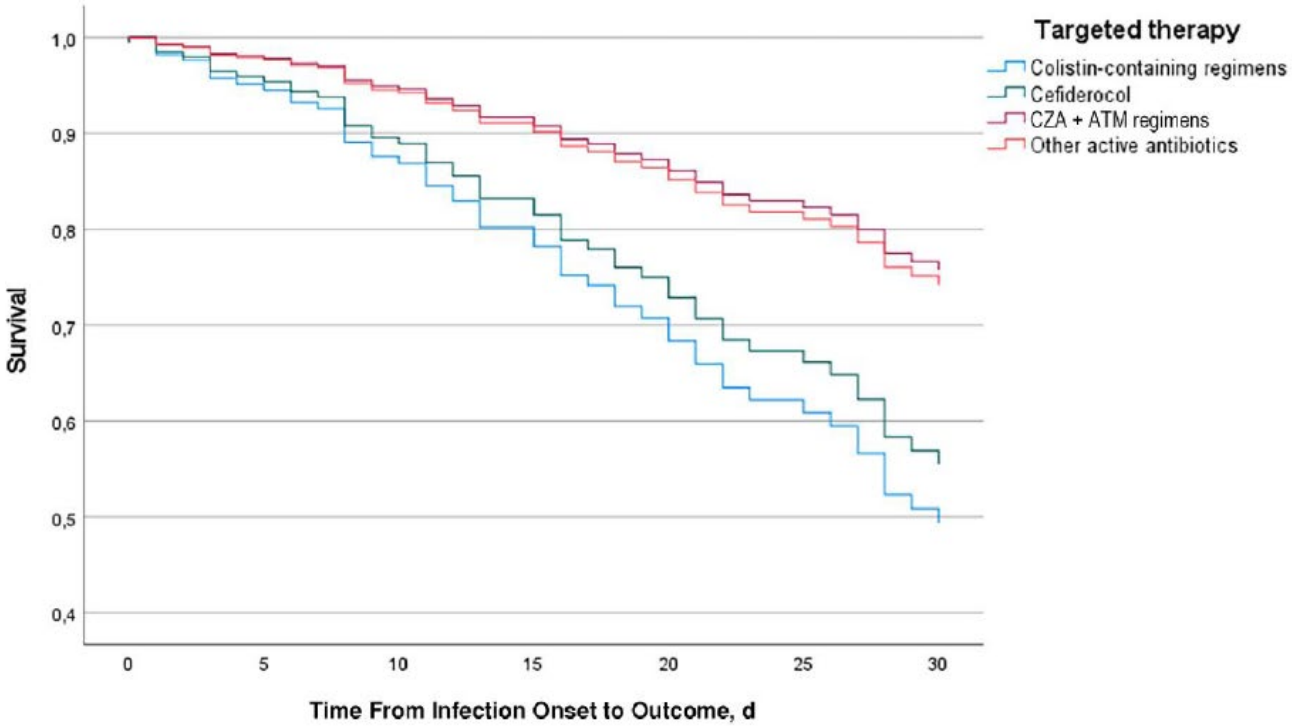
343 patients: 328 with NDM and 15 VIM producing Enterobacterales infections (199 patients (58%) with BSI)

215 (62.7%) received ceftazidime-avibactam plus aztreonam
33 (9.6%) received cefiderocol-containing regimens
26 (7.6%) received colistin-containing regimens
37 (10.8%) received other active antibiotics
32 did not receive in vitro active antibiotic therapy

The 30-day mortality rate was 29.7%.

Table 4. Cox Regression of Factors Independently Associated With 30-Day Mortality Rate[a]

Factor	aHR (95% CI)	*P* Value
Septic shock	3.57 (2.05–6.23)	<.001
Age	1.05 (1.03–1.08)	<.001
Active antibiotic therapy within 48 h after infection onset	0.48 (.26–.8)	.007
Source control	0.43 (.26–.72)	.001



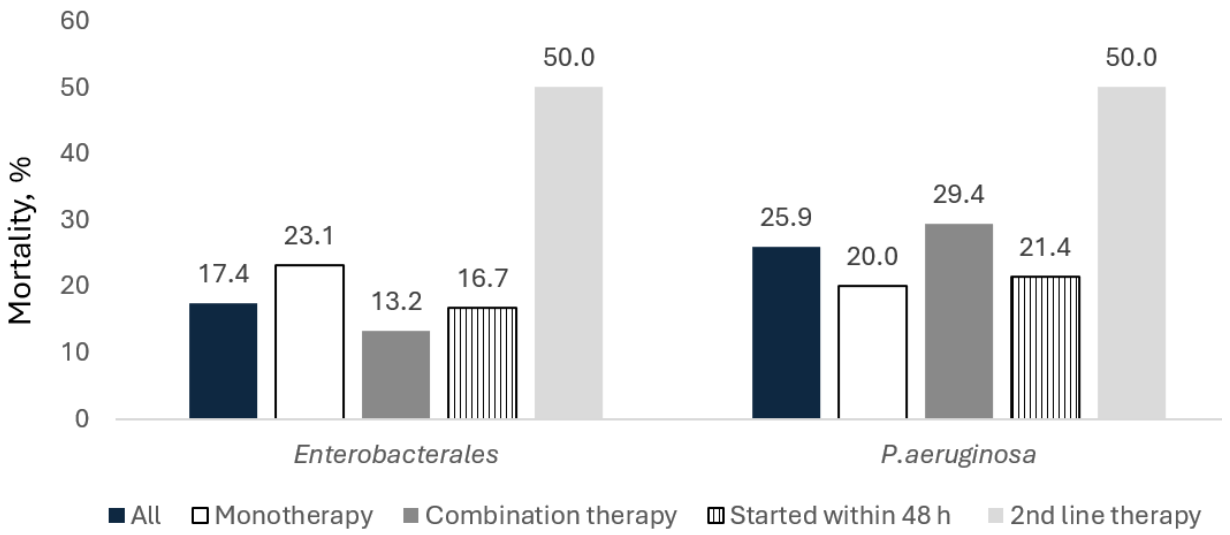
J Antimicrob Chemother
https://doi.org/10.1093/jac/dkae416

Journal of Antimicrobial Chemotherapy

Clinical impact of ceftazidime/avibactam on the treatment of suspected or proven infections in a large cohort of patients with haematological malignancies: a multicentre observational real-world study

Mario Tumbarello [1,2]*, Gabriele Giuliano[2], Marianna Criscuolo[3], Maria Ilaria Del Principe[4], Cristina Papayannidis[5], Nicola Stefano Fracchiolla[6], Michela Dargenio[7], Mariagiovanna Cefalo[8], Gianpaolo Nadali[9], Anna Candoni[10], Caterina Buquicchio[11], Francesco Marchesi[12], Marco Picardi[13], Federica Lessi[14], Monica Piedimonte[15], Lucia Prezioso[16], Matteo Piccini[17], Chiara Cattaneo[18], Alessandro Busca[19], Sara Brunetti[3], Elisa Buzzatti[4], Alessandra Dedola[5,20], Mariarita Sciumé[6], Nicola Di Renzo[7], Laura Cesini[8], Alessandra Vatteroni[9], Francesca Raffaelli[21] and Livio Pagano[3,22]

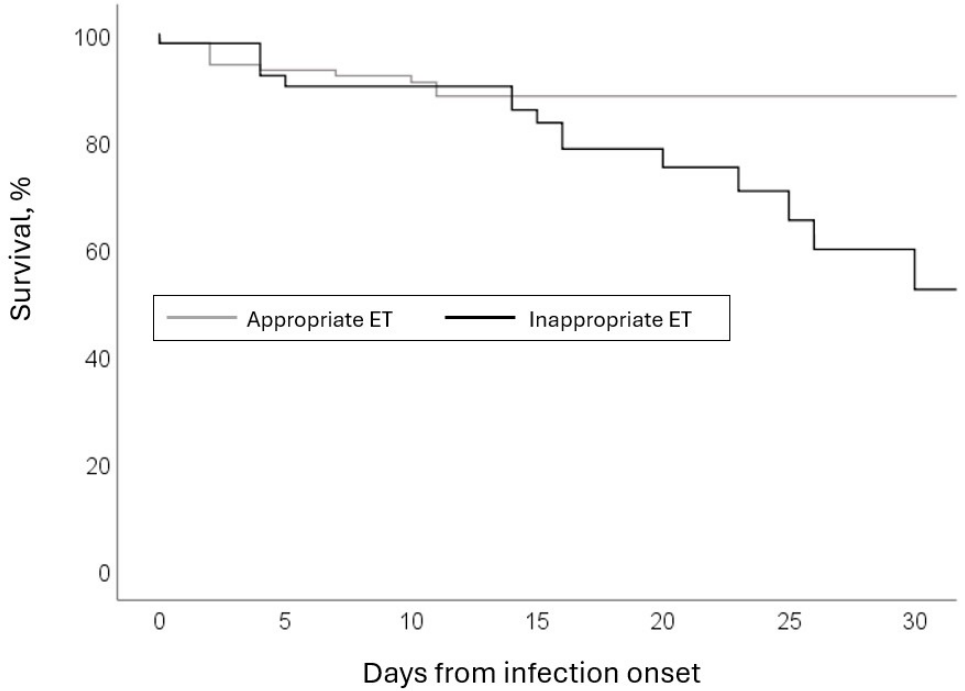
Enterobacterales were responsible for 98 MPIs, with KPC producers accounting for 75% of these, and carbapenem-resistant *Pseudomonas aeruginosa* caused 25% of MPIs.



198 patients (66 FUO and 132 microbiologically proven infections (MPIs).

Thirty days after onset of infection, 35/198 (17.7%) of patients had died: 19.7% (26/132) of those with MPI and 13.6% (9/66) of those with FUO. In patients with MPI mortality rate was 20.0% (24/120) in those with BSI and 40.0% (2/5)

Thirty-day mortality was independently associated with septic shock at infection onset and inappropriate initial antibiotic therapy



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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

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-024-04758-2

ORIGINAL ARTICLE

Real-world experience with meropenem/vaborbactam for the treatment of infections caused by ESBL-producing Enterobacterales and carbapenem-resistant *Klebsiella pneumoniae*

Giusy Tiseo[1] · Valentina Galfo[1] · Niccolò Riccardi[1] · Lorenzo Roberto Suardi[1] · Manuela Pogliaghi[1] · Cesira Giordano[2] · Alessandro Leonildi[2] · Simona Barnini[2] · Marco Falcone[3]

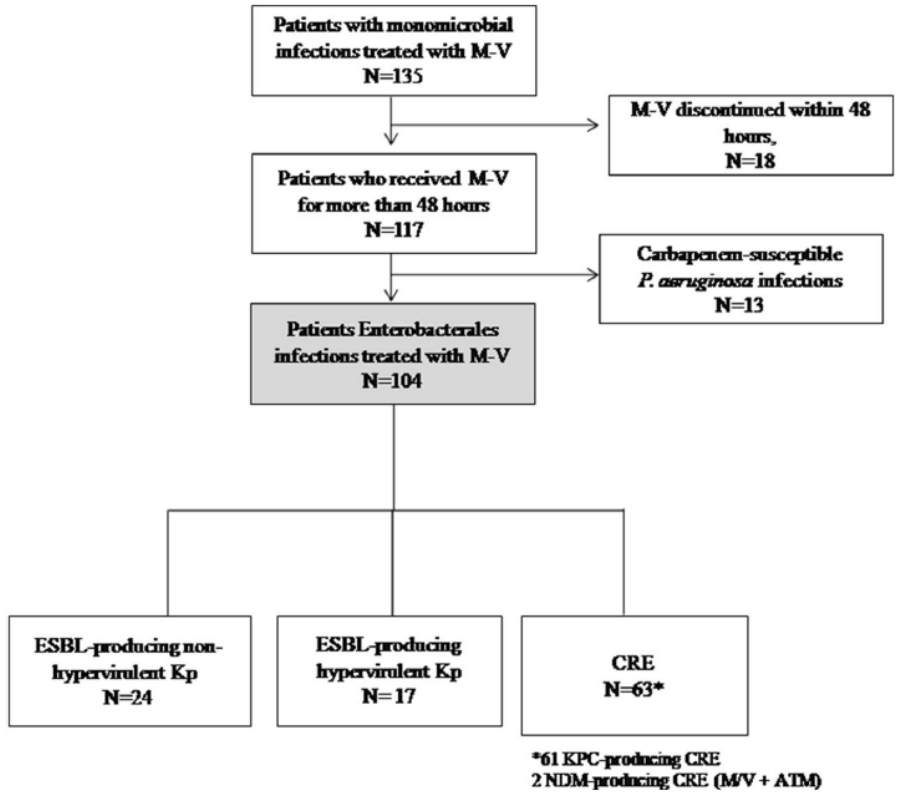

Table 2 Multivariable logistic regression analysis of factors independently associated with clinical failure.

Variables	OR (95% CI)	*p* value
SOFA score, each point increment	1.32 (1.02–1.7)	0.032
Source control	0.16 (0.03–0.89)	0.036

European Journal of Clinical Microbiology & Infectious Diseases
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ORIGINAL ARTICLE

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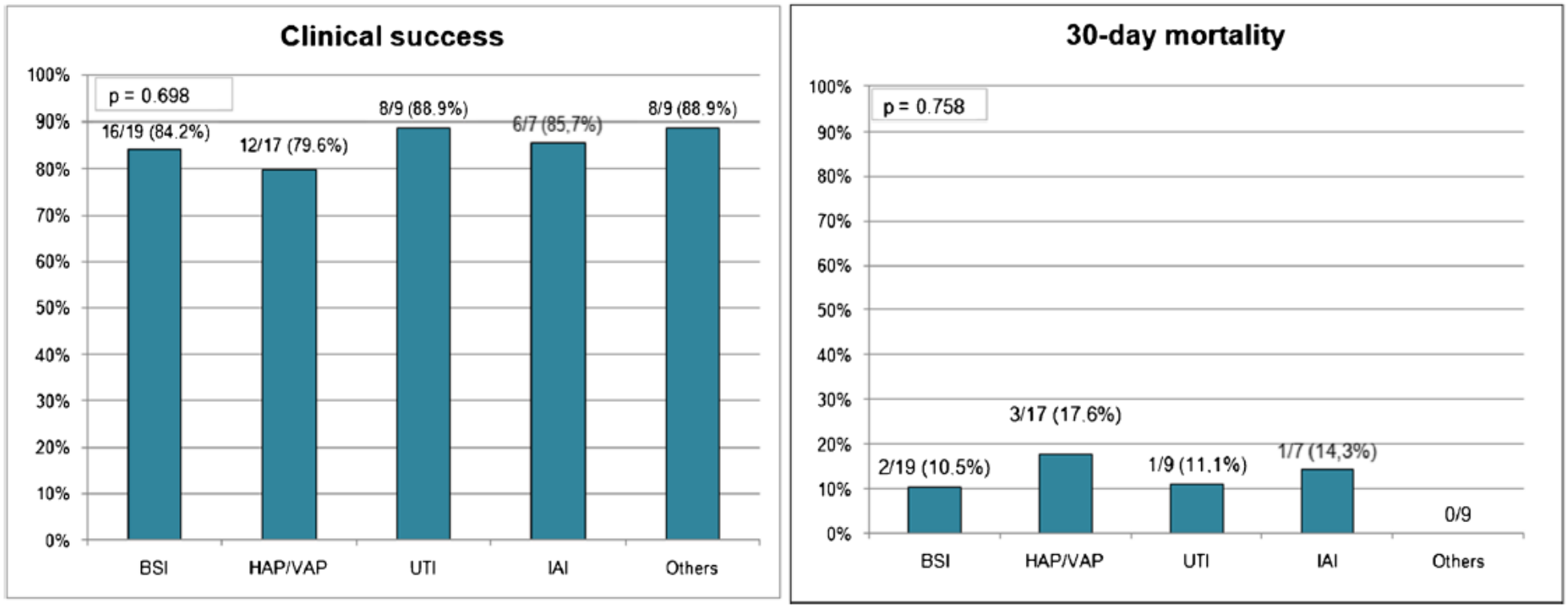


Fig. 2 Outcome of patients with KPC-Kp infections treated with M/V according to type of infection.

Open Forum Infectious Diseases
MAJOR ARTICLE

Outcomes and Predictors of Mortality in Patients With KPC-Kp Infections Treated With Meropenem Vaborbactam: An Observational Multicenter Study

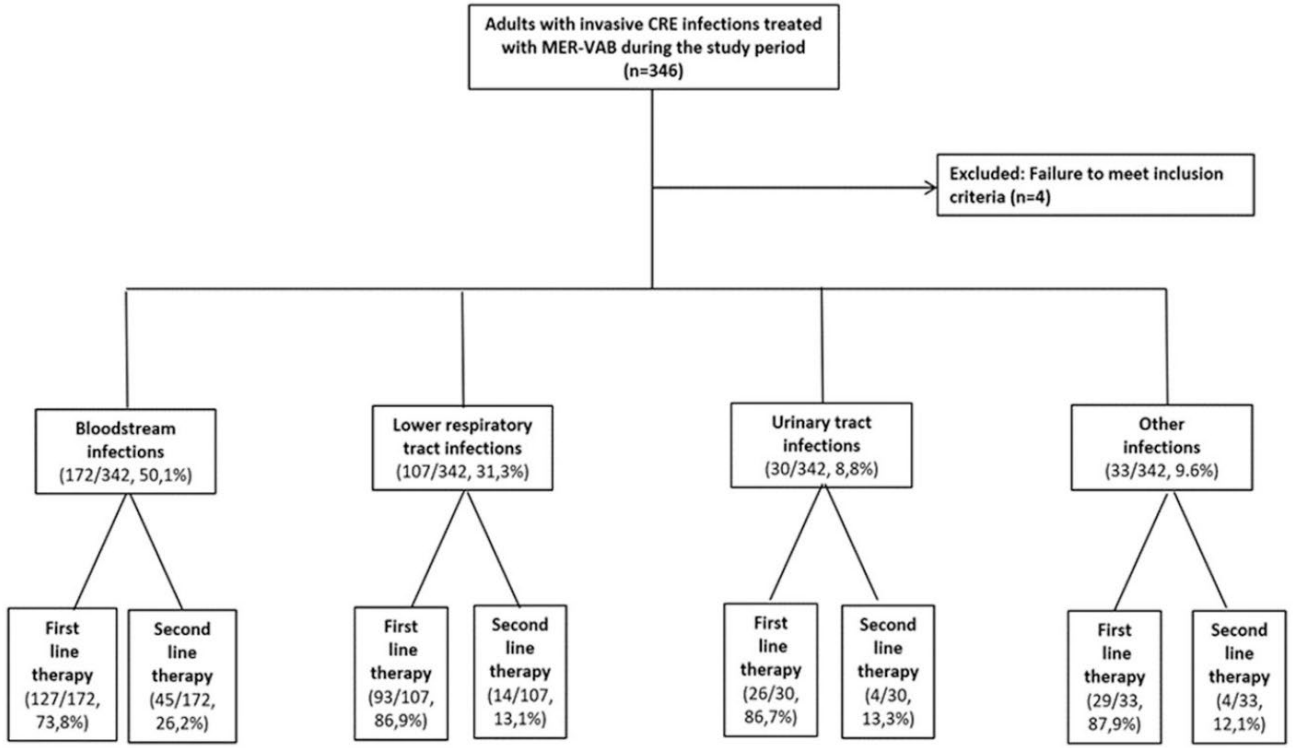
Mario Tumbarello,[1,2] Francesca Raffaelli,[3] Maddalena Giannella,[4] Gennaro De Pascale,[5,6] Antonio Cascio,[7,8] Francesco Giuseppe De Rosa,[9] Anna Maria Cattelan,[10,11] Alessandra Oliva,[12] Annalisa Saracino,[13] Matteo Bassetti,[14,15] Cristina Mussini,[16] Roberto Luzzati,[17] Alessandro Capone,[18] Liana Signorini,[19] Michele Bartoletti,[20,21] Margherita Sambo,[1,2] Loredana Sarmati,[22] Spinello Antinori,[23] Alessandra Mularoni,[24] Carlo Tascini,[25] Alberto Corona,[26] Renato Pascale,[4] Raffaella Rubino,[8] Silvia Corcione,[9] Maria Mazzitelli,[10] Gabriele Giuliano,[2] Antonio Lovecchio,[17] Davide Fiore Bavaro,[13] Marianna Meschiari,[16] Francesca Montagnani,[1,2] Massimiliano Fabbiani,[1,2] Ilaria De Benedetto,[9] Massimo Antonelli,[5,6] Mario Venditti,[12] and Pierluigi Viale[4]

342 patients: 50% BSI and 31% LRTI

43/172 (25.0%) of BSIs were catheter-related
76/107 (71.1%) of LRTI were VAP

Almost half (161/342, 47.1%) were diagnosed during an ICU stay

156, 45.6% were classified as high mortality risk according to INCREMENT score.



Open Forum Infectious Diseases

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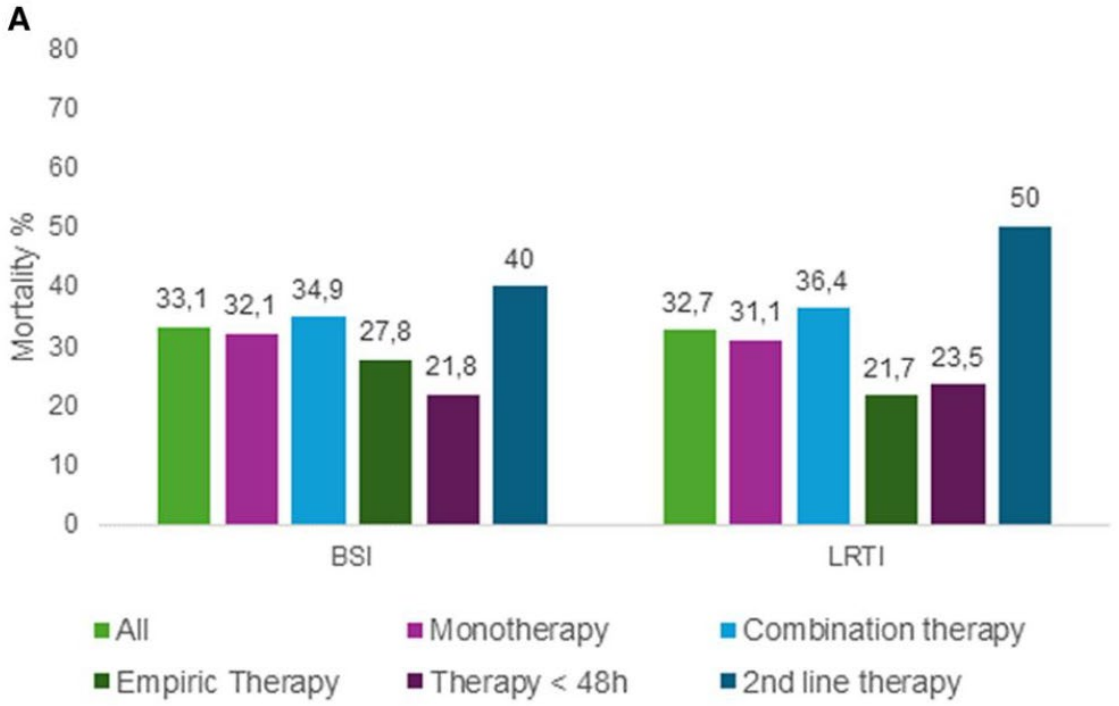

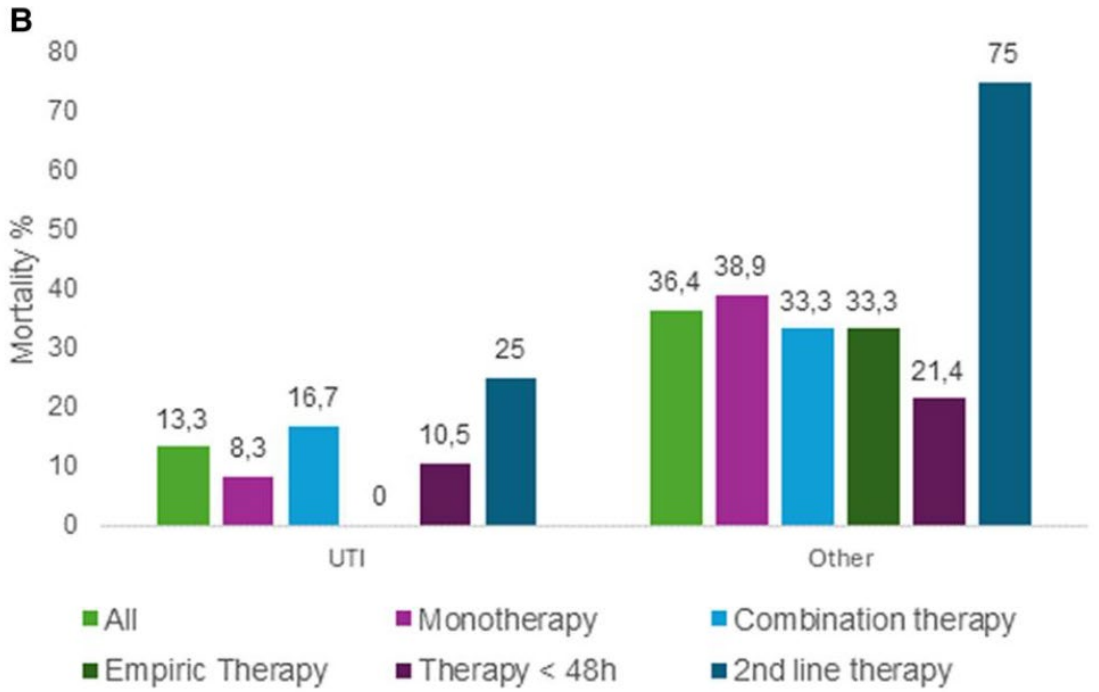

Open Forum Infectious Diseases

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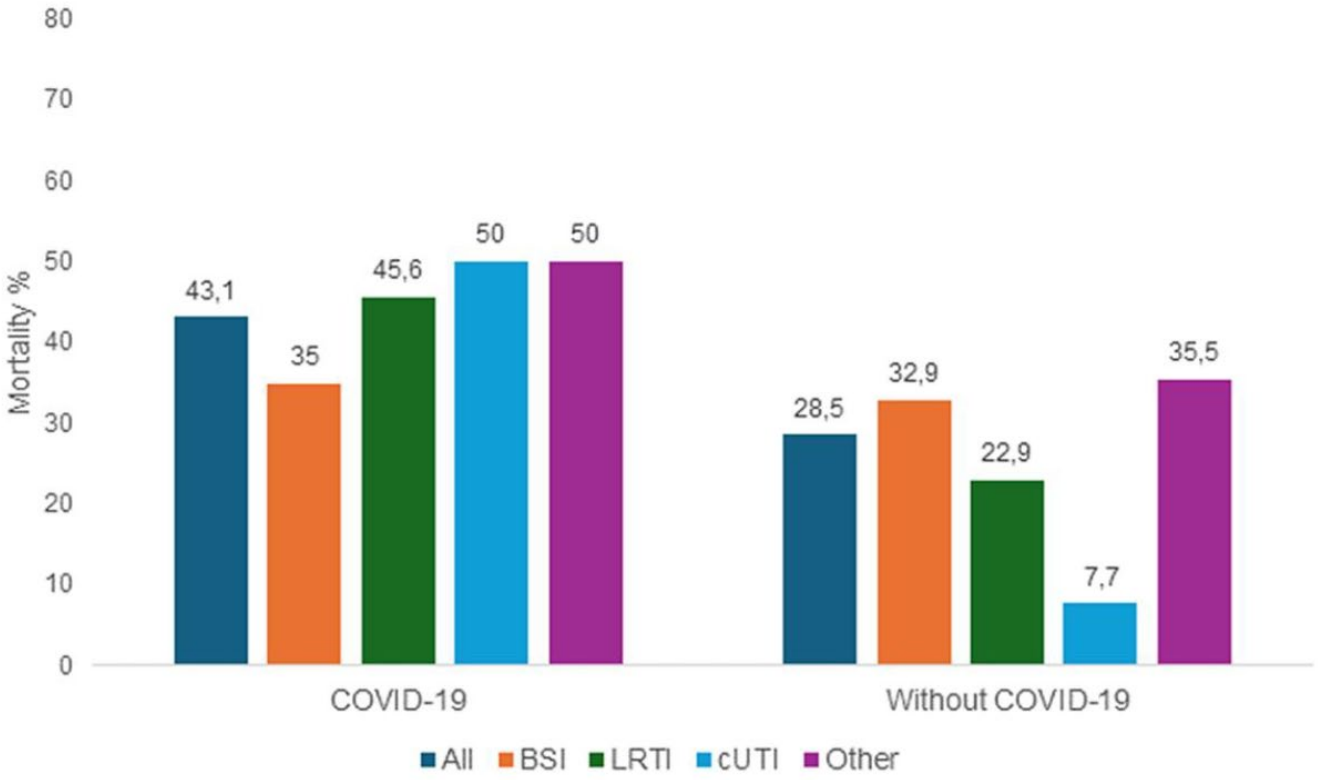
342 patients: 50% BSI and 31% LRTI

43/172 (25.0%) of BSIs were catheter-related
76/107 (71.1%) of LRTI were VAP

COVID-19 was the underlying condition for admission in 21.1% of patients (72/342).



Open Forum Infectious Diseases

MAJOR ARTICLE

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342 patients: 50% BSI and 31% LRTI

43/172 (25.0%) of BSIs were catheter-related
76/107 (71.1%) of LRTI were VAP

Most infections (62.3%) were managed with meropenem-vaborbactam monotherapy

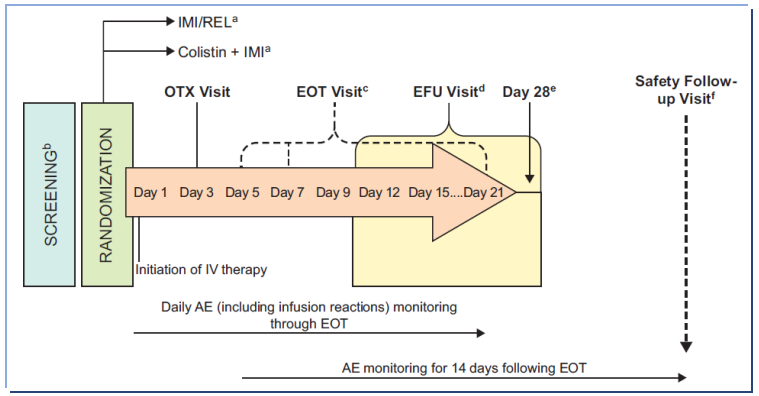
Table 4. Multivariate Analysis of Factors Associated With 30-d Mortality

	Adjusted For The Propensity Score Matching For Combination Therapy			
	No		Yes	
Variables	*P* value	HR (95% CI)	*P* value	HR (95% CI)
Septic shock at infection onset	<.001	3.65 (2.27–5.87)	<.001	2.85 (1.65–4.92)
Charlson Comorbidity Index ≥ 3	.005	2.42 (1.31–4.47)	.01	2.33 (1.22–4.48)
Dialysis[a]	.04	1.69 (1.03–2.78)	.02	1.91 (1.11–3.31)
COVID-19	.03	1.64 (1.05–2.56)	.04	1.62 (1.19–2.63)
INCREMENT score ≥8	.04	1.65 (1.02–2.67)	.01	2.02 (1.13–3.61)
MER-VAB started within 48 h of infection onset	.05	0.69 (0.55–1.06)	.39	0.81 (0.52–1.29)

Clinical Infectious Diseases
MAJOR ARTICLE

RESTORE-IMI 1: A Multicenter, Randomized, Double-blind Trial Comparing Efficacy and Safety of Imipenem/Relebactam vs Colistin Plus Imipenem in Patients With Imipenem-nonsusceptible Bacterial Infections

Johann Motsch,[1] Cláudia Murta De Oliveira,[2] Viktor Stus,[3] Iftihar Köksal,[4] Olexiy Lyulko,[5] Helen W. Boucher,[6] Keith S. Kaye,[7] Thomas M. File Jr,[8] Michelle L. Brown,[9] Ireen Khan,[9] Jiejun Du,[9] Hee-Koung Joeng,[9] Robert W. Tipping,[9] Angela Aggrey,[9] Katherine Young,[9] Nicholas A. Kartsonis,[9] Joan R. Butterton,[9] and Amanda Paschke[9]



Pseudomonas aeruginosa (77%), *Klebsiella* spp. (16%), other Enterobacteriaceae (6%)

31 patients received imipenem/relebactam and 16 colistin+imipenem

Favorable overall response was observed in 71% imipenem/relebactam and 70% colistin+imipenem patients, day 28 favorable clinical response in 71% and 40%, and 28-day mortality in 10% and 30%, respectively. Serious adverse events occurred in 10% of imipenem/relebactam and 31% of colistin+imipenem patients,

Table 2. Primary and Secondary Prospective Efficacy Endpoints (in the Modified Microbiologic Intent-to-Treat Population) and Secondary Prospective Safety Endpoints (in the Safety Population)

	IMI/REL (n = 21)		Colistin + IMI (n = 10)		Unadjusted Difference	Adjusted Difference[a]	
Endpoint	n	% (95% CI)[b]	n	% (95% CI)[a]	%	%	90% CI
Primary endpoint							
Favorable overall response[c]	15	71.4 (49.8, 86.4)	7	70.0 (39.2, 89.7)	1.4	–7.3	(–27.5, 21.4)
Hospital-acquired bacterial pneumonia/ ventilator-associated bacterial pneumonia	7/8	87.5 (50.8, 99.9)	2/3	66.7		20.8	
Complicated intraabdominal infection	0/2[d]	0.0	0/2[e]	0.0		0.0	
Complicated urinary tract infection	8/11	72.7 (42.9, 90.8)	5/5	100.0 (51.1, 100.0)		–27.3 (–52.8, 12.8)	
Secondary endpoints							
Favorable clinical response (day 28)	15[f]	71.4 (49.8, 86.4)	4[g]	40.0 (16.7, 68.8)	31.4	26.3	(1.3, 51.5)
28-day all-cause mortality	2	9.5 (1.4, 30.1)	3	30.0 (10.3, 60.8)	–20.5	–17.3	(–46.4, 6.7)
Treatment-emergent nephrotoxicity[h]	3/29	10.3 (2.8, 27.2)	9/16	56.3 (33.2, 76.9)		–45.9 (–69.1, –18.4)	

Open Forum Infectious Diseases

BRIEF REPORT

Early Multicenter Experience With Imipenem-Cilastatin-Relebactam for Multidrug-Resistant Gram-Negative Infections

Nicholas Rebold,[1] Taylor Morrisette,[1,2,3] Abdalhamid M. Lagnf,[1] Sara Alosaimy,[1] Dana Holger,[1] Katie Barber,[4,5] Julie Ann Justo,[6,7] Kayla Antosz,[7] Travis J. Carlson,[8] Jeremy J. Frens,[9] Mark Biagi,[10,11] Wesley D. Kufel,[12,13] William J. Moore,[14] Nicholas Mercuro,[15,16] Brian R. Raux,[2] and Michael J. Rybak[1,17,18]

- Multicenter, retrospective, observational case series
- 21 patients were treated with imipenem-cilastatin-relebactam.
- There were mixed infection sources, with pulmonary infections (11/21,52%) composing the majority.
- The primary pathogen was *Pseudomonas aeruginosa* (16/21, 76%), and 15/16 (94%) isolates were multidrug-resistant.
- Thirty-day survival occurred in 14/21 (67%) patients
- Two patients experienced adverse effects.

Journal of Global Antimicrobial Resistance 37 (2024) 190–194

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

Short Communication

Real-world evaluation of imipenem/cilastatin/relebactam across US medical centres

Ryan K. Shields[a], Emre Yücel[b,*], Vladimir Turzhitsky[b], Sanjay Merchant[b], Jae S. Min[b], Alexandre H. Watanabe[b]

160 patients who received for ≥2 days imipenem/cilastatin/relebactam.

At treatment initiation, the median Charlson Comorbidity Index was 5, 45% were in the intensive care unit, and 19% required vasopressor support.

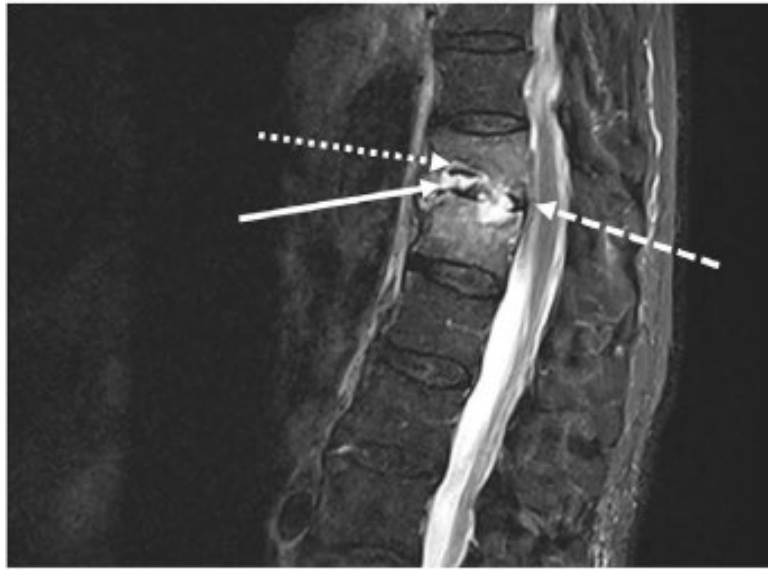
The in-hospital mortality rate was 24%.

Table 2
Microbiologic characteristics of a subset of patients for whom data were available.

Pathogen infection, *n* (%)[a]	Overall (*N* = 37[b])	HABP/VABP (*n* = 24)	cUTI (*n* = 4)	cIAI (*n* = 3)
Pseudomonas aeruginosa	33 (89.2)	21 (87.5)	3 (75.0)	3 (100.0)
MDR PsA positive	28 (75.7)	18 (75.0)	2 (50.0)	2 (66.7)
Enterobacterales				
Escherichia coli	4 (10.8)	4 (16.7)	0	0
Klebsiella pneumoniae	7 (18.9)	4 (16.7)	1 (25.0)	0
Enterobacter cloacae	4 (10.8)	4 (16.7)	0	0
Klebsiella (Enterobacter) aerogenes	1 (2.7)	1 (4.2)	0	0
Klebsiella oxytoca	1 (2.7)	1 (4.2)	0	0
Serratia marcescens	2 (5.4)	2 (8.3)	0	0
CRE positive	1 (2.7)	1 (4.2)	0	0
ESBL positive	4 (10.8)	4 (16.7)	0	0
Polymicrobial infections[c]	13 (35.1)	11 (45.8)	0	0

frontiers | Frontiers in Pharmacology

TYPE Brief Research Report
PUBLISHED 30 October 2024
DOI 10.3389/fphar.2024.1347306



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Laffont-Lozes P, Naciri T, Pantel A, Martin A, Pruvot-Occean A-S, Haignere V, Loubet P, Sotto A and Larcher R (2024) First case report of a vertebral osteomyelitis caused by

First case report of a vertebral osteomyelitis caused by carbapenem-resistant *Enterobacter cloacae* treated with imipenem/cilastatin/relebactam prolonged infusion then meropenem/vaborbactam in continuous infusion

Paul Laffont-Lozes[1], Tayma Naciri[2], Alix Pantel[3,4], Aurélie Martin[2], Anne-Sophie Pruvot-Occean[5], Vincent Haignere[6], Paul Loubet[2,4], Albert Sotto[2,4] and Romaric Larcher[2,7]*

We report a case of a vertebral osteomyelitis caused by carbapenem-resistant *Enterobacter cloacae* successfully treated with extended infusion of I-R (1.25 g q6h over 2 h), then with continuous infusion of MVB (2 g q4h as over 4 h). Therapeutic drug monitoring confirmed that extended-infusion of I-R and continuous infusion of MVB achieved serum concentrations up to 12 mg/L of imipenem and 19 mg/L of meropenem, respectively.

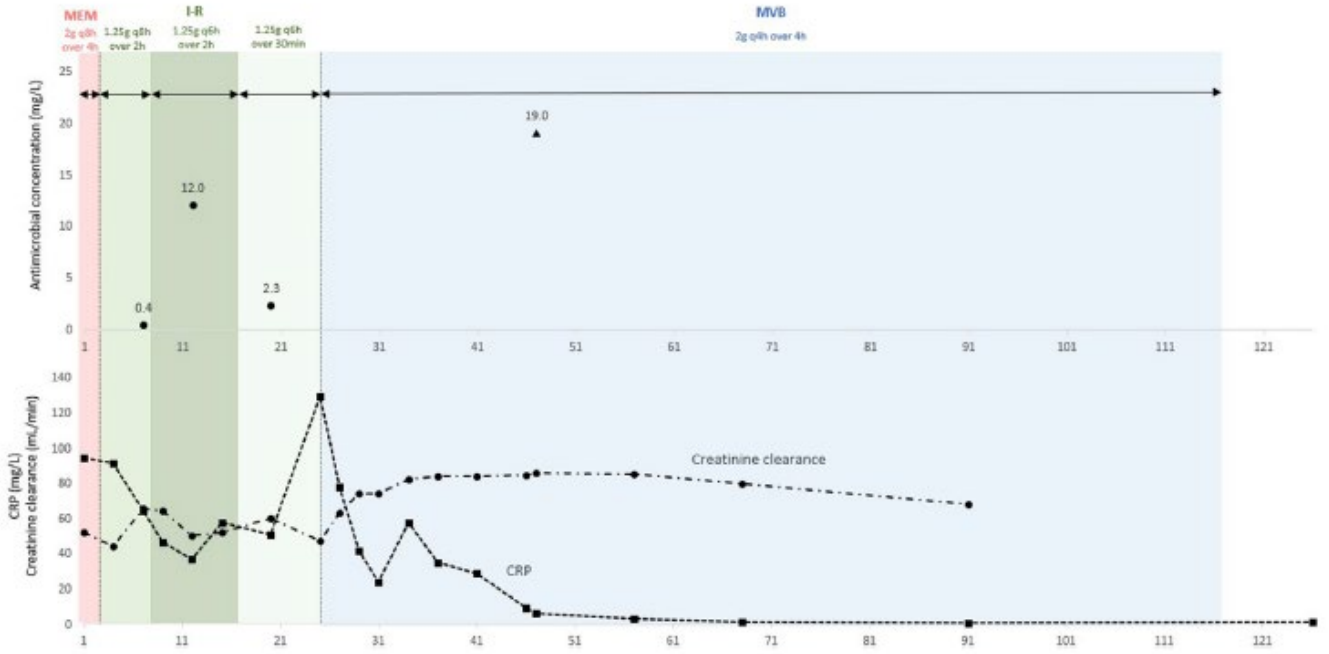


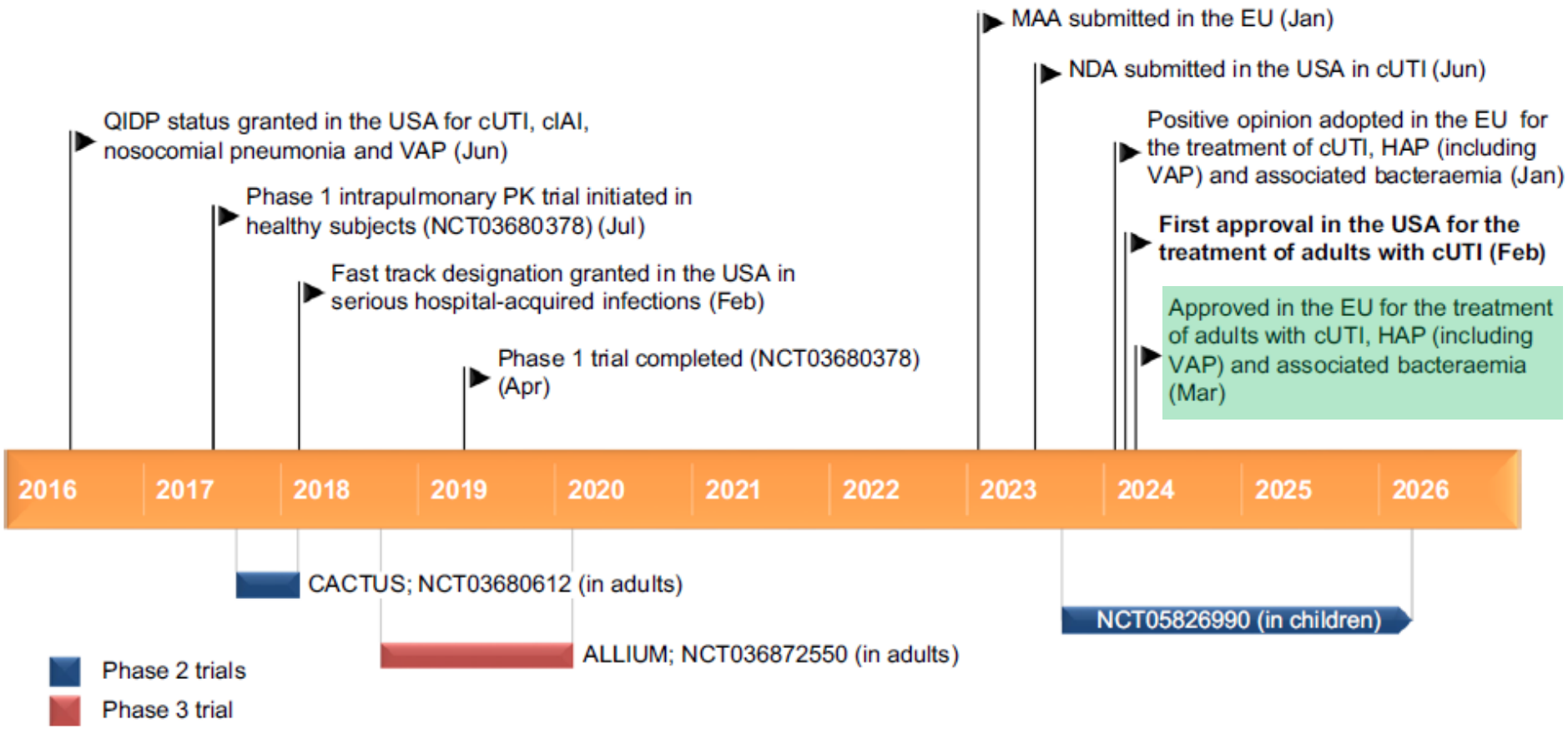
FIGURE 2
Therapeutic drug monitoring of imipenem and meropenem plasma concentrations in the patient. Imipenem through concentrations are represented by black circles and meropenem steady-state concentrations are represented by black triangles. Creatinine clearance is represented by black circles and dotted line, and C-reactive protein (CRP) is represented by black squares and dotted line.

Drugs (2024) 84:737–744
https://doi.org/10.1007/s40265-024-02035-2

ADISINSIGHT REPORT

Cefepime/Enmetazobactam: First Approval

Susan J. Keam[1]



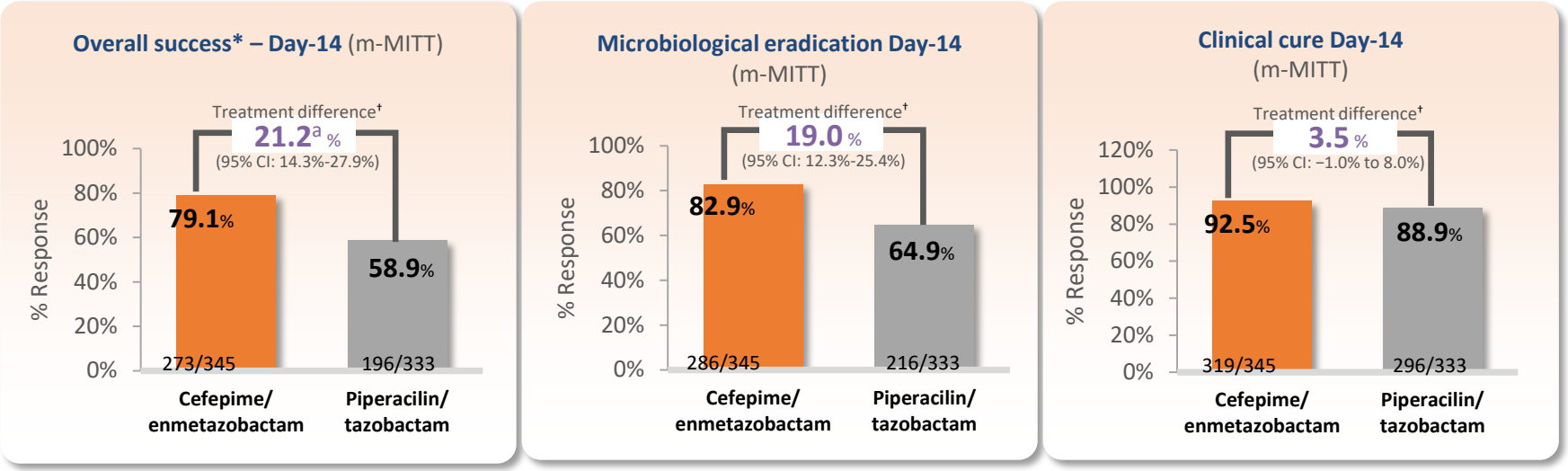
JAMA | Original Investigation

Effect of Cefepime/Enmetazobactam vs Piperacillin/Tazobactam on Clinical Cure and Microbiological Eradication in Patients With Complicated Urinary Tract Infection or Acute Pyelonephritis

A Randomized Clinical Trial

Keith S. Kaye, MD; Adam Belley, PhD; Philip Barth, PhD; Omar Lahlou, PharmD; Philipp Knechtle, PhD; Paola Motta, PhD; Patrick Velicitat, MD

In complicated UTI or pyelonephritis, cefepime/ enmetazobactam increased success vs. PIP/TAZ at Day 14[1]



RBI (95% CI)	NNT (CI)
34% (21 to 50)[a]	5 (4 to 8)

RBI (95% CI)	NNT (CI)
4% (–1 to 9)	Not significant

RBI (95% CI)	NNT (CI)
28% (17 to 41)	6 (5 to 9)

Cefepime/enmetazobactam demonstrated a clinically meaningful, superior composite clinical cure/microbiological eradication versus PIP/TAZ for infections caused by Gram negative pathogens in the ALLIUM cUTI/AP trial

BL/BLI

CEF/BLI

- Caftolozano-tazobactam
- Ceftazidime-avibactam
- Cefepime-enmetazobactam

CARB/BLI

- Meropenem-vaborbactam
- Imipenem-relebactam

SITA
Società Italiana di Terapia Antinfettiva
Antibatterica Antivirale Antifungina

14° CONGRESSO NAZIONALE

GENOVA | 21-22 novembre 2024