Focus sui nuovi antibiotici per le infezioni da microrganismi MDR

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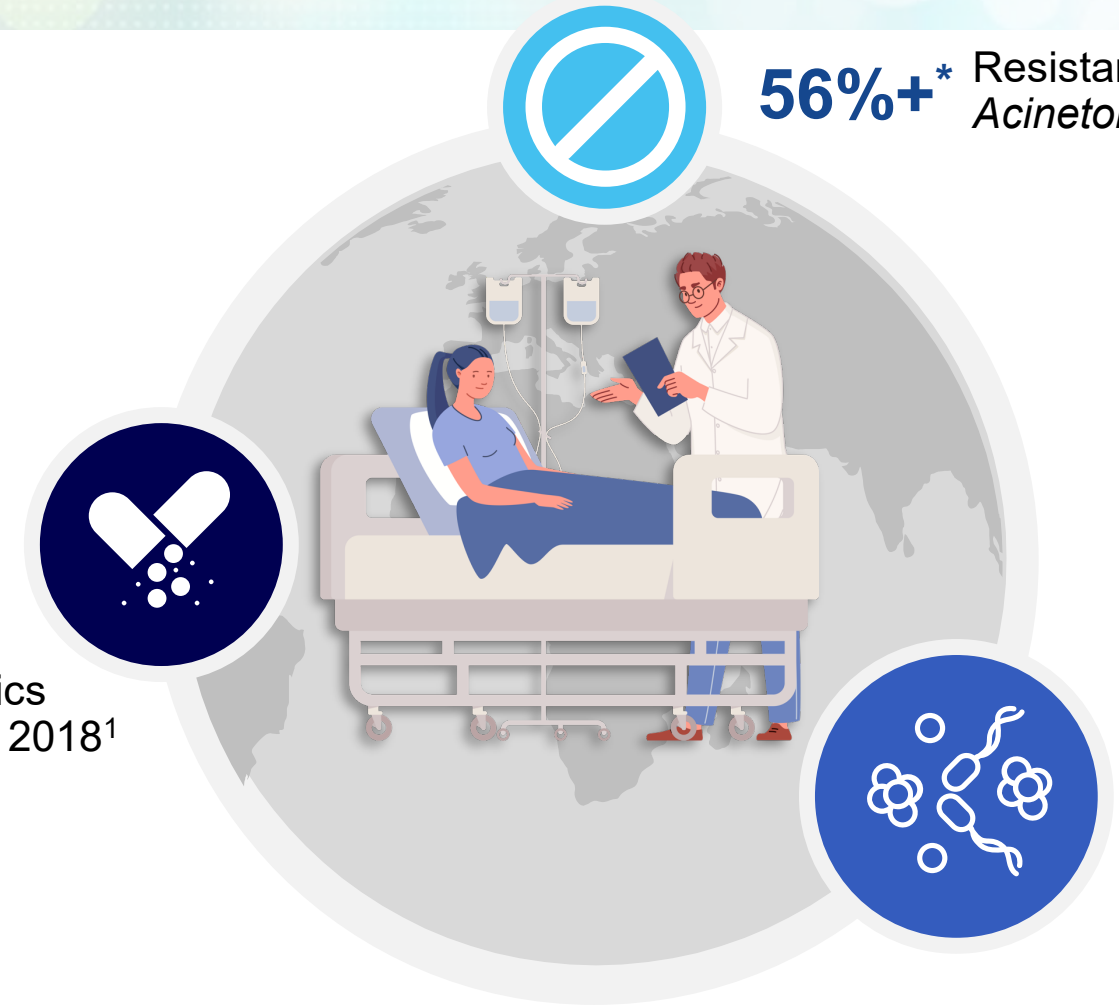
Disclosures (past 2 years)

- Advisor/consultant/speaker bureau
  - Angelini, Biomerieux, Cidara, Gilead, Menarini, Medscape, Mundipharma, MSD, Pfizer, Shionogi

Antimicrobial resistance is a globally unfolding crisis that every healthcare professional can act upon to avert

56%+* Resistance in key pathogens: *Acinetobacter spp.* and *Klebsiella spp.*[2]



46%

Global increase in consumption of prescribed antibiotics between 2000 and 2018[1]

4.95 million

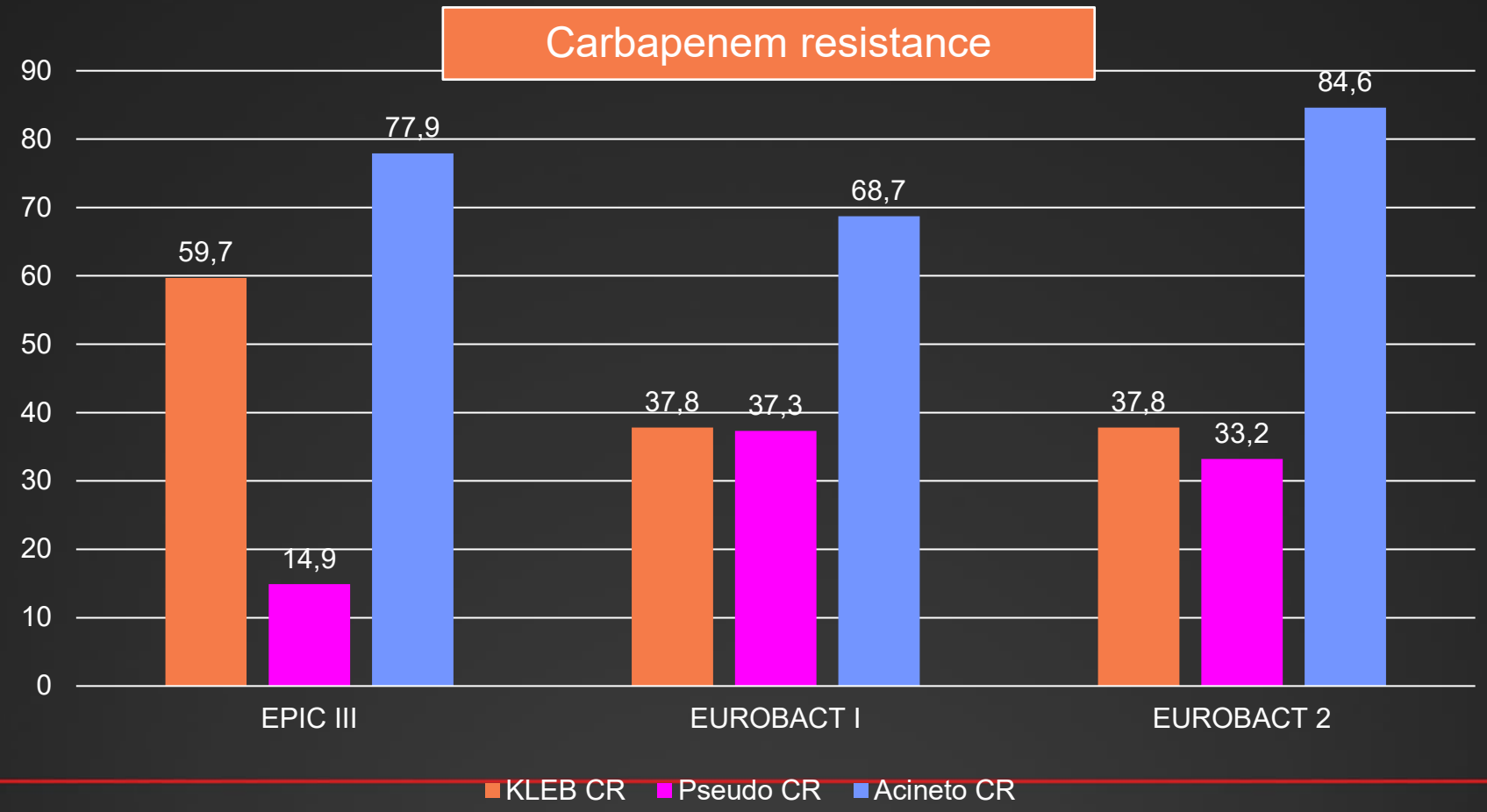
Deaths globally in 2019 associated with bacterial AMR[3]

*Data from the 2022 GLASS report covering 87 CTAs shows a global resistance rate of ≥56% in *Acinetobacter* spp. to carbapenem and aminoglycosides, and ≥57% in *Klebsiella pneumoniae* to third- and fourth-generation cephalosporins. This data accounts for varying testing coverage across different regions.

AMR, antimicrobial resistance.

1. Browne AJ, et al. *Lancet Planet Health*. 2021;5(12):e893-e904.
2. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report: 2022. 2022. https://www.who.int/publications/i/item/9789240062702;
3. Antimicrobial Resistance Collaborators. *Lancet*. 2022;399(10325):629-655.

Characteristics of the pathogens in the initial blood culture in EUROBACT-2 and comparison with EUROBACT-1 and EPIC III studies



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Vincent et al. JAMA. 2020 Apr 21; 323(15): 1478–1487
Tabah A et al. Intensive Care Med. 2023 Feb 10:1-13.
Tabah A et al. Intensive Care Med. 2012 Dec;38(12):1930-45

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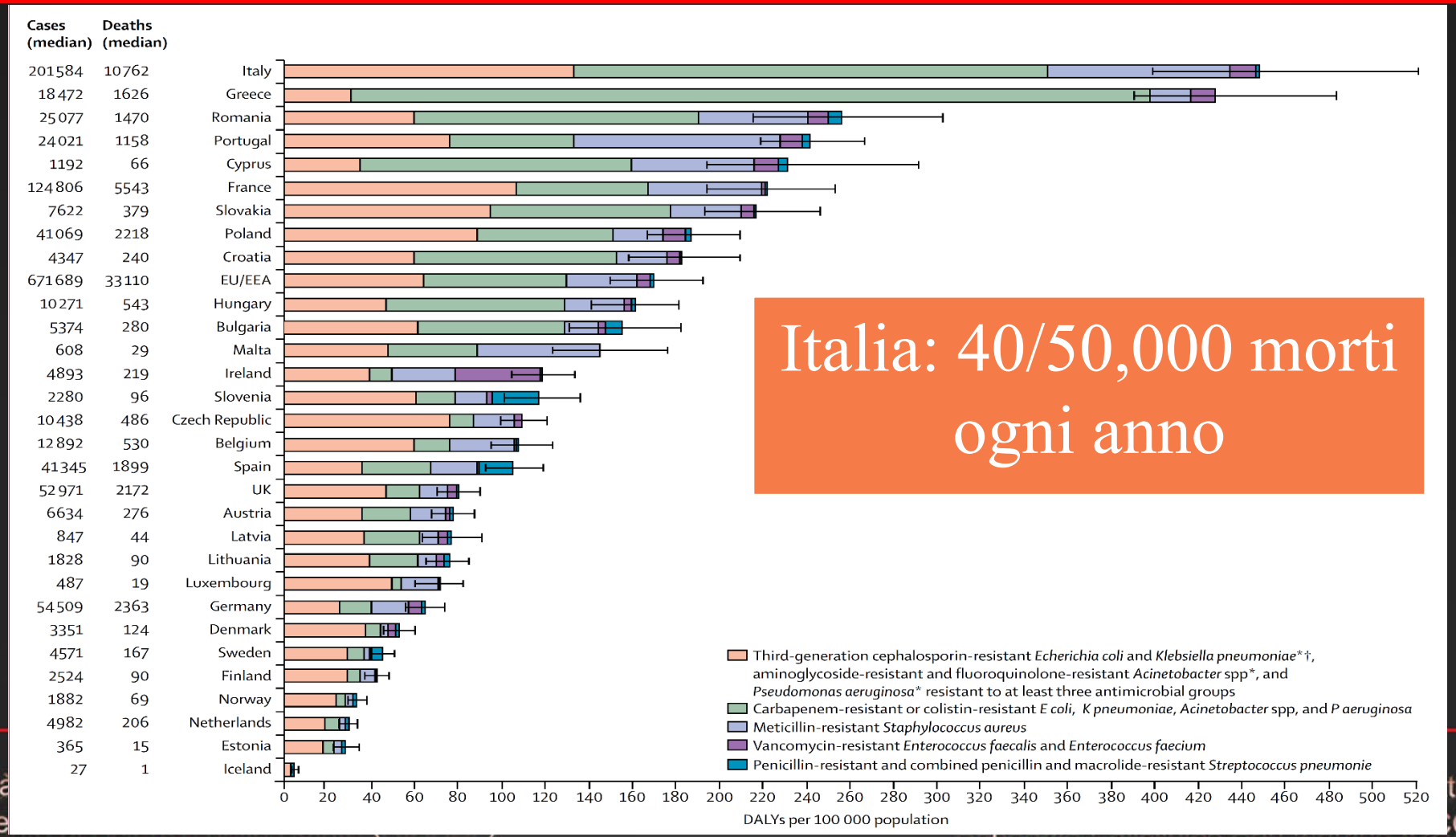
Impact of antibiotic- resistant bacteria in the EU in hospital

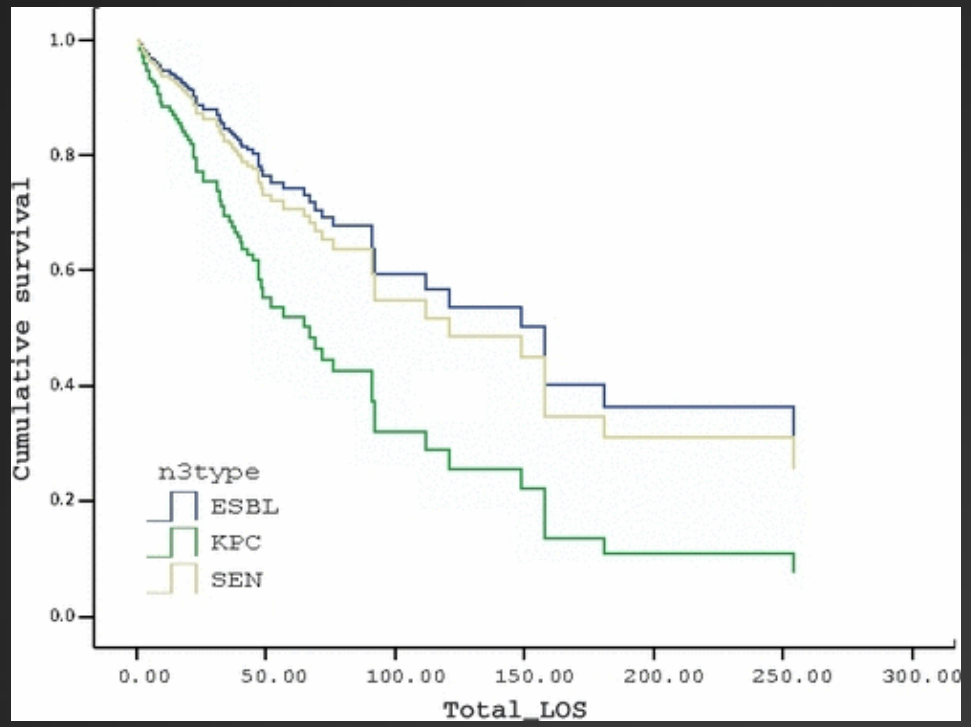


Italia: 40/50,000 morti ogni anno

Cassini A et al. *Lancet Infect Dis.* 2019 Jan;19(1):56-66.

Mortality

Comparison in mortality among patients with carbapenem-resistant (n=42), extended-spectrum β-lactamase producers (ESBL- n=68) and susceptible *K. pneumoniae* bloodstream infections (n=120),



- Infection-related mortality was 48% for carbapenem-resistant, 22% for ESBL producers and 17% for susceptible *K. pneumoniae*.

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Ben David B et al, Clin Microbiol Infect. 2011 Feb 1. doi: 10.1111/j.1469-0691.2011.03478.x

J Antimicrob Chemother
https://doi.org/10.1093/jac/dkad262

Journal of Antimicrobial Chemotherapy

Mortality in KPC-producing *Klebsiella pneumoniae* bloodstream infections: a changing landscape

Daniele Roberto Giacobbe[1,2*], Cristina Marelli[2], Greta Cattardico[1,2], Chiara Fanelli[2,3], Alessio Signori[4], Gabriele Di Meco[2], Vincenzo Di Pilato[5], Malgorzata Mikulska[1,2], Maria Mazzitelli[6], Anna Maria Cattelan[6,7], Carlo Pallotto[8], Daniela Francisci[8], Alessandra Calabresi[9], Andrea Lombardi[10,11], Andrea Gori[11,12], Valerio Del Bono[13], Chiara Aldieri[13], Angela Raffaella Losito[14], Francesca Raffaelli[14], Andrea Cortegiani[15,16], Marta Milazzo[15], Filippo Del Puente[17], Emanuele Pontali[17], Francesco Giuseppe De Rosa[18,19], Silvia Corcione[18], Alessandra Mularoni[20], Giovanna Russelli[20], Mauro Giacomini[21], Flavia Badalucco Ciotta[22], Chiara Oltolini[22], Francesco Saverio Serino[23], Elena Momesso[24], Michele Spinicci[25,26], Lucia Graziani[25], Carlo Torti[27,28], Enrico Maria Trecarichi[27,28], Marco Merli[29], Federico D'Amico[29], Anna Marchese[5,30], Antonio Vena[1,2] and Matteo Bassetti[1,2]† on behalf of the CARBANEW study group

Giacobbe DR et al. J Antimicrob Chemother. 2023 Aug 22:dkad262. doi: 10.1093/jac/dkad262.

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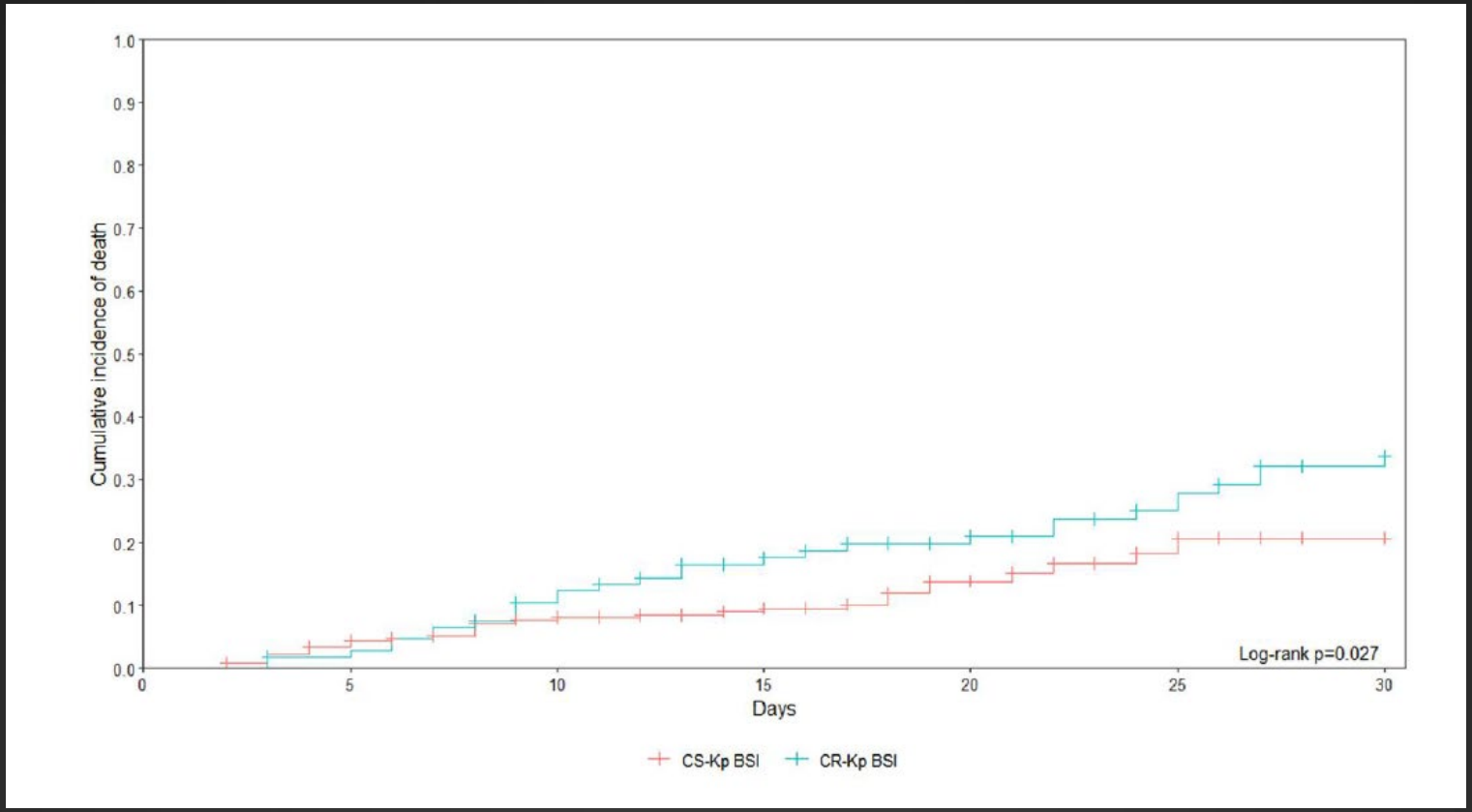
Cumulative mortality up to Day 30 in patients with CR-Kp BSI and CS-Kp BSI



Giacobbe DR et al. J Antimicrob Chemother. 2023 Aug 22:dkad262. doi: 10.1093/jac/dkad262.

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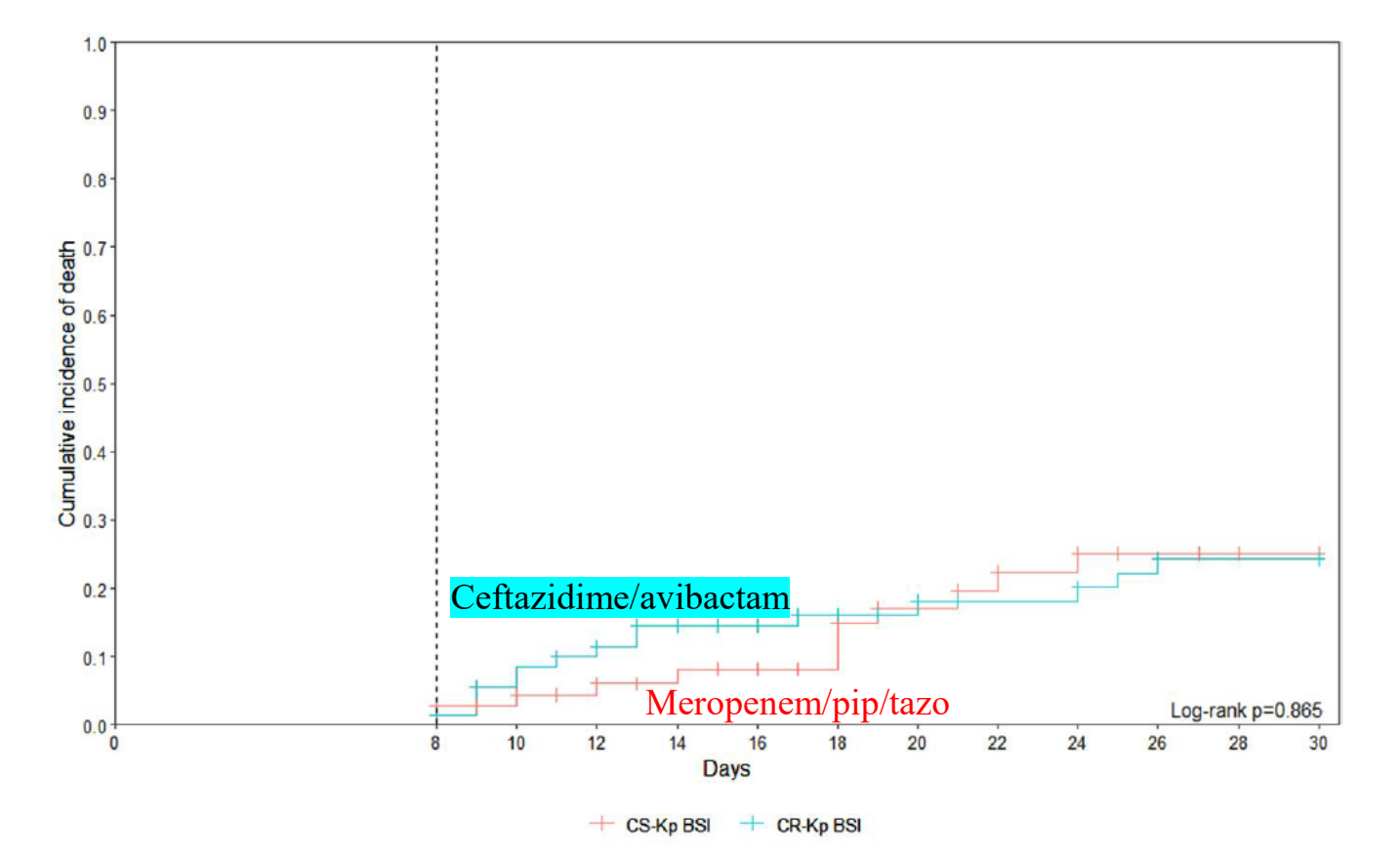
30 days mortality patients with CR-Kp BSI receiving appropriate therapy with ceftazidime/avibactam (cases) versus patients with CS-Kp BSI receiving appropriate therapy with agents other than ceftazidime/avibactam (controls).



Giacobbe DR et al. J Antimicrob Chemother. 2023 Aug 22:dkad262. doi: 10.1093/jac/dkad262.

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Activity of new agents against Gram-negative pathogens.

Grey shading: variable activity; red shading: non-activity; green shading: activity. KPC: Klebsiella pneumoniae carbapenemases; OXA: OXA-β-lactamases; NDM: New Delhi metallo-β-lactamase.

	Enterobacterales					
	Class A Carbapenemase (*e.g.* KPC)	Class B Carbapenemase (*e.g.* NDM)	Class D Carbapenemase (*e.g.* OXA-48)	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Stenotrophomonas maltophilia*
Ceftobiprole						
Ceftolozane-tazobactam						
Ceftazidime-avibactam						
Cefiderecol						
Meropenem-vaborbactam						
Imipenem-relebactam						
Aztreonam-avibactam						
Plazomicin						
Eravacycline						

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Bassetti M et al. Eur Respir Rev. 2022 Dec 31; 31(166): 220119

Ceftazidime/avibactam in Summary for KPC

Tumbarello, CID, 2019	*Tumbarello, CID, 2021*	***Falcone, Crit Care, 2020***	*Shields, CID, 2016*	*Van Duin, CID, 2018*	*Shields, AAC 2017*
Lower mortality rate in 104 BSI in targeted CAZ/AVI combo vs 104 BSI in targeted non CAZ/AVI combo	No differences in 165 CAZ/AVI mono vs 412 CAZ/AVI combo. Overall 25% mortality. **Prolunged infusion was protective**, **LRTI and CAZ/AVI renal dose adjustment were mortality risk factors**	102 BSI in CAZ/AVI vs COL-based showed lower mortality or nefrotoxicity. Time to appropriate therapy start was associated to survival. Primary BSI was mortality risk factor.	No differences in clinical success in 37 CAZ/AVI treated (70% mono vs 30% combo). **Lower clinical success in CRRT**	Higher probability of better outcome in 38 CAZ/AVI combo pts vs 99 COL-combo pts	Higher clinical success rate in 13 BSI in CAZ/AVI vs 25 CB+AG vs 30 CB + COL vs 41 other

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Efficacy and safety of ceftazidime avibactam versus polymyxins in the treatment of carbapenem- resistant Enterobacteriaceae infection

Study or Subgroup	CAZ-AVI Events	CAZ-AVI Total	polymyxins Events	polymyxins Total	Weight	Risk Ratio M-H, Random, 95% CI
Chen 2021	5	26	40	103	9.6%	0.50 [0.22, 1.13]
Falcone 2020	3	13	27	61	6.3%	0.52 [0.19, 1.46]
Falcone 2021	10	52	16	27	15.1%	0.32 [0.17, 0.61]
Hakeam 2021	12	32	12	29	15.8%	0.91 [0.49, 1.69]
Ryan 2017	1	13	9	30	1.8%	0.26 [0.04, 1.82]
Satlin 2022	2	21	8	26	3.4%	0.31 [0.07, 1.30]
van Duin 2018	3	38	33	99	5.4%	0.24 [0.08, 0.73]
Zheng 2022	29	82	57	82	41.6%	0.51 [0.37, 0.70]
Zhou 2021	0	4	17	28	1.0%	0.17 [0.01, 2.34]
Total (95% CI)		281		485	100.0%	0.48 [0.37, 0.63]
Total events	65		219			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 8.85$, $df = 8$ ($P = 0.35$); $I^2 = 10\%$

Test for overall effect: $Z = 5.39$ ($P < 0.00001$)

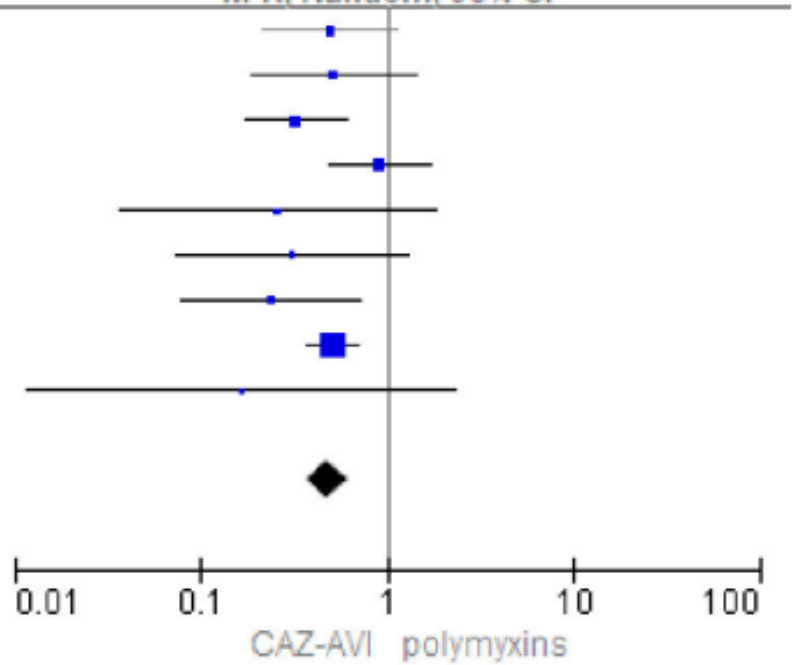
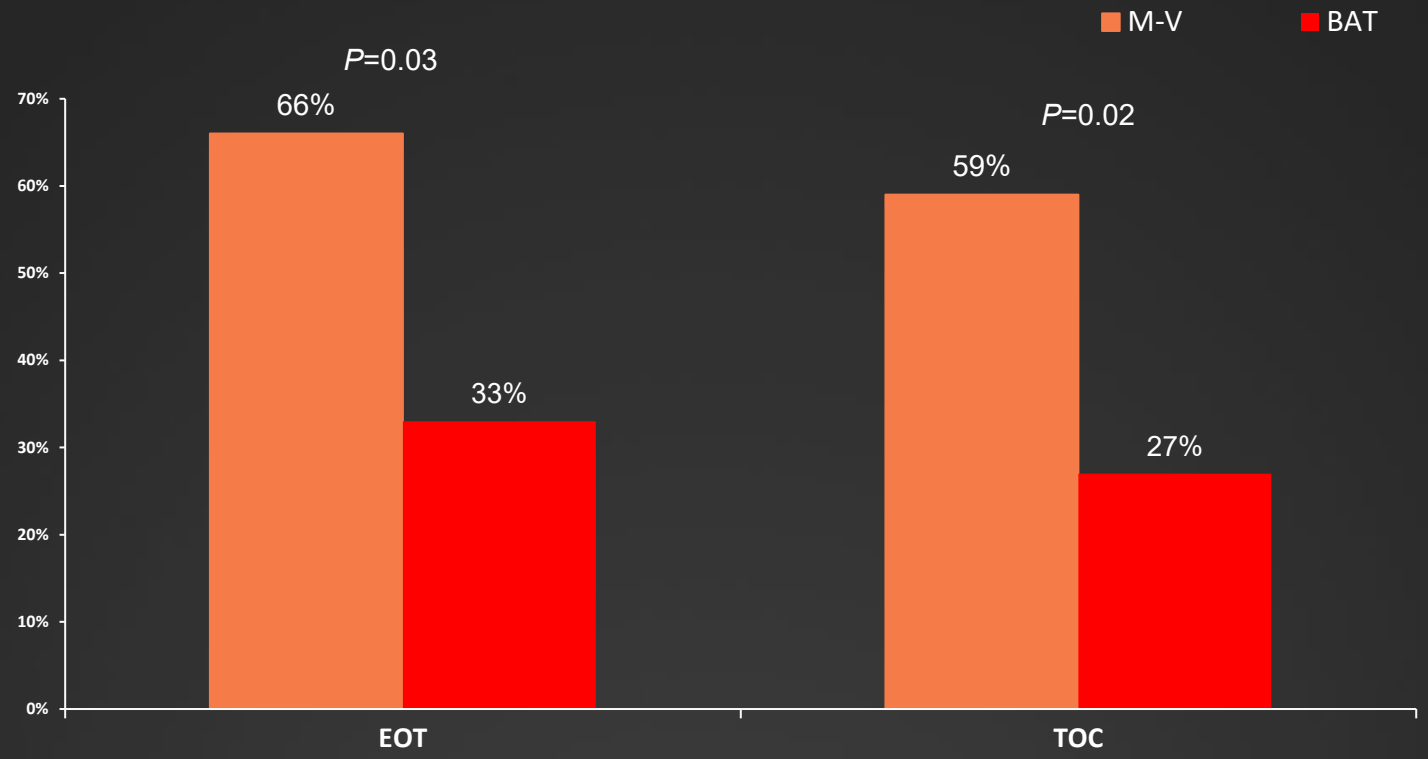


Figure 2 The 30-day mortality of the CAZ-AVI regimens compared with polymyxins regimens. CAZ-AVI, ceftazidime–avibactam.

Meropenem-vaborbactam: TANGO II

Meropenem-vaborbactam showed higher clinical cure rates at end of therapy (EOT) and test of cure (TOC)



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Wunderink RG, et al. Infect Dis Ther. 2018;

TANGO II
Day 28 All-Cause Mortality
All Infection Types (mCRE-MITT)

Endpoint/Statistics	MV N=32 n, (%)	Best Available Therapy N=15 n, (%)	Absolute Percent Difference (MV-BAT)	Relative Percent Difference [(MV-BAT)/BAT]
All-Cause Mortality Rate Day 28	5 (15.6)	5 (33.3)	-17.7	-53.2
Subjects Censored*	27 (84.4)	10 (66.7)		
Kaplan-Meier Estimate (95%CI)	15.6 (6.8 to 33.5)	33.3 (15.4 to 62.5)		

*Subjects whose survival status is unknown due to early termination or lost to follow up will be censored at the last day the subject was known to be alive.

Wunderink RG, et al. Infect Dis Ther. 2018; https://doi.org/10.1007/s40121-018-0214-1

BRIEF REPORT

Efficacy and Safety of Meropenem–Vaborbactam Versus Best Available Therapy for the Treatment of Carbapenem-Resistant *Enterobacteriaceae* Infections in Patients Without Prior Antimicrobial Failure: A Post Hoc Analysis

Matteo Bassetti · Daniele Roberto Giacobbe · Niki Patel · Glenn Tillotson · Jill Massey

Received: March 6, 2019

Table 2 Efficacy results in patients without prior antimicrobial failure in the mCRE-MITT population

Efficacy endpoints (mCRE-MITT)	Meropenem–vaborbactam (*n* = 23)	Best available therapy (*n* = 15)	Absolute difference (95% CI)
Clinical cure at TOC	16 (69.6)	4 (26.7)	+ 42.9 (+ 13.7 to + 72.1)
Clinical cure at EOT	19 (82.6)	5 (33.3)	+ 49.3 (+ 20.8 to + 77.7)
Microbiologic cure[a] at EOT	19 (82.6)	6 (40.0)	+ 42.6 (+ 13.4 to + 71.8)
Microbiologic cure[a] at TOC	16 (69.6)	5 (33.3)	+ 36.2 (+ 5.9 to + 66.6)
Day 28 mortality	1 (4.3)	5 (33.3)	− 29.0 (− 54.3 to − 3.7)

CI confidence intervals, *EOT* end of therapy, *mCRE-MITT* microbiologic carbapenem-resistant *Enterobacteriaceae* modified intent-to-treat, *TOC* test of cure

[a] Microbiologic cure was defined as microbial eradication or presumed eradication

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

Avoid R in vivo

- 131 patients; 105 w C/A VS 26 w M/V
- Overall, 53/105 (40.5%) had BSI.
- Most common sources of BSI: UTI (35.1%) in the C/A and the abdomen (37.5%) in the M/V.
- COMBO therapy: 61.0% pts in C/A VS 15.4% in M/V (p= 0.01).
- No differences in clinical cure and overall mortality.

	Ceftazidime-avibactam group (*n* = 105)	Meropenem-vaborbactam group (n = 26)	*P* value
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

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

Tumbarello M et al. JAC Antimicrob Resist. 2022; 4(1):

Table 1. Baseline characteristics, treatment features and outcomes of the KPC-*Kp* infections treated with meropenem/vaborbactam, stratified according to the isolate's ceftazidime/avibactam susceptibility status

Variables	All infections ($n=37$)	CZA^{a}_{RES} ($n=22$)	CZA_{SUSC} ($n=15$)	*P* value CZA_{RES} vs CZA_{SUSC}
Patient variables				
Males	22 (59.5)	13 (59.1)	9 (60.0)	0.95
Age, years, median (IQR)	65 (31–71)	61 (43–66)	69 (53–74)	0.07
CCI ≥4	19 (51.3)	8 (36.4)	11 (73.3)	0.02
Pre-infection healthcare interventions				
Previous hospitalization[b]	19 (51.3)	12 (54.5)	7 (46.7)	0.64
Previous antibiotic therapy[c]	34 (91.9)	21 (95.4)	13 (86.7)	0.33
Previous CZA therapy[c]	13 (35.1)	12 (54.5)	1 (6.7)	0.002
Infection characteristics				
Hospital acquired[d]				
BSI	23 (62.2)	15 (68.2)	8 (53.3)	0.36
LRTI	10 (27.0)	5 (22.7)	5 (33.3)	0.47
IAI	1 (2.7)	1 (4.5)	0	0.40
cUTI	2 (5.4)	1 (4.5)	1 (6.7)	0.78
ABSSI	1 (2.7)	0	1 (6.7)	0.22
Severity of illness at onset				
INCREMENT score ≥8	19 (51.3)	8 (36.4)	11 (73.3)	0.03
Septic shock	7 (18.9)	1 (4.5)	6 (40.0)	0.007
Ward submitting index culture				
Medical	7 (18.9)	4 (18.2)	3 (20.0)	0.89
Surgical	4 (10.8)	3 (13.6)	1 (6.7)	0.51
ICU	26 (70.3)	15 (68.2)	11 (73.3)	0.73
MEM/VAB treatment variables				
Days before MEM/VAB treatment, median (IQR)[e]	5 (2–8)	4 (1–8)	5 (2–9)	0.91
Monotherapy regimens	14 (37.8)	10 (45.5)	4 (26.7)	0.24
Combination regimens[f]	23 (62.2)	12 (54.5)	11 (73.3)	0.24
MEM/VAB + 1 other active antimicrobial:	17 (45.9)	9 (40.9)	8 (53.3)	0.46
Fosfomycin	6 (16.2)	2 (9.1)	4 (26.7)	0.15
Tigecycline	3 (8.1)	3 (13.6)	0	0.14
Gentamicin	1 (2.7)	1 (4.5)	0	0.40
Colistin	6 (16.2)	3 (13.6)	3 (20.0)	0.61
Amikacin	1 (2.7)	0	1 (6.7)	0.22
MEM/VAB + ≥2 active antimicrobials	6 (16.2)	3 (13.6)	3 (20.0)	0.61
Days of treatment, median (IQR)	13.5 (8.5–15.5)	14 (12–16)	12.5 (7–15)	0.41
Dose adjusted for renal function	14 (37.8)	10 (45.5)	4 (26.7)	0.25
Outcomes				
Clinical cure[g]	28 (75.6)	18 (81.8)	10 (66.6)	0.29
Microbiological eradication[h]	25 (89.3)	16 (88.9)	9 (90.0)	0.93
Microbiological data N/A[h]	3 (10.7)	2 (11.1)	1 (10.0)	0.93
In-hospital infection recurrence[h,i]	3 (10.7)	1 (5.5)	2 (20.0)	0.24
Adverse reactions[j]	1 (2.7)	0	1 (6.7)	0.22
In-hospital mortality	9 (24.3)	4 (18.2)	5 (33.3)	0.29

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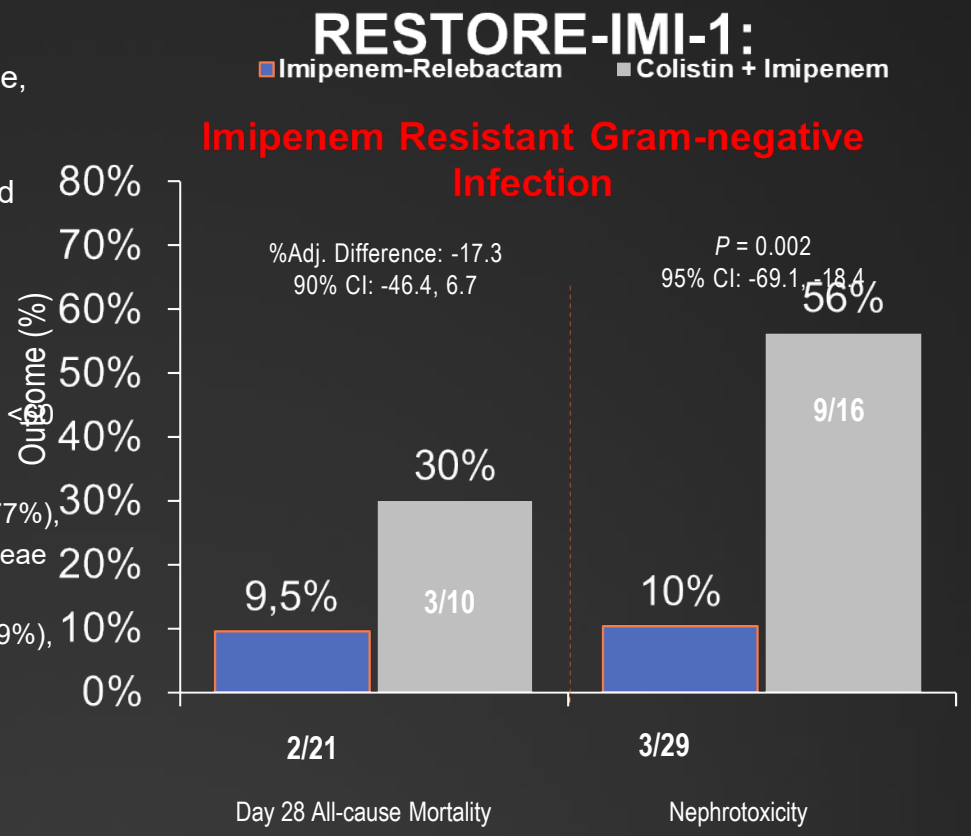
RESTORE-IMI-1: Efficacy & Safety of Imipenem-Relebactam (IMI-REL) in Patients with Imipenem-NS Infections

- RESTORE-IMI-1 is the first prospective comparative, randomized, double blind trial of a β-lactam/β-lactamase inhibitor as monotherapy (imipenem/relebactam) compared to dose optimized colistin + imipenem
  - 47 patients were randomized & treated (31 IMI/REL, 16 colistin+IMI), 31 of whom met mMITT criteria (11 HABP/VABP, 16 cUTI, and 4 cIAI)
    - 29% had APACHE-II scores >15, 23% had CrCl <60 mL/min, 35% were ≥65 yrs old.
    - Qualifying baseline pathogens: *P. aeruginosa* (77%), *Klebsiella* spp (16%), and other Enterobacteriaceae (6%), with the following β-lactamases detected: AmpC (84% of all qualifying isolates), ESBLs (39%), KPC (16%), OXA-48 (3%)
  - Efficacy defined by a favorable overall response (survival for HABP/VABP + clinical for cIAI, + clinical/micro for cUTI)



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Adjusted difference, based on Miettinen and Numiren method stratified by infection site
Motsch J et al..Clin Infect Dis Clin Infect Dis. 2020;70(9):1799-1808 (RESTORE-IMI-1)

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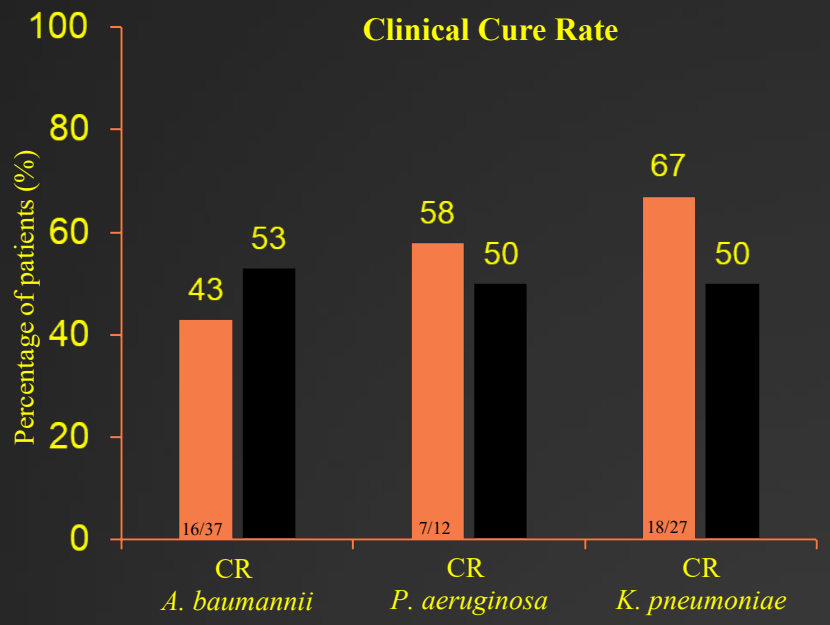
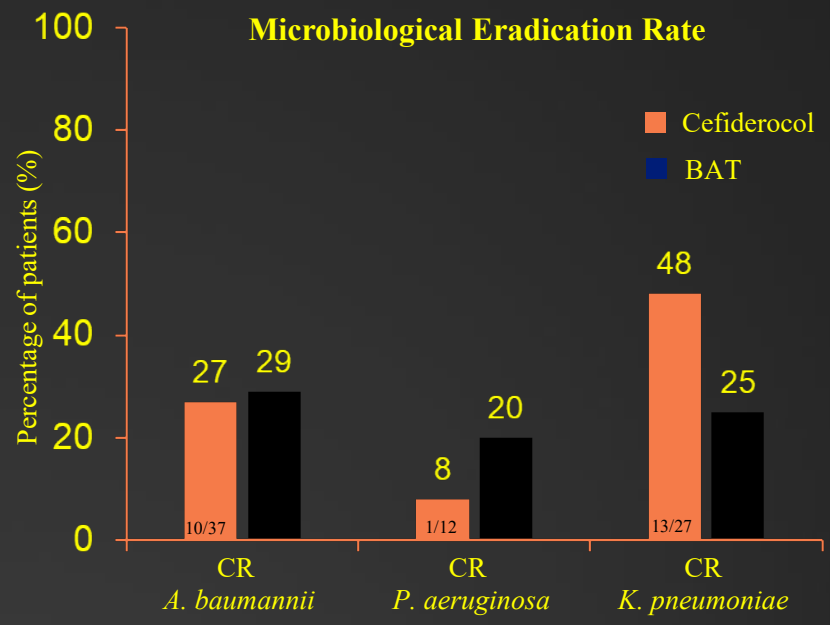
CREDIBLE-CR: similar rates at TOC by baseline pathogen, but higher for cefiderocol in Enterobacterales infection[a]



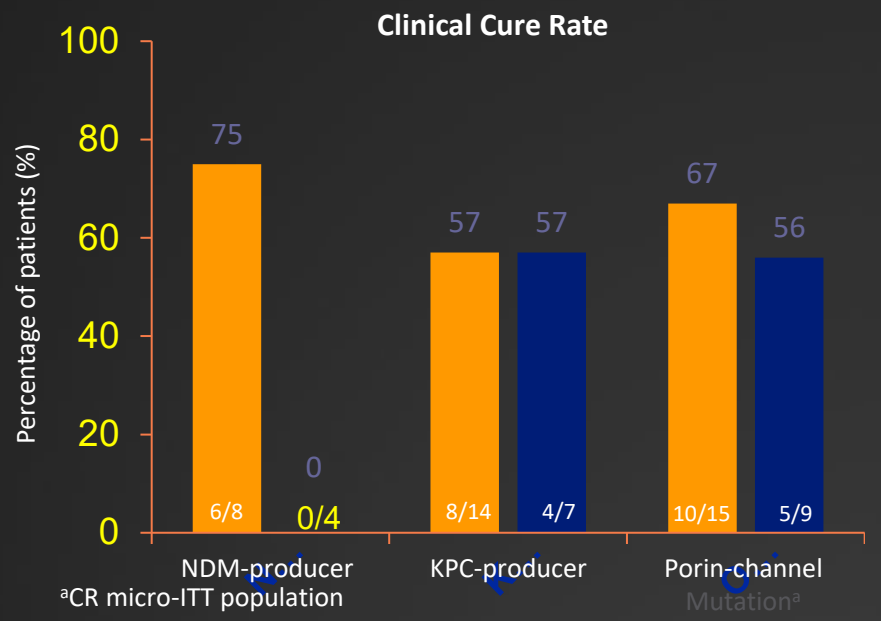


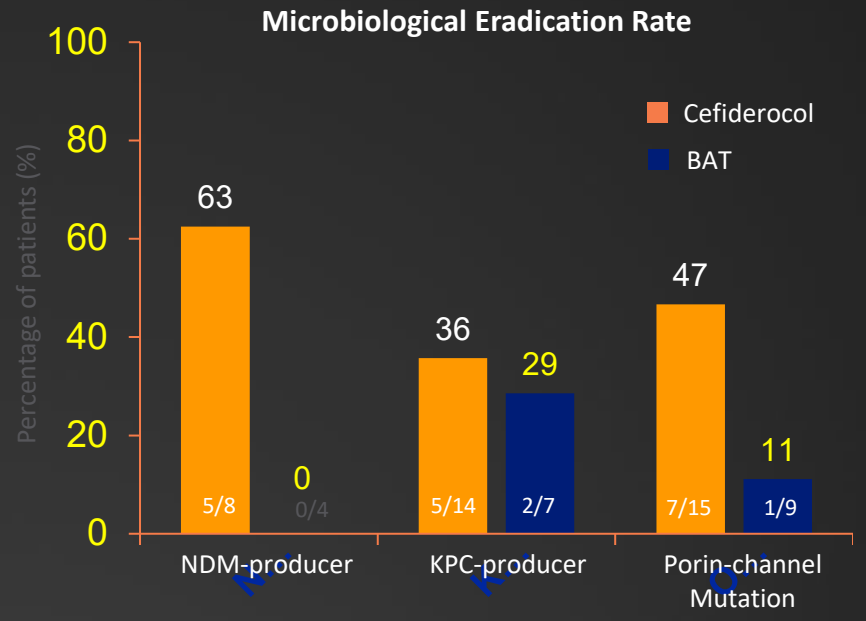
[a]CR micro-ITT population

BAT, best available therapy; CR, carbapenem resistant; CR Micro-ITT, carbapenem-resistant microbiological intention-to-treat population; TOC, test of cure.

Bassetti M, et al. *Lancet Infect Dis* 2020; published online Oct 12. https://doi.org/10.1016/S1473-3099(20)30796–9

CREDIBLE-CR: cefiderocol effective at TOC in resistant Enterobacterales due to carbapenemase producers and porin-channel mutations[a]





[a]CR micro-ITT population

Matsunaga Y, et al. Presented at IDWeek, October 2-6, 2020 (virtual) Abstract 904840, Oral Presentation O165

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Examples of clinical experience of ‘old-style’ vs ‘new-style’ treatment in CRE infections

Study	Treament	Mortality
OLD (mainly colistin)		
Shields *et al. Antimicrob Agents Chemother* 2017	Ceftazidime/avibactam (monotherapy or combination)	8%
Wunderink *et al. Infect Dis Ther* 2018	Meropenem/vaborbactam	15.6%
Motsch *et al. Clin Infect Dis* 2020	Imipenem/relabactam	9.5%
Bassetti *et al. Lancet Infect Dis* 2021	Cefiderocol	13.8%

In vitro activity of eravacycline and comparators in Enterobacteriaceae, including subgroups of strains with an ESBL and a carbapenem-resistant phenotype, isolated from patients in the EU

Organism	N	ERV		TIG		
		$MIC_{50/90}$ (mg/L)	MIC range (mg/L)	$MIC_{50/90}$ (mg/L)	MIC range (mg/L)	%S
Escherichia coli	153	0.12/0.25	0.06-2	0.25/0.5	0.12-2	99.4
E. coli ESBL	43	0.12/0.25	0.06-0.5	0.25/0.5	0.12-0.5	100
Klebsiella oxytoca	150	0.25/0.25	0.12-2	0.5/0.5	0.25-2	98.0
K. oxytoca ESBL	13	0.25/2	0.12-2	0.5/2	0.25-2	84.6
Klebsiella pneumoniae	147	0.5/1	0.12-2	1/2	0.12-4	82.3
K. pneumoniae ESBL	57	0.5/1	0.12-2	1/2	0.12-4	68.4
K. pneumoniae CRE	16	0.5/1	0.25-1	1/2	0.5-2	75.0
Proteus mirabilis	150	2/2	0.25-4	4/4	0.25-8	10.0
P. mirabilis ESBL	18	2/2	0.5-4	4/8	1-8	5.6
P. mirabilis CRE	65	2/2	0.5/4	4/8	0.5-8	7.7
Serratia marcescens	150	1/2	0.5-8	2/2	0.25-4	49.3
S. marcescens ESBL	19	2/4	0.5-4	2/4	0.5-4	36.8
S. marcescens CRE	1	4/4	4-4	4/4	4-4	0.0
Proteus vulgaris	149	1/1	0.12-2	2/4	0.5-8	39.6
P. vulgaris ESBL	17	1/1	0.25-1	2/2	0.5-4	23.5
P. vulgaris CRE	53	1/1	0.25-2	2/4	0.5-4	15.1

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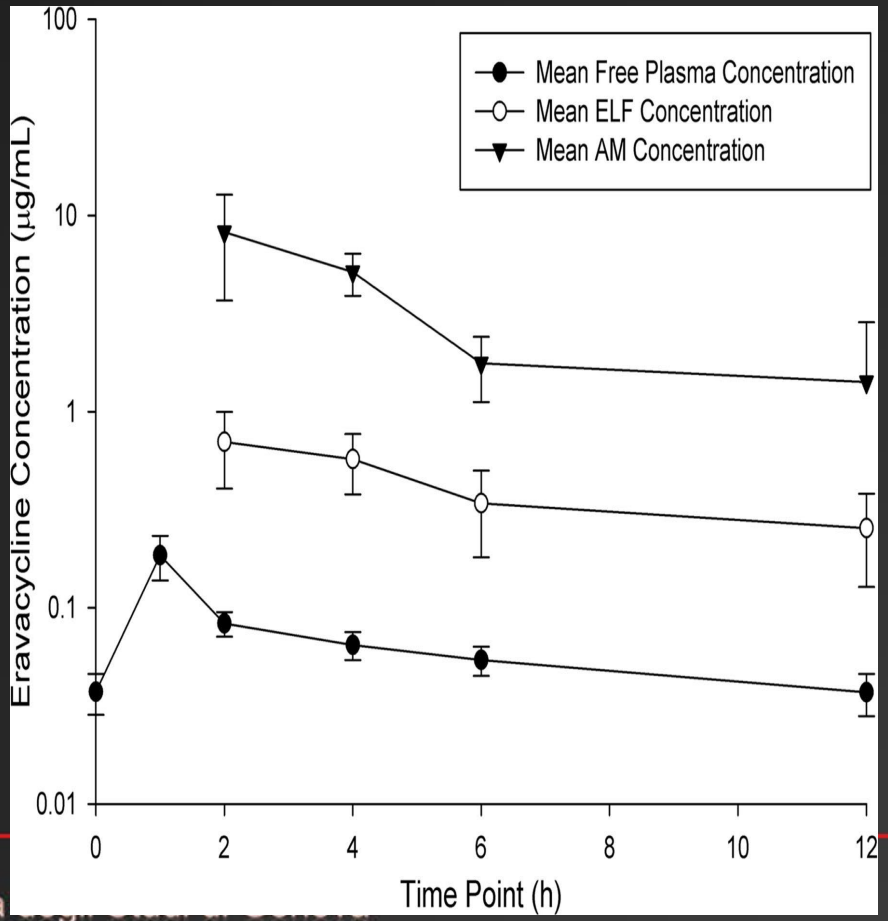
Bassetti M et al. *ECCMID 2016*;

Eravacycline activity vs Acinetobacter baumannii

A. baumannii	Eravacycline	1,600	0.5	1	≤0.015 - 16		NA	NA
	Amikacin	1,101	32	≥128	0.12 - ≥128		49.5	47.1
	Ampicillin-sulbactam	1,101	32	≥128	1 - ≥128		30.9	NA
	Aztreonam	1,600	≥32	≥32	≤0.5 - ≥32		NA	NA
	Cefepime	1,600	≥32	≥32	≤0.25 - ≥32		26.9	NA
	Ceftazidime	1,600	≥32	≥32	≤0.5 - ≥32		29.1	NA
	Ceftriaxone	1,600	≥64	≥64	≤0.5 - ≥64		12.6	NA
	Colistin	1,600	0.5	2	≤0.03 - ≥8		95.4	95.4
	Gentamicin	1,600	≥16	≥16	≤0.03 - ≥16		38.3	38.3
	Imipenem	499	≥16	≥16	≤0.25 - ≥16		37.3	37.3
	Levofloxacin	1,600	≥8	≥8	≤0.25 - ≥8		26.6	24.8
	Meropenem	1,101	32	≥128	≤0.03 - ≥128		32.2	32.2
	Minocycline	1,101	2	16	0.06 - ≥128		66.5	NA
	Piperacillin-tazobactam	1,600	≥128	≥128	≤0.5 - ≥128		24.3	NA
	Tetracycline	1,600	≥16	≥16	≤0.25 - ≥16		25.4	NA
	Tigecycline	1,600	2	4	0.06 - ≥32		NA	NA
	Trimethoprim-sulfamethoxazole	1,101	16	≥128	≤0.03 - ≥128		37.8	37.8

Plasma and Intrapulmonary Concentrations of Eravacycline



Eravacycline 1.0 mg/kg IV q12h for a total of seven doses

Sample Site	AUC_{0-12} (ug-h/mL)	Site:Unbound Plasma Ratio
Plasma (total)	4.56	
Plasma (unbound)	0.77	
ELF	4.59	6.44
AM	39.53	51.63

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Connors KP, et al. *Antimicrob Agents Chemother* 2014;58:2113-2118

Patient Case Report

Use of Eravacycline for *Acinetobacter baumannii* Infections: A Case Series

Journal of Pharmacy Practice
2023, Vol. 0(0) 1–5

DOI: 10.1177/08971900231196076
journals.sagepub.com/home/jpp
Sage

Valerie Buckley, PharmD[1], MaiCuc Tran, PharmD, BCPS[1], Todd Price, MD[2], Sushma Singh, MD[2], and Stefanie Stramel, PharmD, BCIDP, MS[1]

Table 1. Patient Characteristics.

Case	Age, Sex	Culture Specimen	Infection Source	ERV Start, days	ERV Duration, days	ICU Stay, days	Prior Active Antimicrobial Therapy	Combination Antimicrobial Therapy with ERV	ERV MIC, µg/mL
1	59, F	Blood	Respiratory	1	9	0	FEP, VAN	Inhaled TOB, CST	0.5
2	43, F	Respiratory	Respiratory	9	10	14	FEP, VAN, ATM, CST, MEM	One dose ATM	0.5
3	84, F	Sacral wound	Skin/soft-tissue	8	13	0	MEM, VAN, FAM, AMK	VAN, FAM	1.0
4	68, F	Tracheal aspirate	Respiratory	24	4	0	FEP, VAN, MEM	FEP	0.5
5	26, F	Tracheal aspirate	Respiratory	14	11	27	CFZ, FEP, MEM, VAN, MFG	MEM, VAN, CST	1.0
6	47, M	Sputum	Respiratory	22	8	20	CRO, VAN, TZP, MEM, CST, MFG	MEM, CST, MFG	0.5
7	62, M	Blood	Respiratory	2	16	0	MEM, VAN	MEM, FAM, inhaled TOB, VAN, LVX, FEP	.38
8	68, M	Sputum	Respiratory	4	12	30	FEP, VAN, MEM	MEM, CST	0.5
9	68, M	Tracheal aspirate	Respiratory	4	6	7	FEP, VAN	FEP, CST	.75
10	45, M	Suprapubic aspirate	Urinary	4	3	0	MEM	MEM, CST	1.5

Note: Adapted from Early experience with eravacycline for complicated infections, by Alosaimy S, Molina KC, Claeys KC, et al., p. 3. Copyright 2020 by Open Forum Infectious Diseases. In the public domain.
Abbreviations: AMK, amikacin; ATM, aztreonam; CFZ, cefazolin; CRO, ceftriaxone; CST, colistimethate; ERV, eravacycline; FAM, ampicillin-sulbactam; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; MFG, micafungin; TOB, tobramycin; TZP, piperacillin-tazobactam; VAN, vancomycin.

A total of 10 patients were isolated for assessment of clinical course information. All patients had MDR CRAB isolated in cultures; 8 patients (80%) had *Acinetobacter* from a respiratory source, followed by skin (10%) and urinary (10%) sources. All patients were treated with eravacycline for non-FDA recommended infection types. Half of the patients (50%) were admitted to the ICU throughout their hospital stay. There were no patient deaths reported during the documented hospital stay after eravacycline use. A single patient had an MIC of .38 µg/mL (10%), 5 patients had an MIC of .5 µg/mL (50%), 1 with an MIC of .75 µg/mL (10%), 2 with an MIC of 1.0 µg/mL (20%), and one with an MIC of 1.5 µg/mL (10%).

Although there is currently little post-marketing data supporting the use of eravacycline in CRAB infections, this case series describes its clinical use and MIC breakpoint data for 10 patients. More high quality data is needed, however, to confirm the clinical utility of this agent in practice.

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Eravacycline

Pros

- Broad spectrum (Gram+ [MRSA], Gram- [including ESBLs, KPC, NDMs], anaerobes)
- Acinectobacter
- Favorable safety and tolerability profile expected
- Q12-Q24 interval
- Oral dosing
- Good lung penetration

Con

- Failed in cUTI P3 trial
- Oral formulation: low bioavailability?

Relative to tigecycline:
2-4× more potent; 2× higher AUC

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AUC, area under the plasma drug concentration-time curve; NDM, New Delhi metallo-β-lactamase

Infections caused by difficult to treat NFGNB

P.aeruginosa

Current options:
Ceftolozane-tazobactam
OR
Cetazidime-avibactam
OR
Cefiderocol OR
Imipenem-relebactam

Future options:
Cefepime/zidebactam
Sulbactam/Durlobactam
Murepavadin

A.baumaniii

Current options:
Cefiderocol +/-* fosfomycin
or colistin or
HD ampicillin/sulbactam OR
HD tigecycline OR
eravacycline

Future options:
Sulbactam/Durlobactam,
Cefiderocol/xeruborbactam

S.maltophilia

Current options:
Trimethoprim-
sulfamethoxazole OR
minocycline
OR
Ceftazidime/avibactam +
aztreonam OR
Cefiderocol

Future options:
cefepime/taniborbactam
cefepime/zidebactam

B.Cepacia complex

Current options:
Trimethoprim-
sulfamethoxazole OR
meropenem OR
ceftazidime OR
levofloxacin OR
Cefiderocol

Future options:
cefepime/zidebactam

- The second antibiotic should be considered for empirical use in cases of severe infections or high-risk scenarios involving multidrug-resistant pathogens.

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Bassetti M et al. *Curr Opin Infect Dis.* 2023 Dec 1;36(6):615-622

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What Makes Ceftolozane/Tazobactam Different?
Activity vs. *Pseudomonas aeruginosa*

Ceftolozane

- Stable against common *P. aeruginosa* resistance mechanisms, including loss of outer membrane porin (OprD), chromosomal AmpC, and up-regulation of efflux pumps (MexXY, MexAB)[1]
- Isolates resistant to other cephalosporins may be susceptible, although cross-resistance may occur[2]

Resistance Mechanisms	Outer Membrane Porin Loss	β-lactamase Enzyme	Efflux Pump	Efflux Pump
	OprD	AmpC	MexXY	MexAB
Ceftolozane	●	●	●	●
Ceftazidime	◐	○	●	○
Cefepime	●	○	○	○
Piperacillin/tazobactam	●	○	●	○
Imipenem	○	●	●	●
Meropenem	◐	●	○	◐

○ Activity greatly decreased >> ● Retains activity

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1. Castanheira M, et al. *Antimicrob Agents Chemother.* 2014;58:6844-6850.
2. Ceftolozane/Tazobactam prescribing information.

Table adapted from Castanheira M, et al. 2014

Imipenem/Relebactam (IMI/REL) Retains Susceptibility among resistant *P. aeruginosa*

C-T: Ceftolozane-tazobactam
IMI-REL: Imipenem-relebactam
CAZ-AVI: Ceftazidime-avibactam

Figure 1. Antimicrobial susceptibility of *P. aeruginosa* from ICU and non-ICU patients

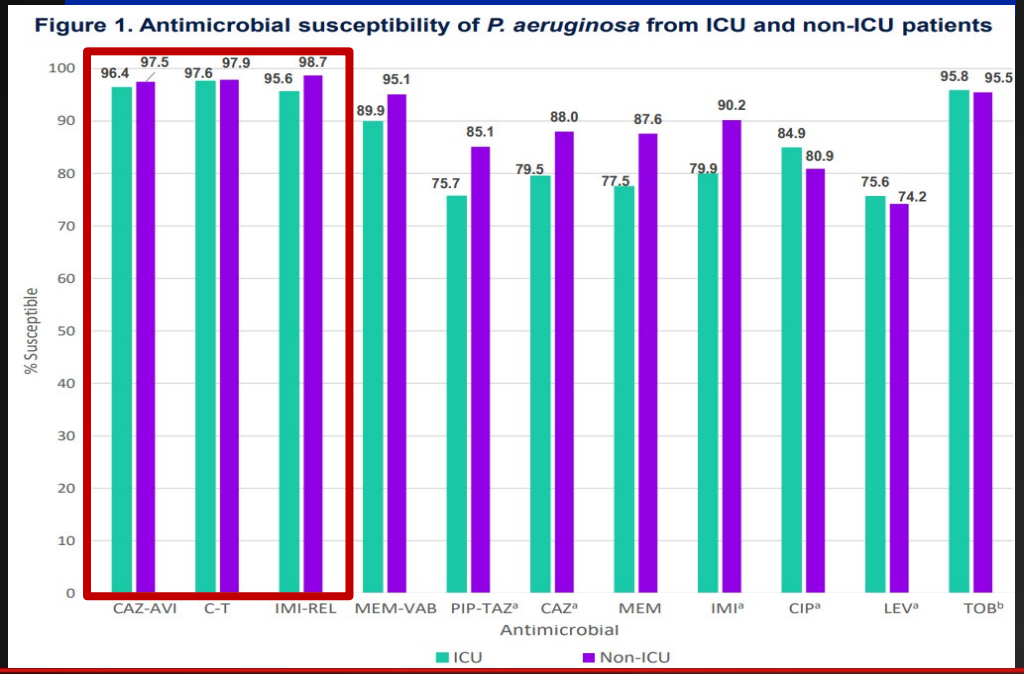

Table 2. Cross Resistance Among New BLIs

Resistance phenotype (no.)	% Susceptible per EUCAST (ICU plus non-ICU)			
	CAZ-AVI	C-T	IMI-REL	MEM-VAB
CAZ-AVI-R-R (41)	--	51.2	69.7	29.3
C-T-R (31)	35.5	--	75.0	51.6
IMI-REL-R (27)	63.0	77.8	--	11.1
MEM-VAB-R (95)	69.5	15.8	70.7	--

- ≥95% activity for C/T, CAZ/AVI, and IMI/REL when evaluating all isolates.
- Against isolates resistant to newer agents, rates of cross-susceptibility varied significantly.
- IMI/REL retained activity against 70-75% of isolates resistant to C/T, CAZ/AVI and MEM/VAB.

Sader H et al. ECCMID 2022, Lisbon, Portugal

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Collateral sensitivity in *P. aeruginosa*

- MDR-*P. aeruginosa* collected before and after treatment-emergent resistance (8->256 mg/L) to ceftolozane-tazobactam
- WGS identified treatment-emergent mutations in *ampC* among 79% (11/14) of paired isolates
- **AmpC mutations** associated with **cross-resistance to ceftazidime-avibactam but increased/maintained susceptibility to imipenem and imipenem-relebactam**
- **High percentage (81%)** of **ceftolozane-tazobactam resistant** isolates were **imipenem-relebactam susceptible**

	Baseline ($n = 23$)		Postexposure ($n = 32$)		
Drug	Median MIC (range) (μg/ml)	Susceptible (%)	Median MIC (range) (μg/ml)	Susceptible (%)	*P* value[a]
Ceftolozane-tazobactam	2 (≤0.25–8)	91	64 (8 to >256)	0	<0.0001
Ceftazidime	32 (1–256)	26	32 (32 to >512)	0	<0.0001
Ceftazidime-avibactam	4 (1–32)	74	64 (4 to >256)	28	<0.0001
Imipenem	16 (0.12–32)	17	4 (0.5 to >32)	50	0.0216
Imipenem-relebactam	2 (0.06–16)	65	2 (0.25–16)	63	0.6625
Piperacillin-tazobactam	128 (1–512)	17	128 (4 to >512)	16	0.6284

[a]Comparison of median MICs, Mann-Whitney U test.

MIC for meropenem-resistant isolates: cefiderocol vs comparators

Attività in vitro di Cefiderocol e comparatori contro isolati italiani di *P. aeruginosa* dello studio SIDERO-WT-2014-2018 resistenti a meropenem (MIC> 8MG/L)

		MIC (mg/L)			
Specie (n)[a]	Antibiotico	Range	MIC_{50}	MIC_{90}	S%
Pseudomonas aeruginosa (39)	Cefiderocol	0,008-2	0,25	2	100
	Colistina	Da 0,5 a >8	1	1	94,9
	Ceftazidime/ avibactam	Da 4 a >64	8	>64	53,8
	Ceftolozane/ tazobactam	Da 0,5 a >64	4	>64	51,3

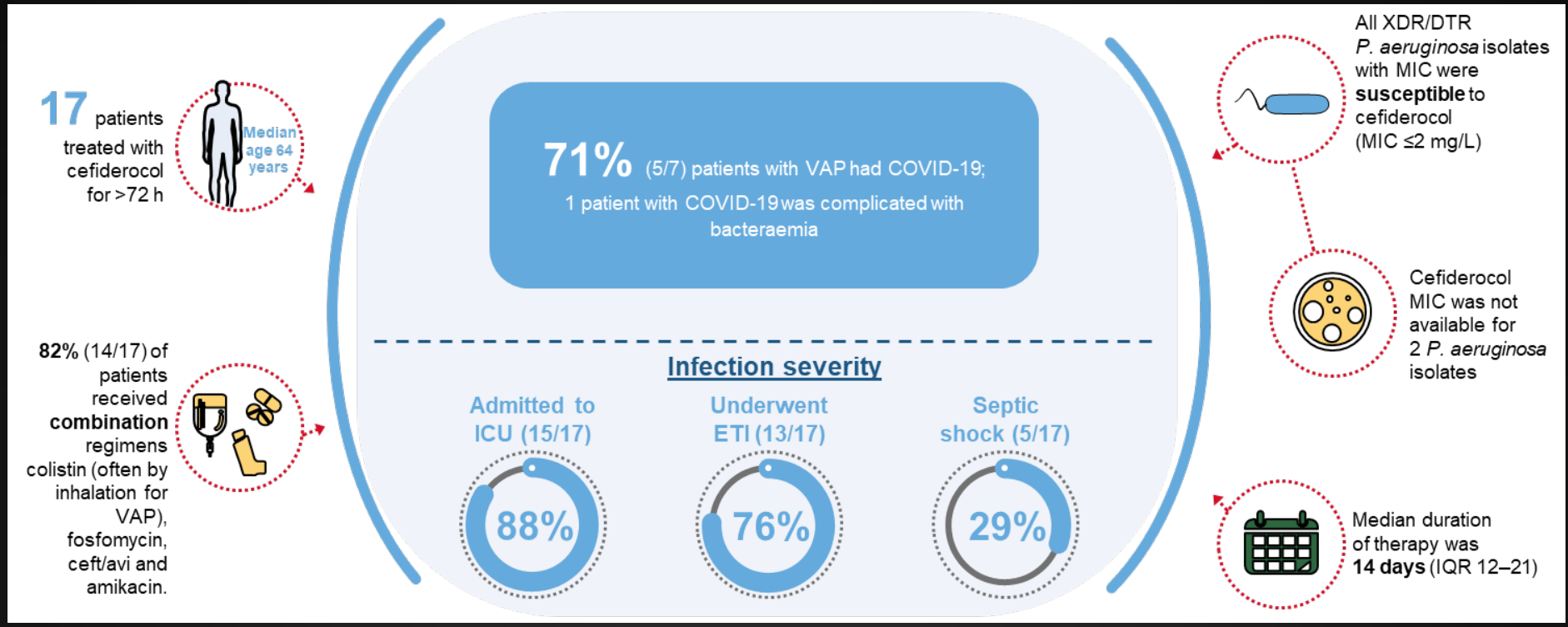
MIC, minima concentrazione inibente; MIC50/90, MIC per il 50% ed il 90% degli isolati testati, rispettivamente; S%, percentuale di suscettibilità

[a]Dove n ≥ 10 isolati

Stracquadanio S, et al. J Glob Antimicrob Resist 2021;25:390–8.

Cefiderocol in patients with XDR/DTR *P. aeruginosa* infection: a prospective, observational study

Prospective observational study including 17 pts (median age 64 yrs) with XDR and DTR *P.aeruginosa* infections, unresponsive to BAT w/o any other available treatment options.



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Meschiari M. et al. JAC Antimicrob Resist 2021;3:dlab188

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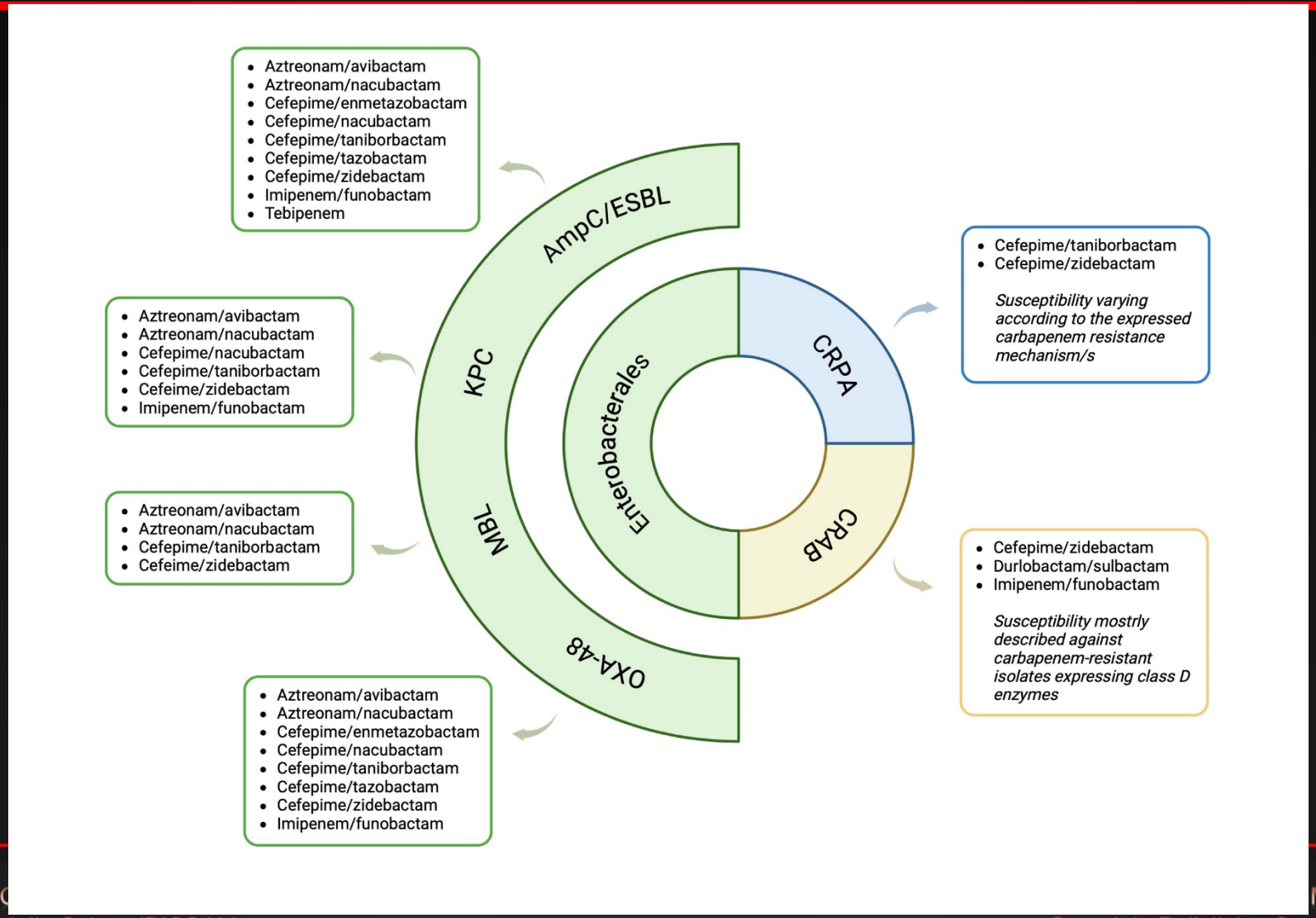
Activity according to *in vitro* studies



Bassetti M, et al. Submitted for publication

Cefepime-enmetazobactam (AAI101)

- Enmetazobactam = penicillanic acid sulfone BLI (no intrinsic activity against GNB)

- *In vitro* activity against ESBL, AmpC, and some OXA producers
- Limited activity against KPC and MBL producers

Papp-Wallace KM, et al. Antimicrob Agents Chemother 2019; 63:e00105-19.
Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20.

Cefepime-enmetazobactam (AAI101)

- Phase 3 study in patients with cUTI/AP (ALLIUM)
- 1034 patients (The primary analysis set included 678 patients who received at least 1 dose of treatment and had a gram-negative bacterium that was not resistant to either treatment)
- Cefepime/AAI101: success 79.1%
- Piperacillin/tazobactam: success 58.9%
- Adjusted difference, 21.2% (95% CI 14.3-27.9)

Kaye KS et al. JAMA 2022;328(13):1304-1314

Cefepime-enmetazobactam (AAI101)

- Approved by FDA for cUTI and AP by designated susceptible organisms (*E. coli, K. pneumoniae, P. aeruginosa, P. mirabilis*, and *Enterobacter cloacae* complex)
- Approved by EMA for cUTI, AP, HAP, and VAP in adults (and of bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above)
- EMA justified the approval of cefepime/enmetazobactam for the treatment of HAP and VAP on the basis of the experience with cefepime alone and pharmacokinetic/pharmacodynamic (PK/PD) analyses for enmetazobactam (e.g., lung penetration similar to cefepime according to data in healthy volunteers)

Cefepime-zidebactam (WCK 5107)

- Zidebactam = non-beta-lactam BLI (and BL enhancer) that inhibits class A carbapenemases, MBL, and OXA-48
- Acitivity against Kp with defective OmpK35/36 porins
- Also active against activity against *P. aeruginosa* with AmpC overexpression and MBL
- Moderate activity against *A. baumannii* OXA-23/24/58

Avery LM, et al. Int J Antimicrob Agents 2020; 55:105863; Joshi P, et al. Diagn Microbiol Infect Dis 2021 Oct;101(2):115481
Thomson KS, et al. Antibiotics (Basel) 2019; 8:32; Khan Z, et al. J Antimicrob Chemother 2020; 74:2938 –2942.
Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20.

Cefepime-zidebactam (WCK 5107)

- Phase 3 ongoing (NCT04979806)
- Cefepime/zidebactam vs. meropenem for cUTI/AP
- Estimated enrollment: 504 patients
- Primary outcome: success at TOC

ClinicalTrials.gov Identifier: NCT04979806

Dubey *et al. Annals of Clinical Microbiology and Antimicrobials* (2023) 22:55
https://doi.org/10.1186/s12941-023-00606-x

Annals of Clinical Microbiology and Antimicrobials

BRIEF REPORT Open Access

Compassionate use of a novel β-lactam enhancer-based investigational antibiotic cefepime/zidebactam (WCK 5222) for the treatment of extensively-drug-resistant NDM-expressing *Pseudomonas aeruginosa* infection in an intra-abdominal infection-induced sepsis patient: a case report

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-024-04791-1

BRIEF REPORT

Successful treatment of sino-pulmonary infection & skull base osteomyelitis caused by New Delhi metallo-β-lactamase-producing *Pseudomonas aeruginosa* in a renal transplant recipient by using an investigational antibiotic cefepime/zidebactam (WCK 5222)

Rajeev Soman[1,2] · Rasika Sirsat[3] · Ayesha Sunavala[4] · Neha Punatar[3] · Jugal Mehta[3] · Camilla Rodrigues[5] · Balaji Veeraraghavan[6]

Successful Use of Cefepime-Zidebactam (WCK 5222) as a Salvage Therapy for the Treatment of Disseminated Extensively Drug-Resistant New Delhi Metallo-β-Lactamase-Producing *Pseudomonas aeruginosa* Infection in an Adult Patient with Acute T-Cell Leukemia

Praveen Kumar Tirlangi,[a] Bala Saheb Wanve,[b] Ramakanth Reddy Dubbudu,[c] Boorgula Sushma Yadav,[d] L. Siva Kumar,[e] Anand Gupta,[e] Racha Amarthya Sree,[f] Hari Priya Reddy Challa,[g] P. Naveen Reddy[h]

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®
August 2023 Volume 67 Issue 8
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Cefepime-taniborbactam (VNRX-5133)

- Taniborbactam = boronic-acid-containing BLI

- *In vitro* activity against producers of class A, B (not IMP) and D carbapenemases
- Active against some CRPA and some KPC-3-producing CAZ-AVI resistant *Enterobacterales*

Hamrick JC et al. Antimicrob Agents Chemother 2019; 64:e01963-19. Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20. Daigle D, et al. Open Forum Infect Dis 2018; 5:S419 –S420

Cefepime-taniborbactam (VNRX-5133)

- Phase 3 (CERTAIN-1)
- Cefepime-taniborbactam vs. meropenem for cUTI/AP
- Primary outcome: composite microbiological eradication and clinical success in the microITT population (436 patients)
- Composite success achieved in 70.6% (FTB) and 58.0% (MEM)
- Treatment difference 12.6%; 95% CI, 3.1 to 22.2

Wagenlehner FM, et al. N Engl J Med 2024;390:611-22.

CellPress

Med

Viewpoint

Cefepime-taniborbactam and CERTAIN-1: Can we treat carbapenem-resistant infections?

Matteo Bassetti[1,2,*] and Daniele Roberto Giacobbe[1,2]

Wagenlehner and colleagues[1] demonstrated non-inferiority and superiority with respect to a primary endpoint of composite success (microbiological plus clinical) of cefepime/taniborbactam vs. meropenem in treating complicated urinary tract infections and acute pyelonephritis caused by carbapenem-susceptible gram-negative bacteria in adults. A major area of interest in real-world application of cefepime/taniborbactam is its potential role in treating carbapenem-resistant infections, which deserves further investigation.

tion baseline of all core symptoms and signs, with no administration of additional antibacterials (for cUTIs or acute pyelonephritis), while microbiological success was defined as reduction of the bacterial load of gram-negative pathogens to less than 10^3 colony-forming units per milliliter. Both drugs were administered intravenously for 7 days (or up to 14 days in presence of bacteremia), and step down to oral agents was not permitted. Overall, the microITT population was composed of 293 and 143 patients randomized to cefepime/taniborbactam and meropenem arms, respectively, with a 2:1 ratio. Most infections were caused by Entero-

Nacubactam

- Nacubactam = non-BL BLI (and BL enhancer)
- First proposed in combination with meropenem
- Active against class A, C, and some B and D beta-lactamases
- *In vitro* activity against ESBL, KPC, NDM, and OXA producing isolates
- Active against some CRPA and against some KPC-3-producing CAZ-AVI resistant *Enterobacterales*

Mushtaq S. J Antimicrob Chemother 2019; 74:953–960. Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20.
Asempa TE, et al. Int J Antimicrob Agents 2020; 55:105838. Monogue ML, et al. Antimicrob Agents Chemother 2018; 62:e02596-17.

Sulbactam-durlobactam (ETX2514)

- Durlobactam = non-BL BLI (and BL enhancer)

- Active against class A, C, and D beta-lactamases
- *In vitro* activity against CRAB

Durand-Reville TF, et al. Nat Microbiol 2017; 2:17104 Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20.
McLeod SM, et al. 2020; Antimicrob Agents Chemother 64:e02534-19.

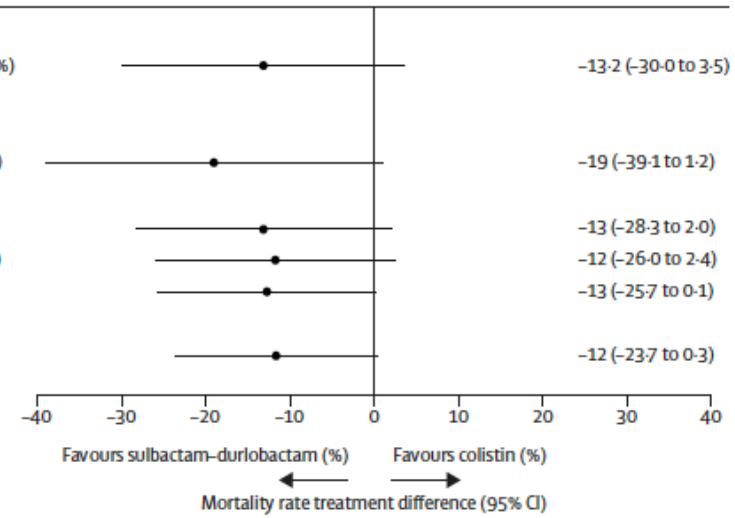
Sulbactam-durlobactam (ETX2514)

- Phase 3 study in patients with *Acinetobacter* infections (ATTACK)
- 125 patients with infection due to CRAB included in primary analysis
- Primary endpoint: 28-day all-cause mortality
- Imipenem/cilastatin in both arms
- Sulbactam/durlobactam: 19.0% (12/63)
- Colistin: 32.3% (20/62)
- Treatment difference -13.2% (95% CI -3.0 to 3.5)

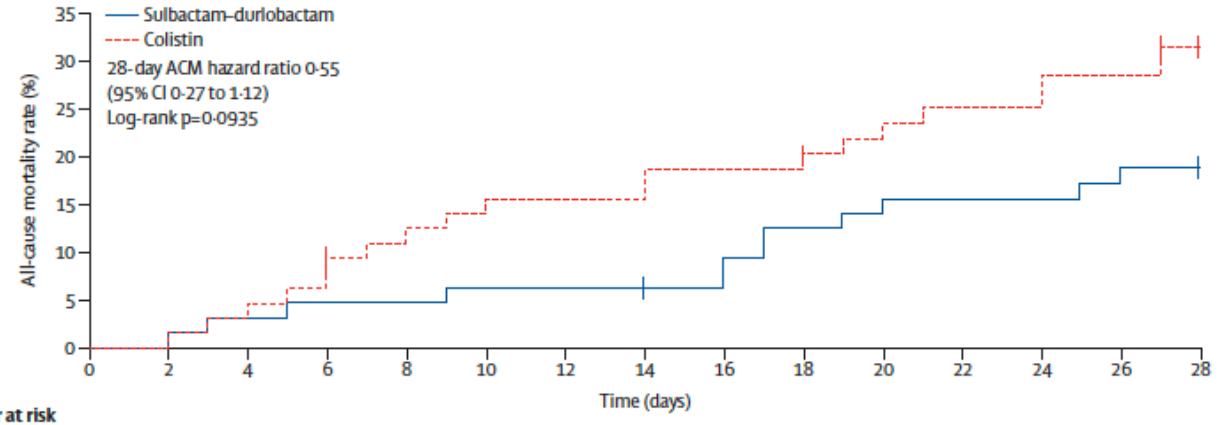
Kaye KS et al. Lancet Infect Dis 2023 May 11;S1473-3099(23)00184-6

A

	Sulbactam–durlobactam, n/N (%)	Colistin, n/N (%)	Treatment difference, % (95% CI)
Primary endpoint			
28-day ACM: carbapenem-resistant ABC microbiologically modified ITT	12/63 (19·0%)	20/62 (32·3%)	−13·2 (−30·0 to 3·5)
Secondary endpoints			
28-day ACM: carbapenem-resistant ABC microbiologically evaluable	8/46 (17%)	16/44 (36%)	−19 (−39·1 to 1·2)
28-day ACM: microbiologically modified ITT	15/76 (20%)	25/76 (33%)	−13 (−28·3 to 2·0)
28-day ACM: ITT	19/90 (21%)	28/85 (33%)	−12 (−26·0 to 2·4)
14-day ACM: carbapenem-resistant ABC microbiologically modified ITT	4/64 (6%)	12/63 (19%)	−13 (−25·7 to 0·1)
14-day ACM: microbiologically modified ITT	6/77 (8%)	15/77 (20%)	−12 (−23·7 to 0·3)



B



Number at risk															
Sulbactam–durlobactam	64	64	62	61	61	60	60	60	59	55	54	53	53	52	51
Colistin	64	64	62	60	56	54	53	53	51	51	48	46	46	44	41

Aztreonam/avibactam

- Combination of aztreonam with a serine BL inhibitor (avibactam)

- Activity against KPC, OXA, and MBL producers
- Activity against some CRPA
- Inactive against CRAB

Sader HS, et al. Antimicrob Agents Chemother 2017; 62:e01856-17. Yahav D, et al. Clin Microbiol Rev 2021; 34:e00115-20. Biedenbach DJ, et al. Antimicrob Agents Chemother 2015; 59:4239-4248.

Aztreonam/avibactam

- Phase 3 (ASSEMBLE) ATM-AVI vs. BAT for MBL infections (NCT03580044) - Terminated
- Phase 3 (REVISIT) ATM-AVI vs. meropenem ± colistin for serious GNB infections (NCT03329092) - Completed

ASSEMBLE

- 5/12 (41.7%) of the ATM-AVI ± MTZ patients with infections due to confirmed MBL-producing Gram-negative bacteria were cured at TOC versus 0/3 (0%) of those on best available therapy (BAT)

- ATM-AVI patients experienced TEAEs that were in line with those of aztreonam alone. No patient treated with ATM-AVI experienced a treatment-related SAE.

https://www.pfizer.com/news/press-release/press-release-detail/phase-3-studies-pfizers-novel-antibiotic-combination-offer

REVISIT

Abstract citation ID: ofad500.2476

2893 A. Efficacy and Safety of Aztreonam-Avibactam for the Treatment of Serious Infections Due to Gram-Negative Bacteria, Including Metallo-β-Lactamase-Producing Pathogens: Phase 3 REVISIT Study

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Session: 262. Late Breaking Abstracts: Clinical Trials
Saturday, October 14, 2023: 2:35 PM

Table 1. Adjudicated clinical response at the TOC visit (ITT and CE analysis sets)

	cIAI		HAP/VAP		Overall	
ITT analysis set	**ATM-AVI + MTZ (n=208)**	**MER ± COL (n=104)**	**ATM-AVI (n=74)**	**MER ± COL (n=36)**	**ATM-AVI ± MTZ (n=282)**	**MER ± COL (n=140)**
Cure, n (%) [95%CI]	159 (76.4) [70.3, 81.8]	77 (74.0) [65.0, 81.7]	34 (45.9) [34.9, 57.3]	15 (41.7) [26.7, 57.9]	193 (68.4) [62.8, 73.7]	92 (65.7) [57.6, 73.2]
Difference, % (95% CI)	2.4 (–12.4, 19.1)		4.3 (–25.6, 32.2)		2.7 (–11.4, 17.8)	
CE analysis set	**ATM–AVI + MTZ (n=168)**	**MER ± COL (n=83)**	**ATM–AVI (n=45)**	**MER ± COL (n=22)**	**ATM–AVI ± MTZ (n=213)**	**MER ± COL (n=105)**
Cure, n (%) [95%CI]	143 (85.1) [79.2, 89.9]	66 (79.5) [69.9, 87.1]	21 (46.7) [32.7, 61.1]	12 (54.5) [34.3, 73.7]	164 (77.0) [71.0, 82.3]	78 (74.3) [65.3, 81.9]
Difference, % (95% CI)	5.6 (–8.9, 23.1)		–7.9 (–42.8, 29.4)		2.7 (–11.9, 19.2)	

ATM-AVI, aztreonam-avibactam; CE, clinically evaluable; CI, confidence interval; cIAI, complicated intra-abdominal infection; COL, colistin; HAP, hospital-acquired pneumonia; ITT, intent-to-treat; MER, meropenem; MTZ, metronidazole; TOC, test-of-cure; VAP, ventilator-acquired pneumonia.

Single arm CIs were computed using Jeffrey's method.

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REVISIT

All-cause 28-day mortality was 4/208 (1.9%) for ATM-AVI ± MTZ vs. 3/104 (2.9%) for MER ± COL in cIAI

All-cause 28-day mortality was 8/74 (10.8%) for ATM-AVI ± MTZ vs. 7/36 (19.4%) for MER ± COL in HAP/VAP

Abstract citation ID: ofad500.2476

Aztreonam/avibactam

- Recently approved by EMA for cIAI, HPA, VAP, and cUTI, as well as for the treatment of infections due to aerobic GNB with limited treatment options, in adult patients
- Marketing authorization applications are also planned for submission in other countries

RACCOMANDAZIONI PER UNA STRATEGIA EFFICACE CONTRO LA RESISTENZA ANTIMICROBICA

FARMINDUSTRIA

Università degli Studi di Genova
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Genoa, Italy

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Genoa, Italy

1. **Metodologia di valutazione dei nuovi antibiotici contro i ceppi batterici resistenti**

   Adattare le attuali metodologie per la determinazione del valore degli antibiotici alle caratteristiche di questi farmaci, considerando il loro ruolo salvavita, tenendo presente che questo richiederà una prospettiva più ampia e l'analisi di scenari ed evidenze oltre a quelle necessarie per le attuali richieste di registrazione.

2. **Criteri per il conferimento dello status di farmaco "innovativo" ai nuovi antibiotici contro i ceppi batterici resistenti**

   Utilizzare indicatori specifici capaci di misurare efficacemente il grado di innovatività dei nuovi antibiotici, adattando, se necessario, gli attuali elementi di valutazione a supporto della richiesta

3. **Modelli di rimborso ad hoc per i nuovi antibiotici attivi per le resistenze batteriche**

   Visto che la stewardship antimicrobica fornisce indicazioni restrittive sull'uso dei nuovi antibiotici nel trattamento delle infezioni causate dai ceppi resistenti per ridurre la probabilità che si sviluppino nuove forme di resistenza, è necessario identificare delle modalità di rimborso[9] che garantiscano agli sviluppatori un ritorno economico tale da aumentare e mantenere nel tempo gli investimenti in ricerca e sviluppo in quest'area.

2. Formazione degli operatori sanitari

Garantire che i fondi previsti dal PNRR in merito all'avvio di un piano straordinario di formazione sulle infezioni correlate all'assistenza a tutto il personale sanitario e non sanitario degli ospedali e delle cure primarie, siano indirizzati verso programmi specifici sulla stewardship antimicrobica e sul controllo delle infezioni.

3. Team multidisciplinari

Garantire la presenza di un team multidisciplinare (medici specialisti, microbiologi, farmacisti ospedalieri, ecc.) all'interno delle strutture sanitarie con la responsabilità di definire i programmi di stewardship e la loro applicazione.

4. Governo dei nuovi antibiotici

Garantire un accesso tempestivo ai nuovi antibiotici in situazioni di urgenza ed emergenza estendendo la prescrivibilità di questi farmaci "salvavita" ad altri specialisti, con competenze specifiche sull'uso degli antibiotici (intensivisti, ematologi, ecc.), prevedendola nell'ambito di progetti di stewardship antimicrobica.

Inoltre, nel contesto di precise raccomandazioni terapeutiche potrebbe essere utile prevedere una finestra di accesso libero e regolamentato che permetta così ai pazienti di ricevere tempestivamente il trattamento necessario nelle prime decisive ore.

5. Integrazione tra stewardship antibiotica e stewardship diagnostica

Sviluppare programmi di stewardship antibiotica fortemente integrata con la stewardship diagnostica nella definizione del Percorso Diagnostico Terapeutico Assistenziale in maniera uniforme a livello nazionale, con il coinvolgimento di tutti gli operatori sanitari ed in particolare della medicina territoriale.

Potenziare, inoltre, l'utilizzo degli strumenti di diagnostica di primo livello (ad es. tampone faringeo per SBEGA, dosaggio PCR, strisce reattive per i test delle urine, otoscopia pneumatica, ecc.) che, nell'ambito delle cure primarie, permette una maggiore precisione diagnostica e una conseguente maggiore appropriatezza prescrittiva.

6. Informazione ai cittadini

Promuovere campagne di comunicazione rivolte alla popolazione sull'uso appropriato e consapevole di antibiotici, puntando ad accrescere il livello di consapevolezza del cittadino.

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