INFEZIONI GRAVI DEL TORRENTE CIRCOLATORIO: QUALI VANTAGGI DALLE NUOVE MOLECOLE

Milano, 9 Giugno 2025

Centro Congressi StarHotels Ritz

Enterococchi quando e come trattare

Michele Bartoletti

Humanitas University -Department of Biomedical Sciences -
Infectious Disease Unit IRCCS Humanitas Research Hospital

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ENTEROCOCCAL INFECTION

- Top 10 cause of BSI
- Fourth cause of HA infection
- Third cause of IE (first case of TAVI endocarditis)
- Up to 26% of E. faecalis BSI are associated to endocarditis
- Persistent bacteremia 13% of cases (when follow-up BC are performed)

Roguerio JAMA 2016; Dahl JACC 2019; Rosselli del Turco CMI 2021 Bussini JGAR 2022

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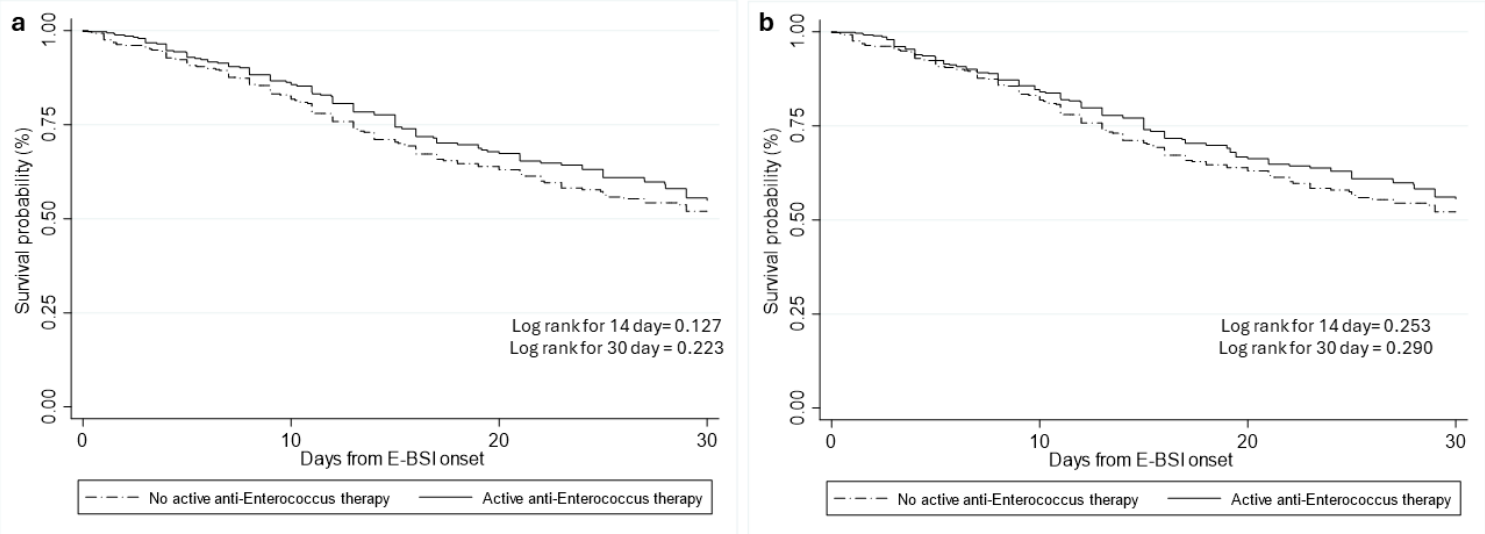
Empirical therapy?

What is the impact of anti-enterococcal empirical therapy on survival of patients with enterococcal bloodstream infections?

Bussini L et al. CID 2025

758 patients
416 received no active antienterococcal empirical therapy
342 received active antienterococcal empirical therapy

The primary outcome was 14-day all-cause mortality from index BC



IPTW-adjustment:

- number of comorbidities (aHR 1.16 [95%CI 1.09-1.24)
- EBSI without identified source (aHR 1.59 [95%CI 1.00-2.51])
- anti enterococcal empirical therapy (aHR 0.80 [95%CI0.59-1.1])

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Enterococcus faecium bacteremia: a multicenter observational study focused on risk factors for clinical and microbiological outcomes

Rinaldi M et al J Antimicrob Chemother 2025

391 patinets from 2 centers
VRE 30%

Multivariable analysis for 30-day mortality

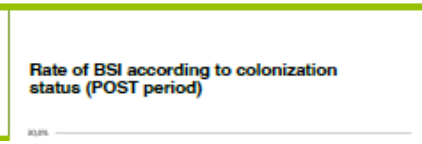
Variable	HR	95%CI	p-value
Male gender	0.761	(0.534-1.084)	0.130
CCI	1.059	(0.990-1.133)	0.097
Immunosuppression	1.638	(1.022-2.625)	0.040
BSI onset in ICU	0.883	(0.514-1.514)	0.650
Monomicrobial BSI	1.032	(0.708-1.505)	0.871
VRE	1.187	(0.820-1.719)	0.364
Primary BSI	1.839	(1.221-2.770)	0.004
SOFA score	1.205	(1.144-1.268)	<0.001
Appropriate empirical therapy	0.859	(0.575-1.284)	0.458
Appropriate targeted therapy	0.841	(0.574-1.230)	0.372
FUBC^	0.403	(0.280-0.581)	<0.001
Source control^	0.534	(0.260-0.972)	0.042

EXTENDED MICROBIOLOGICAL SCREENING in hematological patients with FEBRILE NEUTROPENIA: a quasi-experimental PRE/POST single-center study

THIS PRELIMINARY ANALYSIS SHOWS THAT MDRO-ES IS ABLE TO BETTER STRATIFY RISK OF MDRO INFECTIONS DURING FN AND TO IMPROVE THE RATE OF ADEQUATE EMPIRICAL ANTIBIOTIC TREATMENT

Bussini L[1], Ambretti S[2], Scolz K[3], Cilli A[3], Vatamanu O[3], Miselli F[3], Tazza B[3], Nigrisoli G[2], Banchini I[2], Barbiero A[2], Vignudelli E[2], Papayannidis C[4], Pellegrini C[4], Maffini E[4], Cavo M[4], Bonifazi F[4], Zinzani P[4], Vianelli N[4], Viale P[3], Giannella M[3], Bartoletti M[1]

[1]*Infectious Disease Division, IRCCS Humanitas Research Hospital – Rozzano (Italy),* [2]*Operative Unit of Clinical Microbiology, Sant'Orsola Malpighi University Hospital – Bologna (Italy),* [3]*Infectious Disease Unit, Department of Medical and Surgical Science, Policlinico Sant'Orsola; Bologna (Italy),* [4]*Institute of Hematology "L. e A. Seragnoli" University of Bologna – Bologna (Italy)*



We aimed to study the role of an extended screening for multidrug-resistant organisms (MDRO-ES) in patients with hematologic malignancies (HM) before chemotherapy to individualize empirical treatment in case of febrile neutropenia (FN).

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Bussini L et al. ECCMID 2023

METHODS:

Study design: prospective, pre/post, single-center study
Population: all adult patients with HM hospitalized for CHT, HSCT or CAR-T therapy and hospitalised in Haematology and transplant units
Primary endpoint: concordance between screening results and results of blood cultures collected during FN episodes using a phenotypic approach (identical susceptibility test)

INTERVENTION:

Period	MDRO-ES
PRE Oct 2019 – Jan 2022	Rectal swab (RS) for CPE
POST Feb 2022 – Jun 2022	• RS and stool culture for: ▪ CPE ▪ ESBL ▪ VRE • Nasal swab for MRSA • Multi-site (throat, groin, axillary) swabs for MDR Enterobacterales and non-fermenting gram-negative bacteria • Urine culture

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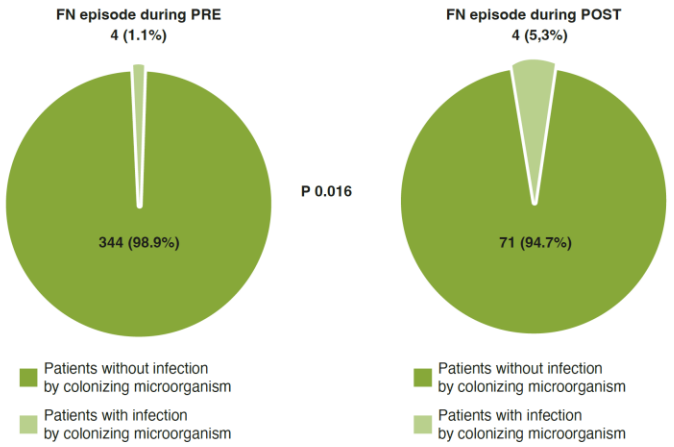
Bussini L et al. ECCMID 2023

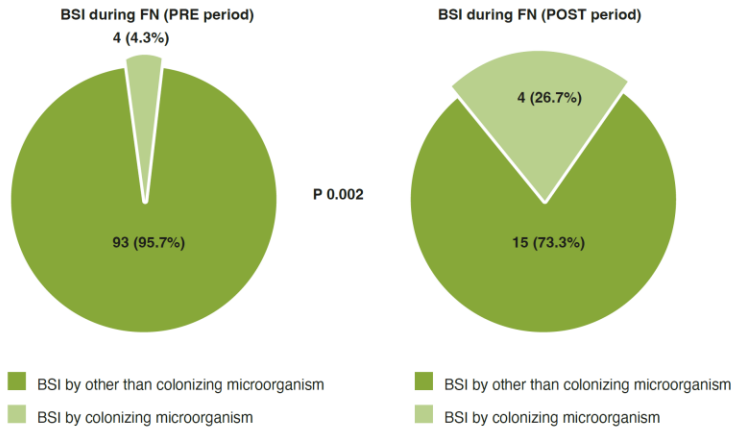
TABLE 1: General characteristics of patients in the PRE and the POST period

	Admission in pre-period N=547 (%)	Admission in the post-period N=197 (%)	p
Demographics			
Age (year), mean (±SD)	54.0 (±14.9)	54.9 (±13.7)	0.45
Gender, male	314 (58.3)	116 (59.5)	0.76
Charlson's comorbidity index, median (IQR)	3 (2-4)	3 (2-5)	0.41
Underlying disease			
Acute Myeloid leukemia	151 (28.2)	53 (28.2)	
Acute Lymphoblastic Leukemia	73 (13.6)	17 (9.0)	
Chronic Lymphocytic Leukemia	7 (1.3)	5 (2.7)	
Chronic Myeloid Leukemia	10 (1.9)	3 (1.6)	
Non-Hodgkin Lymphoma	179 (33.4)	63 (33.5)	
Hodgkin Lymphoma	28 (5.2)	6 (3.2)	
Multiple Myeloma	70 (13.1)	34 (18.1)	
Myelodysplastic Syndrome	13 (2.4)	6 (3.2)	
Aplastic Anemia	5 (0.9)	1 (0.5)	
Disease Status			0.037
Onset	152 (27.9)	57 (29.1)	
Complete response	139 (25.6)	63 (32.1)	
Partial response	79 (14.5)	28 (14.3)	
Stable disease	30 (5.5)	16 (8.2)	
Progressive disease	144 (26.5)	32 (16.3)	
Admission reason			0.007
Induction chemotherapy (CHT)	120 (22.0)	32 (16.2)	
Consolidation CHT	53 (9.7)	27 (13.7)	
Salvage CHT	73 (13.4)	25 (12.7)	
Hematopoietic stem cell transplantation	150 (27.5)	55 (27.9)	
CAR-T	46 (8.4)	5 (2.5)	
Other	104 (19.0)	53 (26.9)	

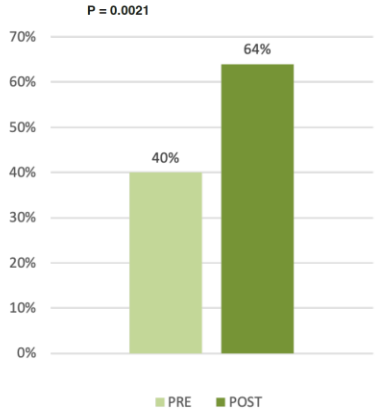
Matching between colonization and infection among 423 patients with FN



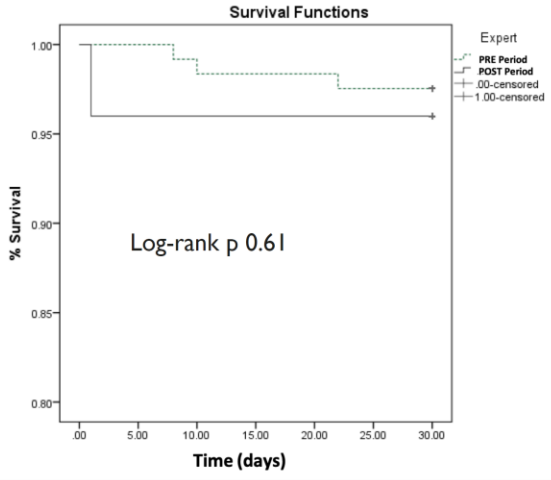
Matching between colonization and BSI among 108 patients with BSI during FN



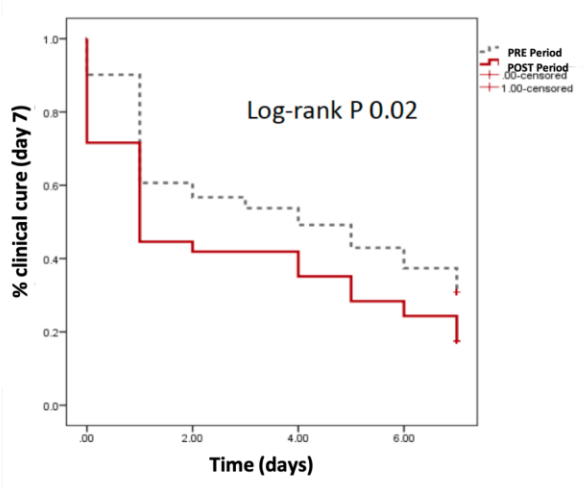
Rate of adequate empirical screening-guided antibiotic treatment



Kaplan-Meier of 30-day mortality in 148 patients with BSI



Kaplan-Meier curve for clinical cure on day 7 of 423 patients with febrile neutropenia



Bussini L et al. ECCMID 2023

Enterococcus spp resistance to anitmicrobials

Antibiotic	Representative gene(s)/operon(s)	Mechanism of resistance	Innate/Clonal and relative prevalence of resistance data		Comments
			E. faecalis	E. faecium	
β-lactams	Penicillin-binding protein (PBPs)	Reduced affinity for the antibiotic	Innate	Innate	PBP4 in E. faecalis, PBP5 in E. faecium
	β-lactamases	β-lactamases hydrolysis	Clonal (0.4%)	Clonal (89.8%)	Inoculum effect (≥10^7 CFU)
Glycopeptides	VanA	Reduced affinity for the antibiotic	Clonal (1.9%)	Clonal (91.0%)*	Both vancomycin and teicoplanin resistance
	VanB	Reduced affinity for the antibiotic	Clonal (0.6%)	Clonal (75.3%)**	Vancomycin only resistance
Daptomycin	LiaFSR, gdpD,cls, YycFG, YycHIJ	Alteration in membrane charge and fluidity	Clonal (<0.2%)	Clonal (<0.2%)	Increasing risk with previous daptomycin exposure
Linezolid	23s rRNA	Reduced affinity for the antibiotic	Clonal (<1%)	Clonal (<1%)	Initial point mutation
	RplC/RplD, Cfr, Cfr(B) and variants	Methylation of 23s rRNA			Expression does not necessary result in resistance to linezolid
	OptrA	ABC-F protein			
Sulfonamides		Absence of molecular target	Innate	Innate	
Fluoroquinolones	gyrA, parC	Reduced affinity for the antibiotic	Clonal (87%)	Clonal (53%)	Increasing with fluoroquinolones exposure, especially in E. faecalis
	gnr	Efflux pump			
Tetracycline	TetK, TetL	Efflux pump	Clonal (30-40%)	Clonal (30-40%)	Globally increasing
Tigecycline	Resistance Nodulation-cell Division (RND)	Efflux pump	Clonal (<1%)	Clonal (0.2%)	For MIC > 0.5 mg/L (EUCAST)
Macrolides	ermB	Reduced affinity for the antibiotic	Clonal (43%)	Clonal (43%)	
	mef	Efflux pump	Clonal (N/D)	Clonal (N/D)	
Aminoglycosides		Impermeability of cell wall	Innate	Innate	Low-level resistance, overwhelmed by association with β-lactams
	Adenylyltransferase	Inactivation of the antibiotics	Clonal (27.1%)§	Clonal (>75%)§	

Rosselli Del Turco E, Bartoletti M, Dahl A, Cervera C, Pericàs JM. Clin Microbiol Infect. 2021 Mar;27(3):364-371

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ENTEROCOCCUS
Beta-lactam resistance

- **Intrinsic**
  - Penicillin «tolerance»
    - Absence of bactericidal effect
  - Aztreonam
  - Cephalosporins (exceptions ceftobiprole and ceftaroline)
  - Carbapenems (exception imipenen)

- **Genetically acquired**
  - PBP5 (i.e enterococcus faecium)
  - Penicillase/beta-lacatamase

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Enterococcal endocarditis. An analysis of 38 patients observed at the New York Hospital-Cornell Medical Center

Mandell Arch Intern Med 1970 Feb;125(2):258-64

Table 4.—Antibiotic Therapy in Patients With Enterococcal Endocarditis Prior to Admission to the New York Hospital-Cornell Medical Center

	Treatment Before Admission to New York Hospital-Cornell Medical Center				
Year Treated	Antibiotics	Daily Dose	Duration of Therapy (Days)	Result	Result of Retreatment With Penicillin and Streptomycin at New York Hospital-Cornell Medical Center
1948	Chlortetracycline hydrochloride, PO *	3-12 gm	41	Became afebrile but blood cultures continued to be positive	Died with heart failure and septic emboli on day 16 of therapy
1949	Penicillin G potassium, IM †; with chlortetracycline hydrochloride, PO	6 million units; 3 gm	42	Relapse with positive blood cultures 6 weeks after cessation of therapy	Cured; doing well 11 years later
1950	Penicillin G potassium, IM	1-3 million units	60	Relapse with positive blood cultures 8 days after cessation of therapy	Died with mesenteric embolus on day 29 of therapy; cultures negative at autopsy
1952	Penicillin G potassium, IV ‡	20 million units	42	Relapse with positive blood cultures 14 days after cessation of therapy	Cured; died 5 years later after prefrontal lobotomy
1956	Penicillin G potassium, IM	2-3 million units	21	Relapse with positive blood cultures 7 days after cessation of therapy	Cured; doing well 5 years later
1961	Chloramphenicol, PO; followed by oxytetracycline, PO	3 gm 1 gm	20 14	Relapse with positive blood cultures 14 days after cessation of therapy	Cured; doing well 7 years later
1964	Penicillin G potassium, IM	0.6-4 million units	18	Fever and positive blood cultures during therapy	Died of massive intestinal hemorrhage secondary to vasculitis on day 40 of therapy
1965	Cephalothin sodium, IV; followed by ampicillin, PO	6 gm 3 gm	24 30	Relapse with positive blood cultures 10 days after cessation of therapy	Cured; died 1 year later following open heart surgery
1967	Cephalothin sodium, IV	4-6 gm	30	Relapse with positive blood cultures 7 days after cessation of therapy	Cured; doing well 1 year later
1967	Ampicillin, PO; followed by cephalothin sodium, IV	2 gm 4 gm	4 12	Fever and positive blood cultures during therapy	Endocarditis initially developed after placement of prosthetic mitral valve; patient living and well 1.5 years after therapy but continues to receive ampicillin
1968	Cephalothin sodium, IV; followed by ampicillin, IV	24 gm 4 gm	14 28	Became afebrile but blood cultures continued to be positive during cephalothin therapy	Cured; doing well 1 year later

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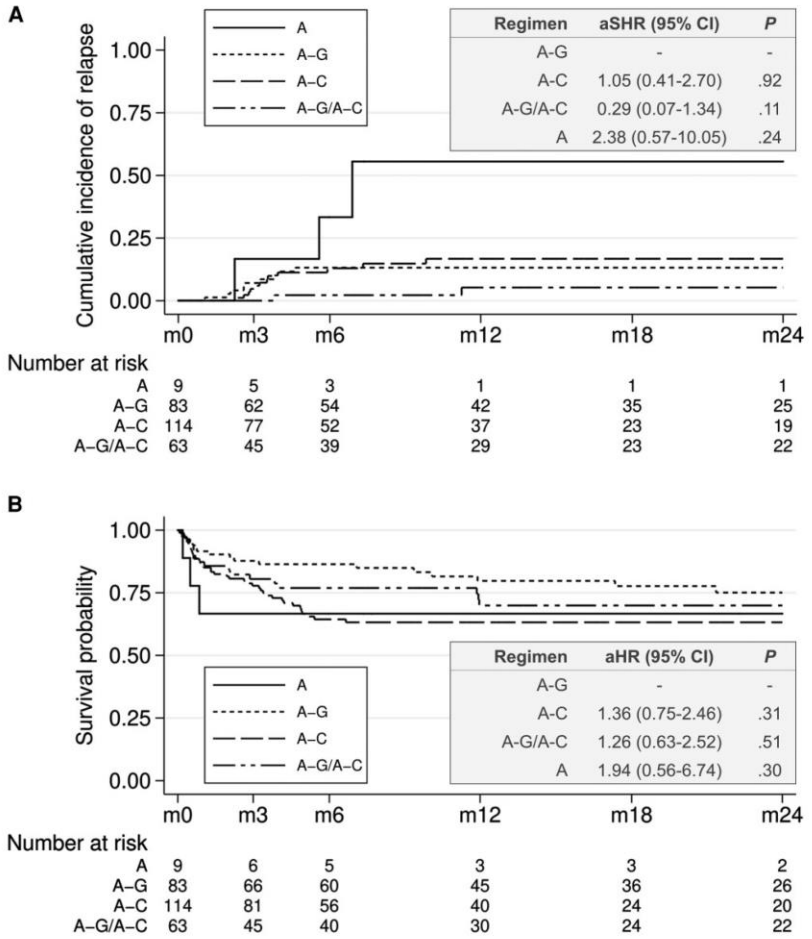
Impact of Enterococcus Faecalis Endocarditis Treatment on Risk of Relapse

279 patients included,

- 83 (29.7%) received the amoxicillin-gentamicin (A-G) combination,
- 114 (40.9%) amoxicillin-ceftriaxone (A-C),
- 63 (22.6%) A-G and A-C (A-G/A-C) sequentially,
- 9 (3.2%) amoxicillin (A),

- 10 received other treatments.

One-year-relapse rate was 9.3%
(26 patients)



Dannells et al Clin Infect Di. 2022 Sep 19;ciac777. doi

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Treatment of *Enterococcus faecalis* Endocarditis with Ampicillin plus Ceftriaxone

Gavalda J et al Ann Intern Med 2007;146:574-579

- To evaluate the efficacy and safety of ampicillin plus ceftriaxone for treating endocarditis due to *E. faecalis* with and without HLAR
- Observational, open-label, non-randomized, multicenter (13 centers in Spain) clinical trial
- 21 patients with HLAR *E. faecalis* endocarditis and 22 patients with non-HLAR *E. faecalis* endocarditis. All were at risk for nephrotoxicity related to aminoglycoside use
- 6-week course of intravenous ampicillin, 2 g every 4 hours, plus intravenous ceftriaxone, 2 g every 12 hours

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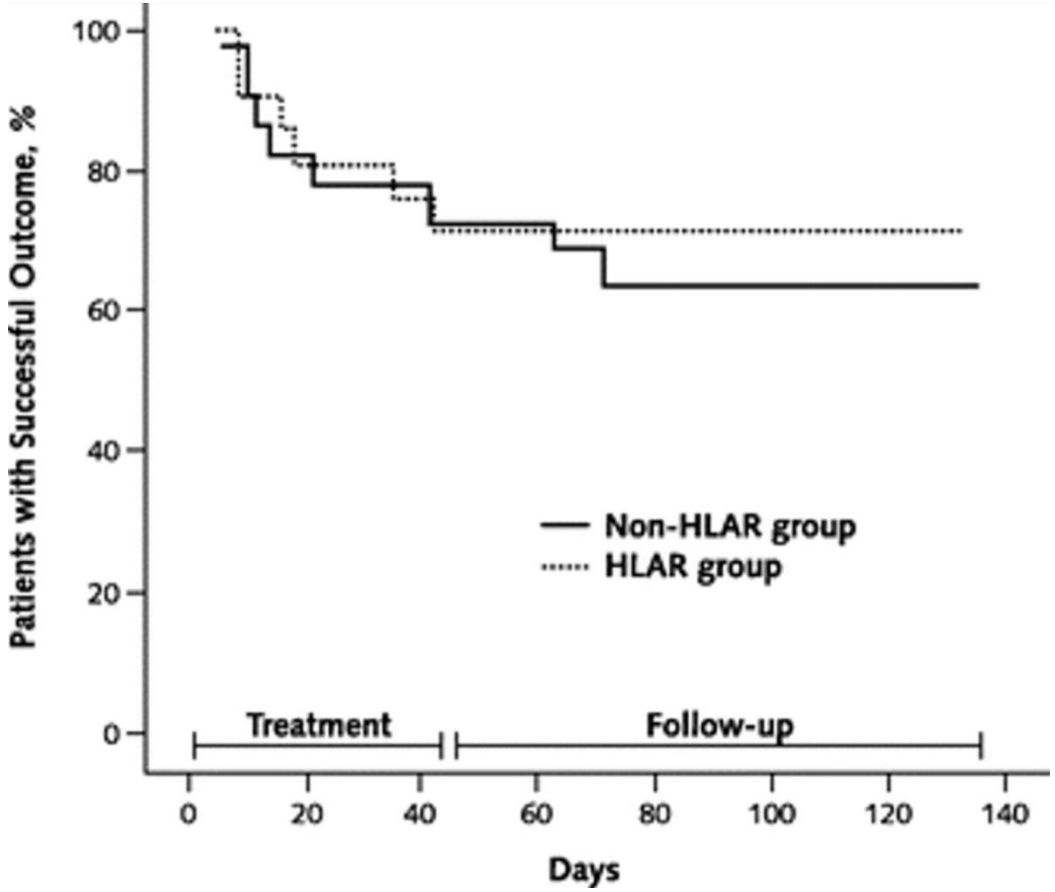
Treatment of *Enterococcus faecalis* Endocarditis with Ampicillin plus Ceftriaxone

Gavalda J et al Ann Intern Med 2007;146:574-579



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Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating Enterococcus faecalis Infective Endocarditis

- An observational, nonrandomized, comparative multicenter cohort study was conducted at 17 Spanish and 1 Italian hospitals. Consecutive adult patients diagnosed of EFIE were included.

	Ampicilln+ Ceftriaxone (n=159)	Ampicillin + Gentamicin (n= 87)	P
In-hospital mortality	42 (26%)	22 (25%)	0.85
Operated	10/53 (19%)	10/35 (29%)	0.29
Non operated (with Indication)	24/39 (62%)	8/19 (42%)	0.16

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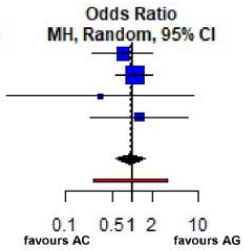
Fernandez Hidalgo et al CID 2013

Time to abandon ampicillin plus gentamicin in favour of ampicillin plus ceftriaxone in Enterococcus faecalis infective endocarditis? A meta-analysis of comparative trials

a In-hospital mortality

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	10	46	9	32	27.7%	0.71 [0.25; 2.01]
Fernández-Hidalgo et al., 2013	35	159	18	87	57.0%	1.08 [0.57; 2.05]
Shah et al., 2021	0	56	1	56	3.4%	0.33 [0.01; 8.21]
El Rafei et al., 2018	2	18	6	67	11.8%	1.27 [0.23; 6.90]
Total (95% CI)		**279**		**242**	**100.0%**	**0.94 [0.56; 1.59]**
Prediction interval						**[0.26; 3.35]**

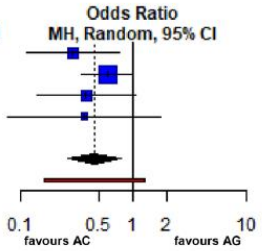
Heterogeneity: $Tau^2 = 0.0596$; $Chi^2 = 0.99$, df = 3 (P = 0.80); $I^2 = 0\%$



b Nephrotoxicity

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	15	46	20	32	20.8%	0.29 [0.11; 0.75]
Fernández-Hidalgo et al., 2013	53	159	40	87	52.8%	0.59 [0.34; 1.00]
Shah et al., 2021	6	100	13	90	18.3%	0.38 [0.14; 1.04]
El Rafei et al., 2018	2	18	17	67	8.1%	0.37 [0.08; 1.77]
Total (95% CI)		**323**		**276**	**100.0%**	**0.45 [0.26; 0.77]**
Prediction interval						**[0.16; 1.26]**

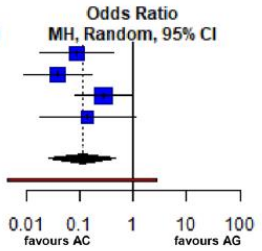
Heterogeneity: $Tau^2 = 0.0280$; $Chi^2 = 1.93$, df = 3 (P = 0.59); $I^2 = 0\%$



c Adverse events requiring drug withdrawal

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio MH, Random, 95% CI
Pericàs et al., 2018	2	46	11	32	24.0%	0.09 [0.02; 0.43]
Fernández-Hidalgo et al., 2013	2	159	22	87	26.5%	0.04 [0.01; 0.16]
Shah et al., 2021	4	49	12	49	33.1%	0.27 [0.08; 0.92]
El Rafei et al., 2018	1	18	20	67	16.5%	0.14 [0.02; 1.11]
Total (95% CI)		**272**		**235**	**100.0%**	**0.11 [0.03; 0.46]**
Prediction interval						**[0.00; 2.73]**

Heterogeneity: $Tau^2 = 0.3575$; $Chi^2 = 4.32$, df = 3 (P = 0.23); $I^2 = 31\%$



Mirna Clin Res Cardiol 2022 Oct;111(10):1077-1086.

- **AC was non-inferior to AG in**
  - in-hospital mortality,
  - 3-month mortality,
  - relapses
  - treatment failure.

- **AC was associated with a lower prevalence of**
  - nephrotoxicity (OR 0.45 [0.26–0.77], *p* = 0.0182)
  - drug withdrawal due to adverse events (OR 0.11 [0.03–0.46], *p* = 0.0160)

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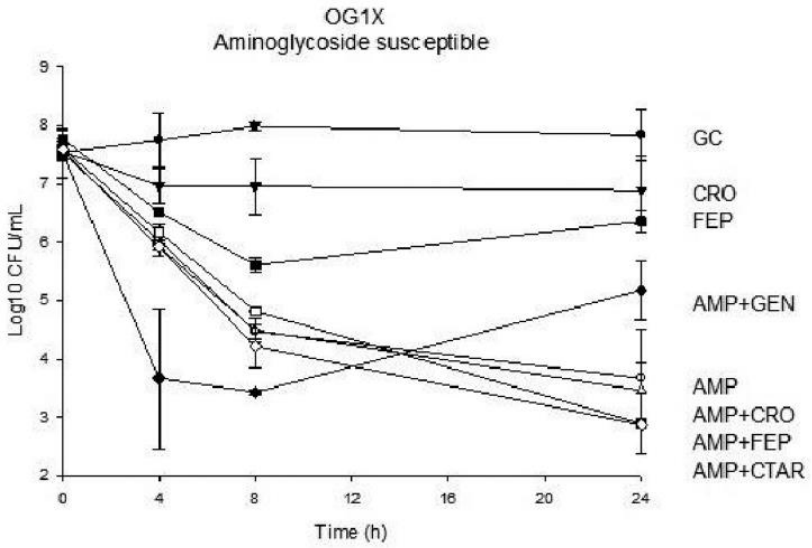
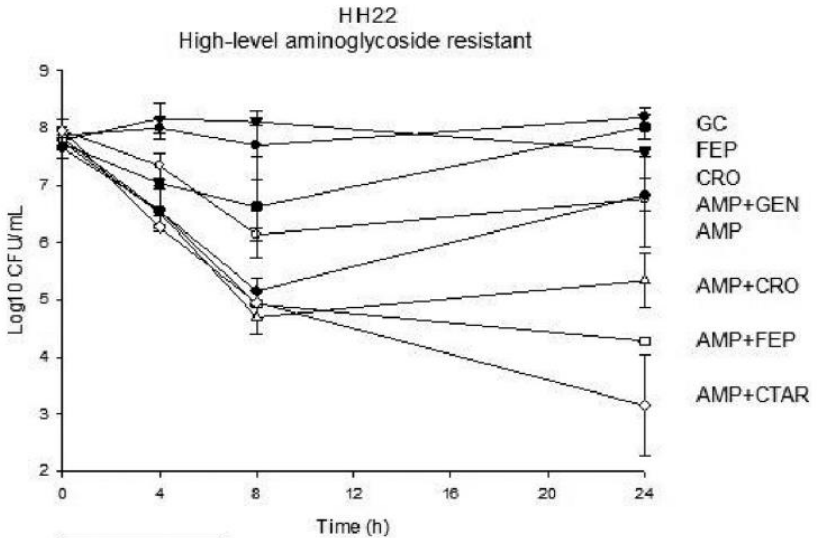
Ampicillin in Combination with Ceftaroline, Cefepime, or Ceftriaxone Demonstrates Equivalent Activities in a High-Inoculum *Enterococcus faecalis* Infection Model





- Ampicillin-cephalosporin combinations demonstrated the most activity against both strains of *E. faecalis* over 24
- Ampicillin-cefepime and ampicillin-ceftaroline significantly increased activity over that of ampicillin alone for one strain

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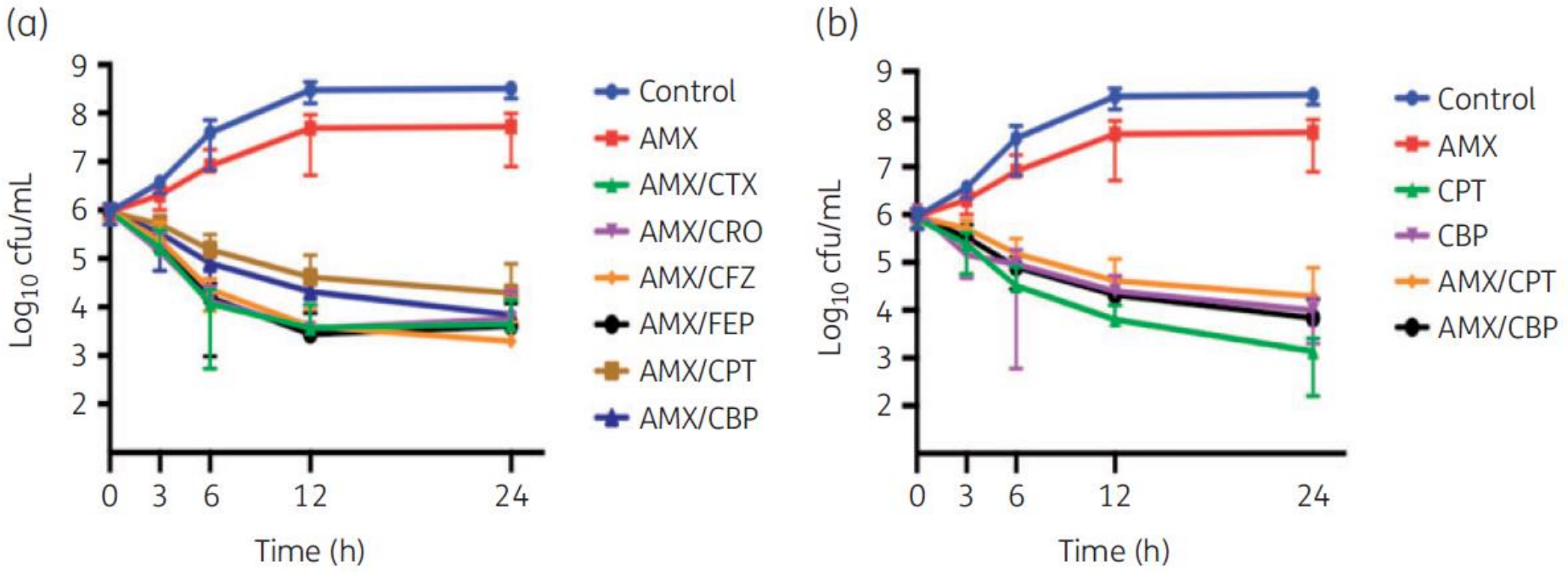
Luther MK Antimicrob Agents Chemother. 2016 Apr 22;60(5):3178-82

In vitro bactericidal activity of amoxicillin combined with different cephalosporins against endocarditis-associated Enterococcus faecalis clinical isolates



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Nathan Peiffer-Smadja J Antimicrob Chemother 2019; 74: 3511–3514

Combination treatment for *Enterococcus faecalis* bacteremia: a prospective, multicenter, observational study (EFFAECT study)

Bartoletti M et al (Manuscript in preparation)

Aim:

- compare monotherapy vs combination therapy

Design:

- Multicenter (26 centres) prospective observational study

Population

- Enterococcal BSI – No endocarditis

Endpoints

cure defined as a composite outcome at 90 days from EOT, including both

A. variables collected at end-of-treatment (EOT):

B. • Patient alive

• fever resolved

• stable or improved SOFA

• blood cultures negative for E. faecalis

B. variables collected during follow-up

• no relapse of EF-BSI within 90 days from EOT

• no need to modify initial therapy

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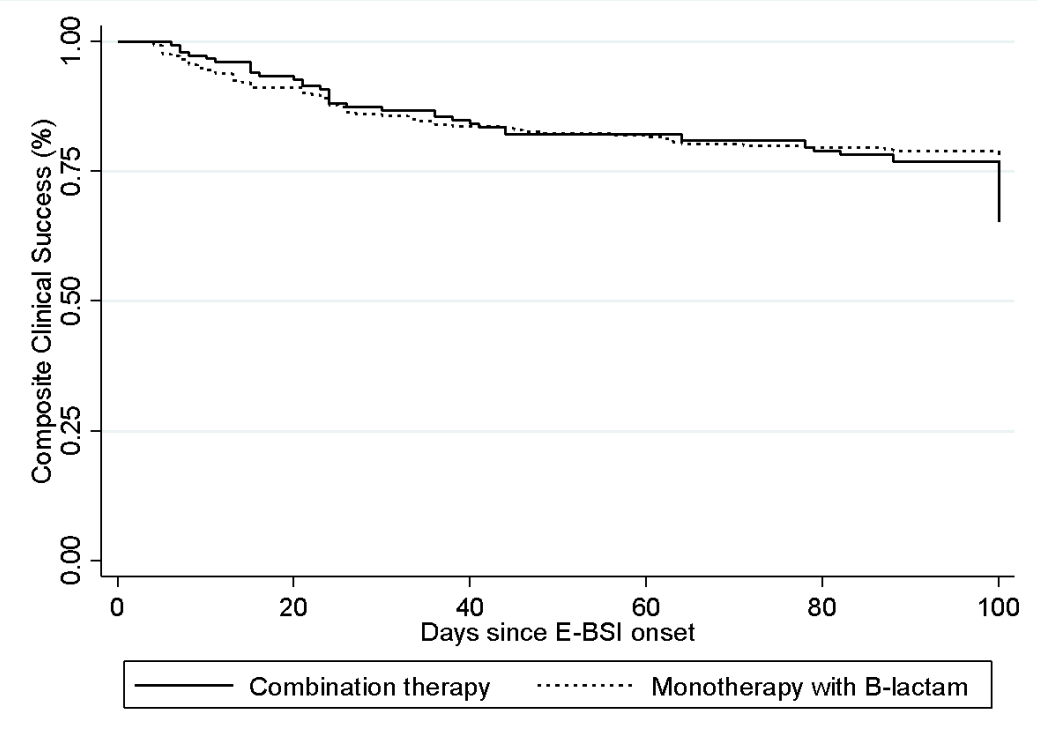
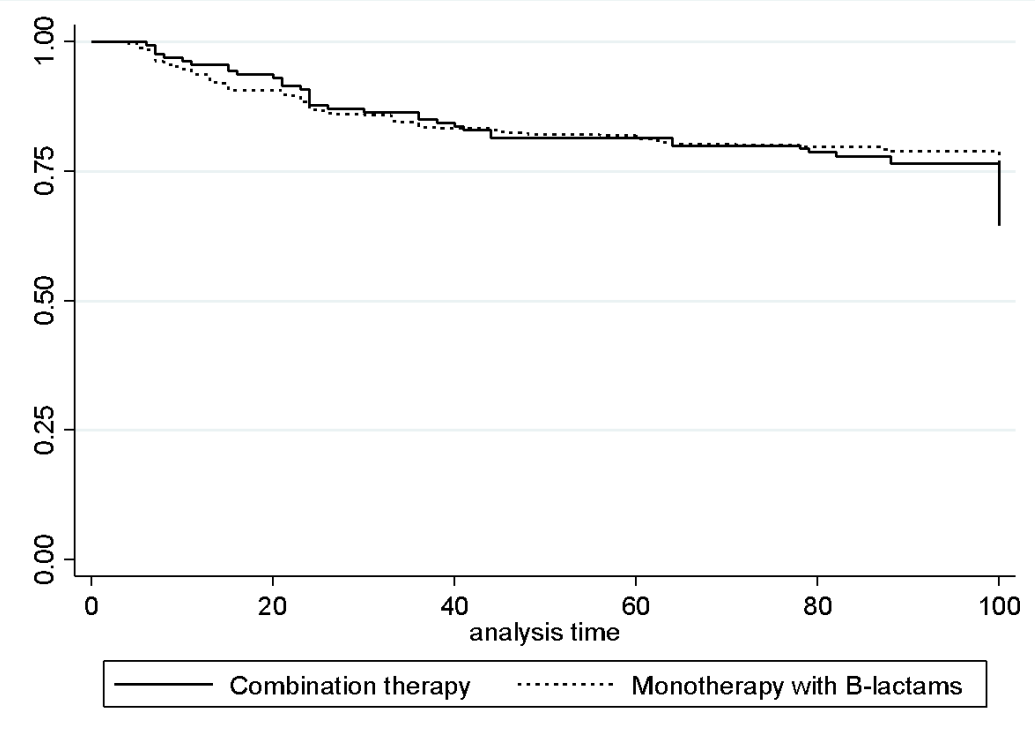
EFFAECT: main results

- 295 subjects (66%) beta-lactam monotherapy
- 152 (34%) were treated with combination therapy





1A) Legend: full population; Log rank p= 0.378

1B) Legend: IPTW-adjusted population; Log rank p= 0.231

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Bartoletti M et al (Manuscript in preparation)

Enterococcus faecium
(VRE)

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Comparison of the Effectiveness and Safety of Linezolid and Daptomycin in Vancomycin- Resistant Enterococcal Bloodstream Infection: A National Cohort Study of Veterans Affairs Patients

Britt N CID 2015

644 patients were included (linezolid, n = 319; daptomycin, n = 325).

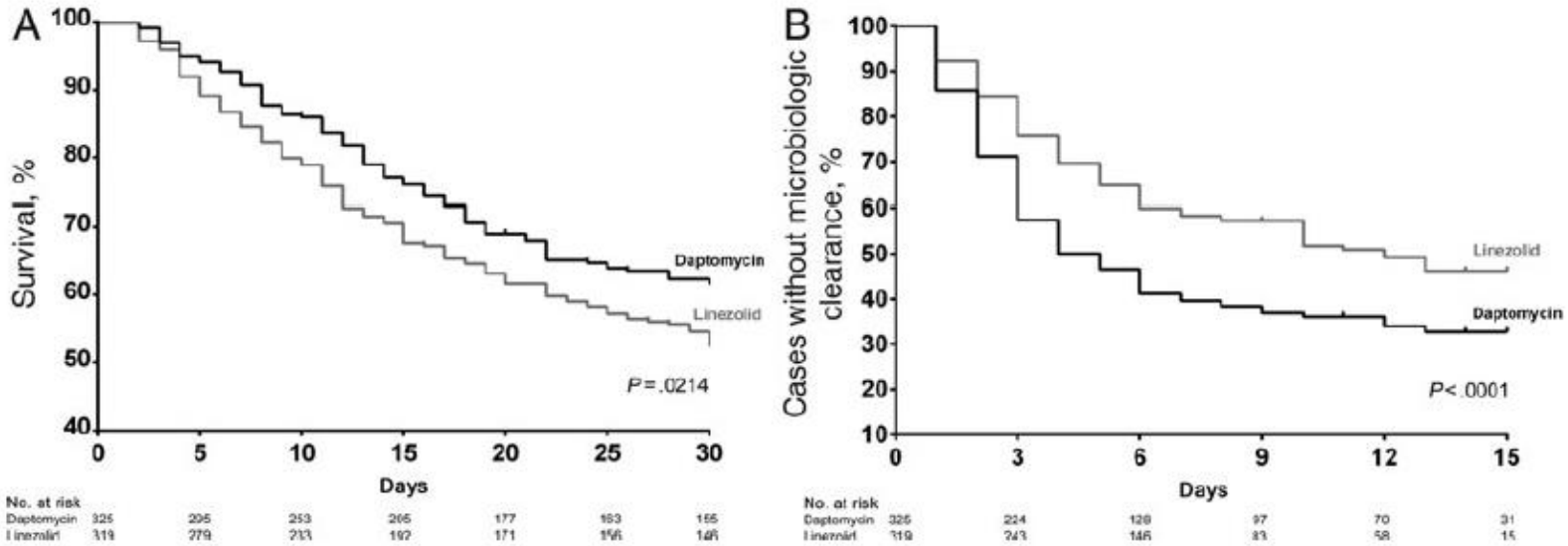

Figure 1. Kaplan–Meier curves for outcomes (*A*) 30-day mortality and (*B*) microbiologic failure.

Linezolid was associated with higher 30-day mortality (42.9% vs 33.5%; RR, 1.17; 95% CI, 1.04–1.32; P = .014) and microbiologic failure rates (RR, 1.10; 95% CI, 1.02–1.18; P = .011).

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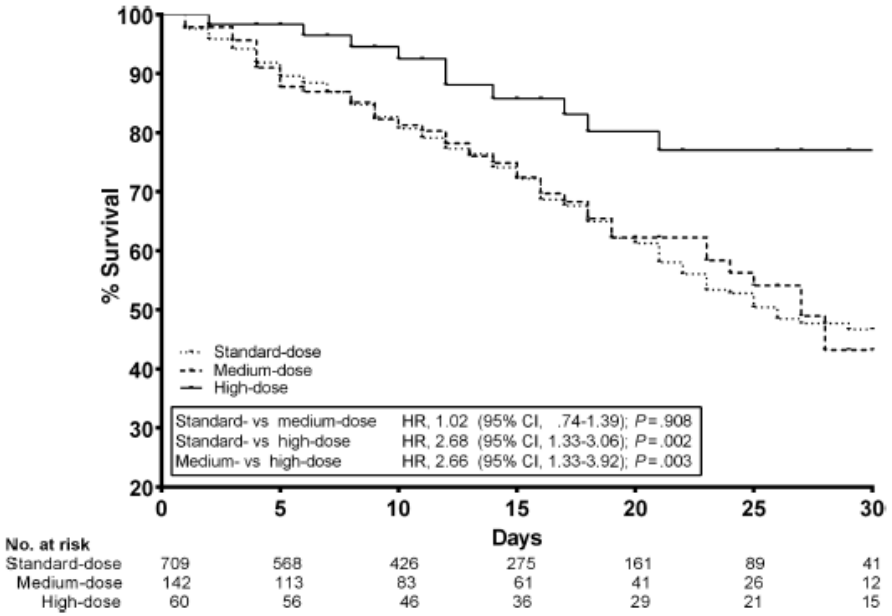
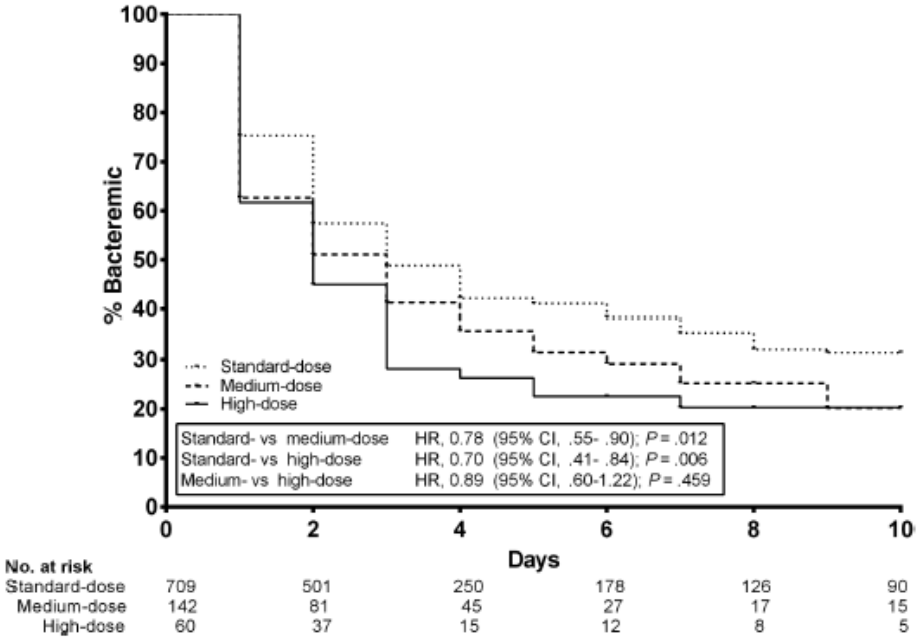
Comparative Effectiveness and Safety of Standard-, Medium-, and High-Dose Daptomycin Strategies for the Treatment of Vancomycin-Resistant Enterococcal Bacteremia Among Veterans Affairs Patients

Britt N CID 2017

standard- dose (6 mg/kg total body weight),
medium-dose (8 mg/kg total body weight), or high-dose (≥10 mg/kg total body weight)





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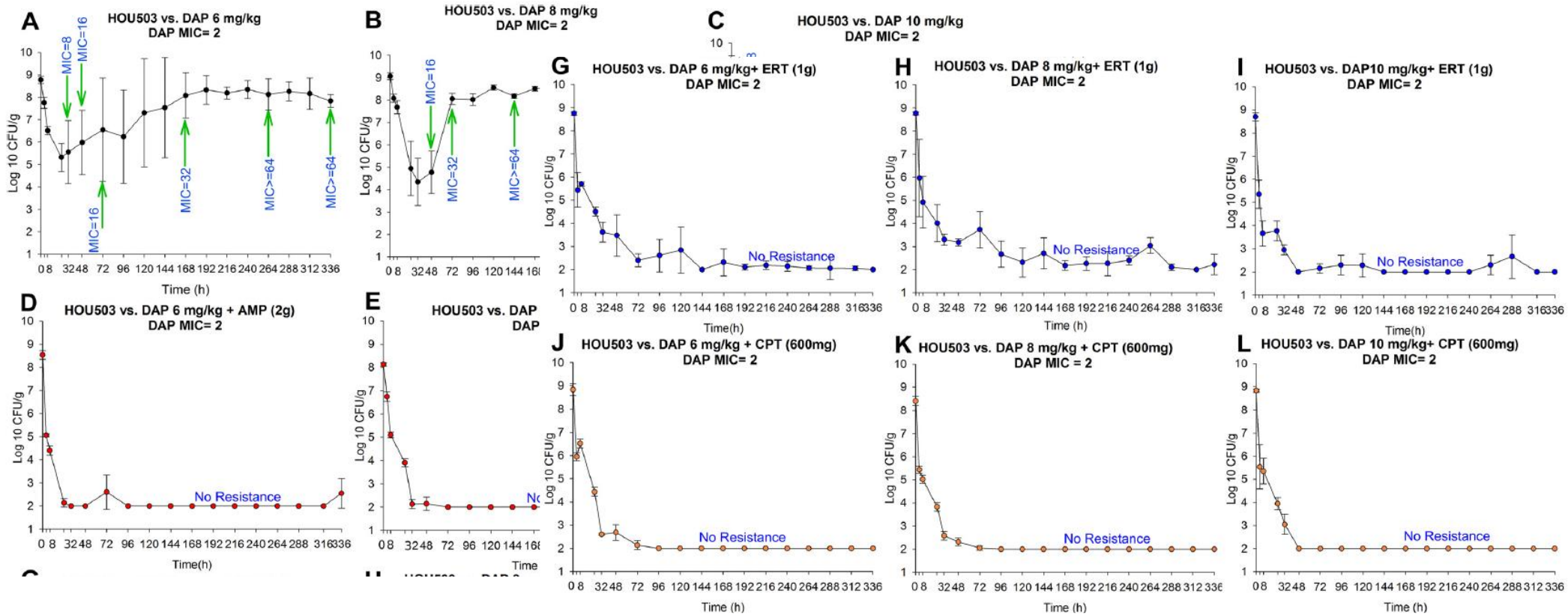
Influence of Inoculum Effect on the Efficacy of Daptomycin Monotherapy and in Combination with -Lactams against Daptomycin-Susceptible Enterococcus faecium Harboring LiaSR Substitutions



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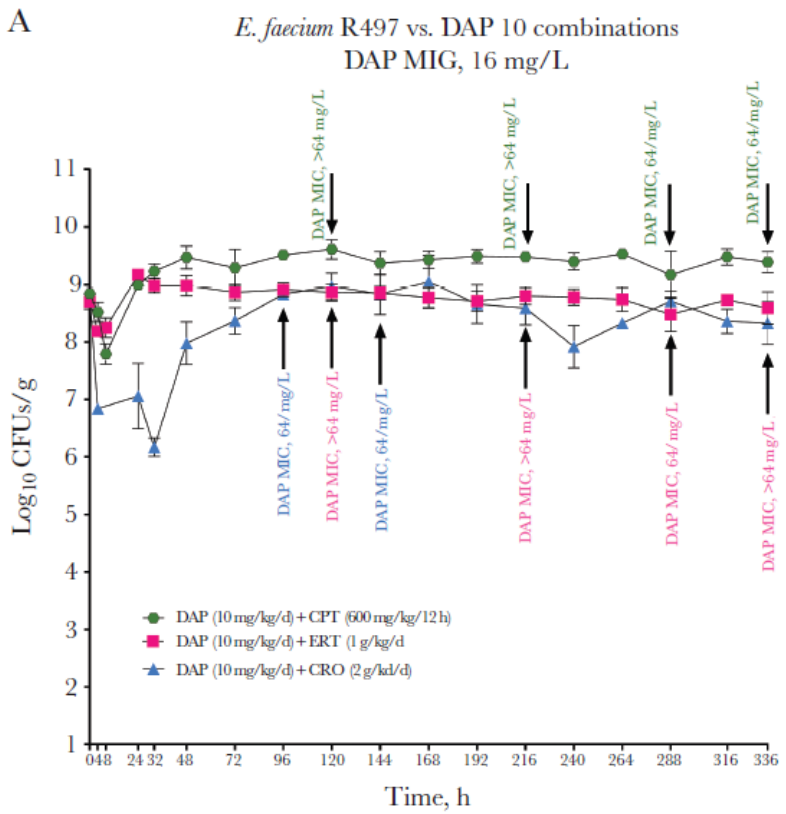
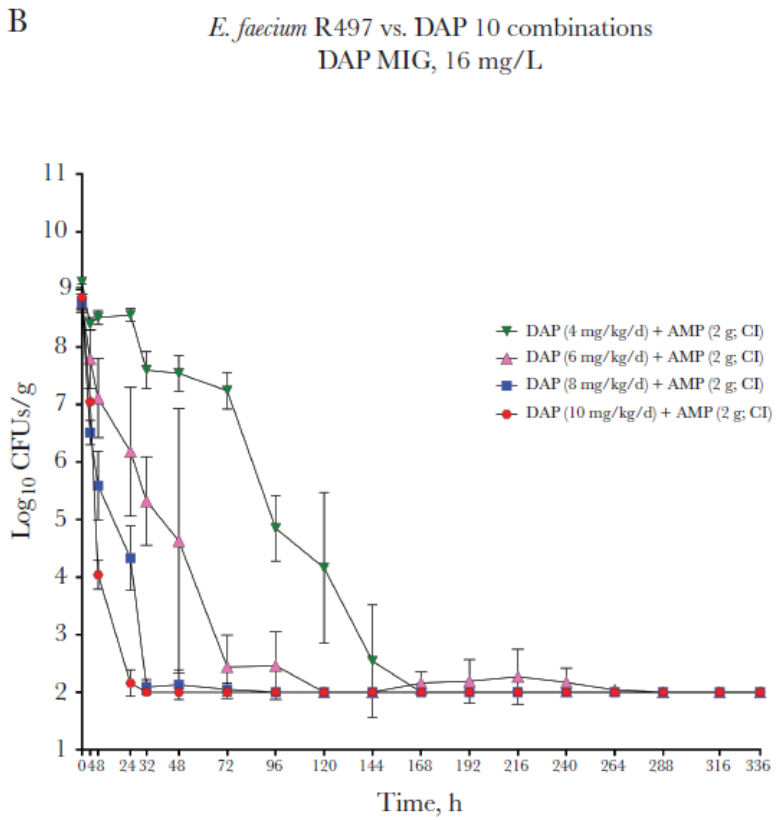
Kebriaei R Antimicrob Agents Chemother. 2018 Aug; 62(8): e00315-18

Mechanistic Insights Into the Differential Efficacy of Daptomycin Plus β-Lactam Combinations Against Daptomycin-Resistant *Enterococcus faecium*





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A Review of Combination Antimicrobial Therapy for *Enterococcus faecalis* Bloodstream Infections and Infective Endocarditis

Beganovic M Clin Infect Dis 2018 Jul 2;67(2):303-309

Synergistic Combination[a]	Study Design	Result	Author (Year)
Human data			
Daptomycin + ampicillin	Patient case report of infective endocarditis	Successful treatment up to follow-up	Sierra-Hoffman et al (2012) [26]
Daptomycin + ceftaroline	Patient case report of infective endocarditis	Successful treatment	Sakoulas et al (2013) [24]
In vitro and in vivo data			
Ampicillin + ceftaroline	Two-compartment simulated endocardial vegetation model	Synergy for dual β-lactam combinations	Werth and Shireman (2017) [23]
Ampicillin + cefepime; ampicillin + ceftaroline	In vitro high-inoculum *Enterococcus faecalis* endocarditis model	Synergy for dual β-lactam combinations	Luther et al (2016) [22]
Ampicillin + ceftaroline	In vitro time-kill experiments	Synergy for dual β-lactam combinations	Werth (2015) [41]
Daptomycin + ceftaroline; daptomycin + ampicillin; daptomycin + ertapenem; daptomycin + ceftriaxone; daptomycin + cefepime	Combination minimum inhibitory concentrations and in vitro time-kill experiments	Synergy demonstrated between daptomycin and β-lactam combinations	Smith et al (2015) [25]
Daptomycin + gentamicin	Stationary-phase in vitro pharmacodynamics model with simulated endocardial vegetation and *Galleria mellonella* survival assays	Synergy demonstrated between daptomycin and gentamicin	Luther et al (2014) [39]
Fosfomycin[b] + rifampin; fosfomycin[b] + tigecycline; fosfomycin[b] + teicoplanin[c]	In vitro time-kill experiments and biofilm assays	Synergy demonstrated between various fosfomycin combinations against planktonic and biofilm-forming bacteria	Tang et al (2013) [33]
Tigecycline + daptomycin; tigecycline + rifampin	In vitro time-kill experiments and in vivo mouse models	Synergy demonstrated with tigecycline combinations of daptomycin and rifampin	Silvestri et al (2012) [40]
Fosfomycin[b] + daptomycin; fosfomycin[b] + gentamicin	In vitro time-kill experiments and foreign-body infection model in guinea pigs	Synergy demonstrated between various fosfomycin combinations against planktonic and biofilm-forming isolates	Oliva et al (2014) [36]
Fosfomycin[b] + ceftriaxone	In vitro assays evaluating fractional inhibitory concentration	Synergy demonstrated with fosfomycin and ceftriaxone	Farina et al (2011) [32]
Ciprofloxacin + rifampin; linezolid + rifampin	In vitro biofilm eradication determined via Calgary Biofilm Device method	Ciprofloxacin and linezolid with rifampin demonstrated antibiofilm activity	Holmberg et al (2012) [38]
Ceftobiprole[c] + gentamicin or streptomycin	In vitro time-kill synergism experiments	Demonstrated synergy between ceftobiprole and aminoglycosides	Arias et al (2007) [37]

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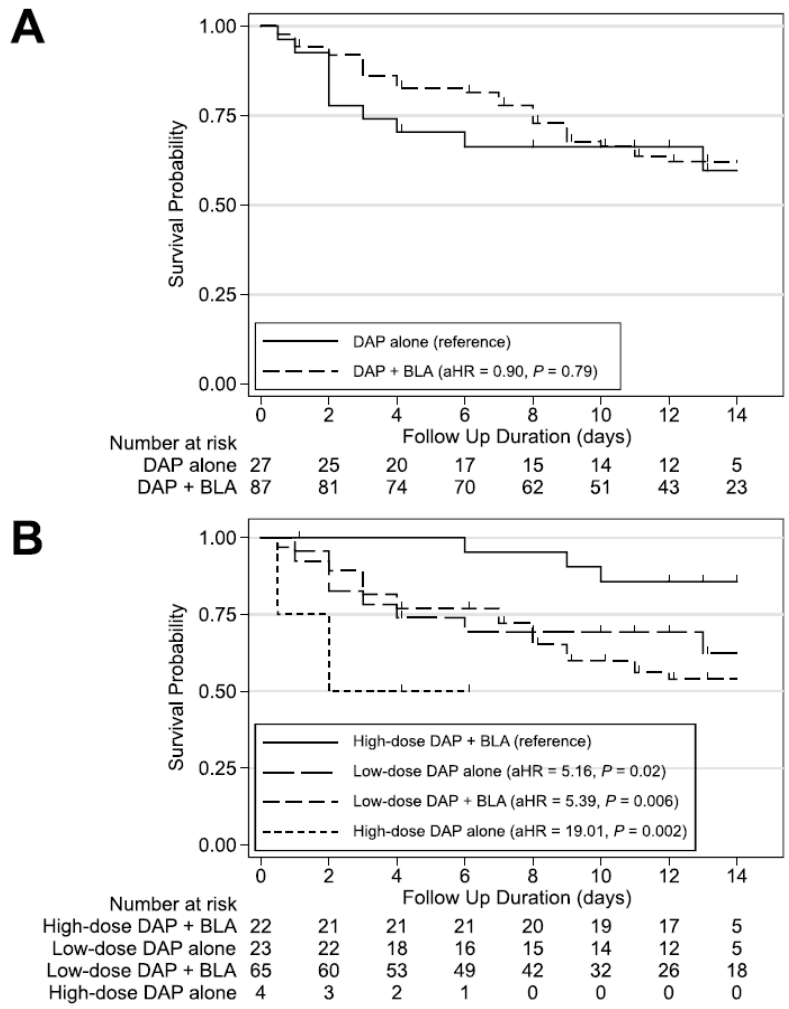
A retrospective clinical comparison of daptomycin vs daptomycin and a beta-lactam antibiotic for treating vancomycin-resistant *Enterococcus faecium* bloodstream infections

Chuang Sci Rep 2018

114 patients who received DAP for VRE-BSI.

87 (76.3%) received DAP + BLA.

In a subgroup analysis of patients with enterococcal DAP MIC ≤2 mg/L,
DAP + BLA had a lower mortality aHR 0.23;
(95% CI, 0.06–0.93; *P* = 0.04)



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The combination of daptomycin with β-lactam antibiotics is more effective than daptomycin alone for vancomycin-resistant Enterococcus faecium bloodstream infection

Chuang YC et al Journal of Infection and Public Health 15 (2022) 1396–1402

- 430 patients were enrolled (DAP, n = 45; DAP+BL, n = 385)
- Combo with carba (65%)

- Clinical success was achieved in 19 (42.2%) patients in tl group and 244 (63.4%) in the DAP+BL group [adjusted od 3.19; 95% confidence interval (CI) 1.61–6.33; *P* = 0.001

Table 3
Multivariable logistic regression analysis of the factors associated with clinical success.

Variables	Adjusted odds ratio	95% confidence interval	*P*
Men	1.70	1.12–2.59	0.01
Charlson comorbidity index	0.91	0.83–0.99	0.03
Platelet count ($\times 10^4/\mu L$)	1.03	1.01–1.04	0.003
Pitt bacteremia score	0.86	0.78–0.95	0.002
Steroid use	0.51	0.31–0.84	0.008
β-lactam combinations	3.19	1.61–6.33	0.001
Daptomycin dose (mg/kg)[a]	1.01	0.84–1.21	0.92

Pearson's goodness-of-fit test, P = 0.32; estimated area under the ROC curve = 0.69.
[a] Daptomycin doses are forced to be selected into the model.

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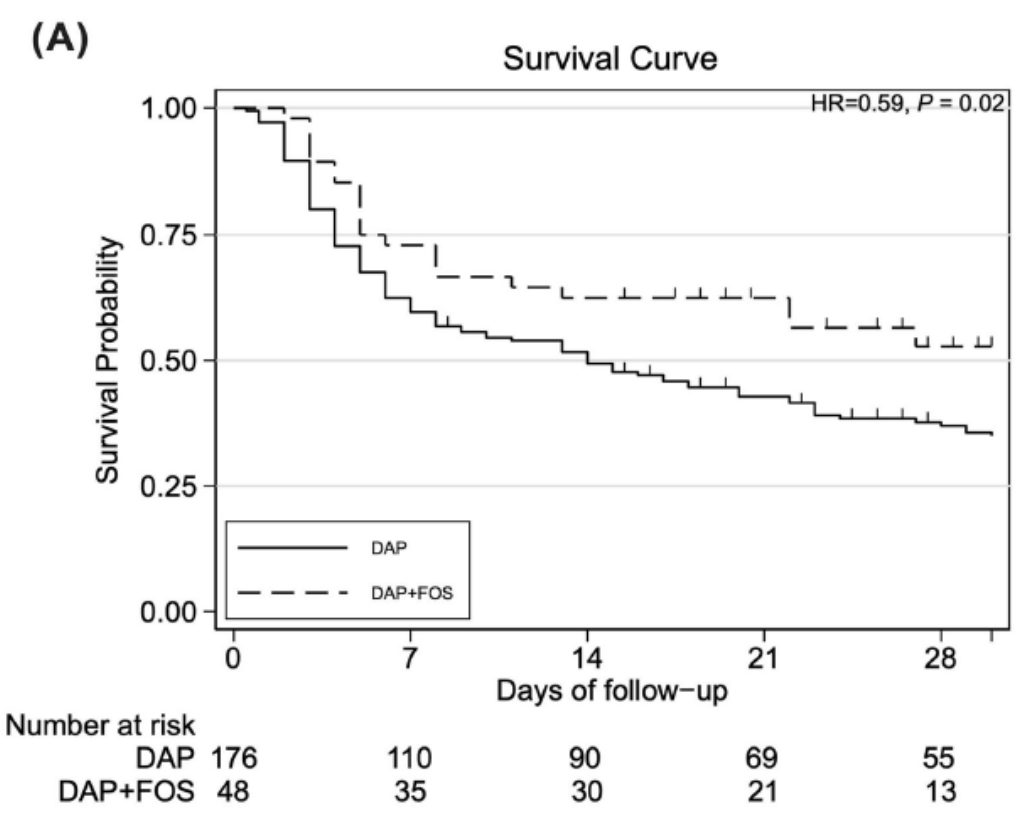
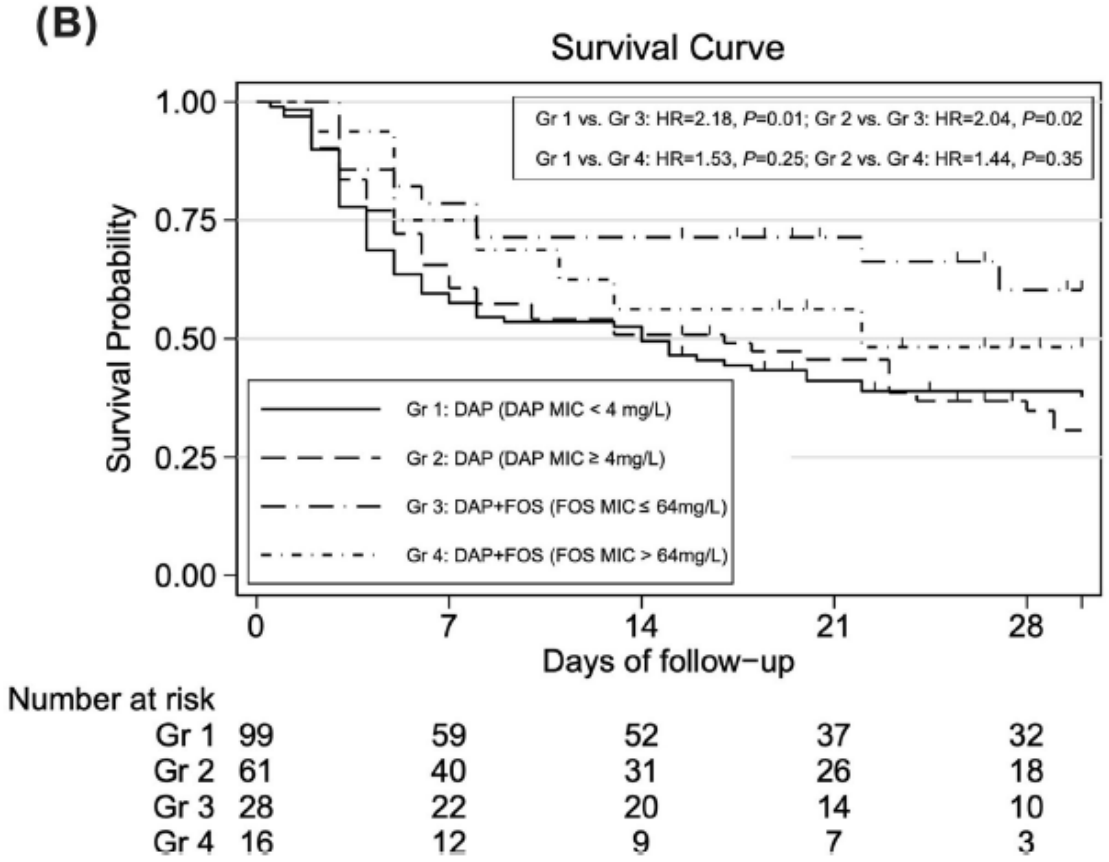
The Combination of Daptomycin with Fosfomycin is More Effective than Daptomycin Alone in Reducing Mortality of Vancomycin-Resistant Enterococcal Bloodstream Infections: A Retrospective, Comparative Cohort Study

Chuang YC et al Journal of Infection and Public Health 15 (2022) 1396–1402





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Clinical characteristics, therapy and outcome of bloodstream infections caused by vancomycin-resistant enterococci: a multicentre clinical experience

Serapide F et al. J Antimicrob Chemother 2025 May 2;80(5):1241-1247.

- 517 VRE BSI
- Most common Tx: linezolid (48.1%) and daptomycin (43.7%).
- 30 day mortality was 32.1%.
- After propensity score adjustment, a daptomycin-based regimen (P = 0.003) was associated with 30 day survival.

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Oritavancin RWE studies and off-label use

Infection source	Cases	Pathogen	Outcome	AE	Note
Endocarditis	14	3 MRSA 3 MSSA, 2 GBS, 1 VRE, 1 E. faecalis, 4 NA	Failure in 2 cases 1 non reprted	Reported in 2 patients	
Device-related infection	15	Mostly NA	Failure not reported	Reported in 1 patient	1 patient received 11 doses for vascular graft infection
BSI	16	5 MRSA 9 MSSA 1 E. faecalis	Failure reported in 5 cases	None	

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Tran Antimicrob Agents Chemother 2022 Jun 21;66(6):e0261420.
Lupia T et al. Life (Basel)- 2023 Apr 6;13(4):959. doi: 10.3390/life13040959.

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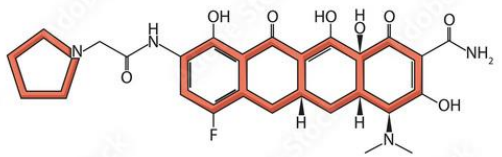
CLINICAL THERAPEUTICS

In Vitro Activity of Eravacycline against Gram-Positive Bacteria Isolated in Clinical Laboratories Worldwide from 2013 to 2017

Ian Morrissey,[a] Stephen Hawser,[a] Sibylle H. Lob,[b] James A. Karlowsky,[c] Matteo Bassetti,[d] Joseph Newman,[f] Corey Fyfe[f]



Eravacycline

TABLE 1 Cumulative percentage of clinical isolates of staphylococci, enterococci, and streptococci tested from 2013 to 2017 inhibited by eravacycline, by MIC

Organism[g]	No. of isolates	Cumulative % of isolates inhibited by the following eravacycline MIC (μg/ml)[a]: ≤0.001	0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2
S. aureus[b]	2,588				0.4	3.8	33.4	84.5	94.8	97.6	99.4	100	
S. aureus, MR[b]	1,304				0.2	4.1	32.8	80.8	91.6	95.5	98.8	100	
S. aureus, MS[b]	1,284				0.5	3.5	34.0	88.3	98.0	99.8	100		
S. epidermidis[b]	1,012				1.4	11.5	28.2	45.7	63.4	84.6	97.1	99.8	100
S. epidermidis, MR[b,c]	480				1.9	10.8	30.8	43.8	66.7	90.4	97.9	99.8	100
S. epidermidis, MS[b,c]	255				2.0	24.3	47.8	59.6	75.7	96.9	99.6	99.6	100
S. haemolyticus[b]	731				1.2	13.5	34.6	45.6	64.8	89.9	96.0	98.8	100
S. haemolyticus, MR[b,c]	440				0.5	11.4	30.9	36.8	60.2	90.0	95.2	98.0	100
S. haemolyticus, MS[b,c]	134				5.2	35.8	76.9	85.8	94.8	97.8	99.3	100	
E. faecalis	1,586				0.2	2.6	28.9	94.5	99.4	99.7	100		
E. faecalis, VR[d]	59						23.7	89.8	98.3	100			
E. faecalis, VS	1,505				0.2	2.7	29.4	94.8	99.5	99.7	100		
E. faecium	1,221				0.6	4.3	60.2	95.0	97.7	99.1	99.8	100	
E. faecium, VR[d]	510				0.6	3.7	54.9	93.1	96.1	98.0	99.6	100	
E. faecium, VS	702				0.6	4.6	63.8	96.3	98.9	99.9	100		
S. pneumoniae[e]	596	0.8	2.0	14.8	73.0	97.8	100						
S. agalactiae	1,239				0.7	13.4	70.5	98.0	99.8	100			
S. pyogenes	1,192			0.2	3.6	47.8	96.0	100					
S. anginosus group[f]	346	5.2	5.5	8.7	19.9	46.5	86.4	99.1	100				

[a]The MIC_{90} is shaded gray.
[b]For staphylococci, the lowest dilution of eravacycline tested was 0.008 μg/ml.
[c]Defined using oxacillin MICs, which were available only for 2015 to 2017.
[d]Defined using CLSI breakpoint criteria.
[e]Collected only in 2013 to 2014 and 2017.
[f]The *S. anginosus* group (n = 346) includes *S. anginosus* (n = 302), *S. constellatus* (n = 36), *S. intermedius* (n = 7), and *S. intermedius*/*S. milleri* (n = 1).
[g]MR, methicillin resistant; MS, methicillin susceptible; VR, vancomycin resistant; VS, vancomycin susceptible.

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IRCCS Humanitas Rozzano
Use of eravacycline: IAI

Type of IAI

- Post surgical peritonitis 5/9 (55%)
- Intrabdominal collection 3/9 (33%)

Clinical conditions

Sepsis 33%, Septic Shock 11%

Pathogens: E.coli 2/9, Enterococcus spp 5/9 (all VRE) Klebsiella 1/9, Enterobacter 1/9 Klebsiella oxytoca 1/9 Polymicrobial 4/9

Use of eravacycline:

30-day mortality 1/9 (11%)
90-day mortality 2/9 (22%)
Relapse 1/9 (11%)

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