Cas clinique

M. P, 83 ans, résidant en EHPAD est admis au SAU pour douleurs hypogastriques fébriles (T : 38,9°C).

Antécédents :
- Troubles cognitifs, GIR=2
- TAVI posé en 2019 pour RAC serré, FEVG=49%. FA sous AOD
- Epilepsie traitée, équilibrée (exogénose sevrée)
- Insuffisance rénale chronique (CKD-EPI : 32 mL/min)

Au SAU :
TDR grippe/COVID/VRS négatifs
Globe vésicale : sondé. BU leuco +++/nitrites-
CRP : 159 mg/L, hémocultures : 1 paire prélevée

Le patient est traité par ceftriaxone 1g/24h IV, et est hospitalisé en médecine.

A H48 : apyrexie, ECBU stérile. Le patiente souhaite rentrer dans son EHPAD.
Que proposez-vous ?

Cas clinique

A H48 : apyrexie, ECBU stérile. Le patiente souhaite rentrer dans son EHPAD.
Que proposez-vous ?

A. Poursuite ceftriaxone 1g/24h IV en EHPAD pendant 7 jours

B. Poursuite ceftriaxone 1g/24h IV en EHPAD pendant 14 jours

C. Relai ceftriaxone 1g/24h SC en EHPAD pour 14 jours au total

D. Relai levofloxacine per os pour 14 jours au total

E. Relai cotrimoxazole per os pour 14 jours au total

F. Arrêt de l'antibiothérapie

Cas clinique

Le service qui le prend en charge décide de poursuivre l'antibiothérapie 14 jours en IV en EHPAD.
A J12, le patient présente à niveau de la fièvre.
Il est toujours sondé, l'ECBU est stérile
Veinite au point de perfusion (depuis son retour en EHPAD selon IDE)
2 paires d'hémocultures reviennent positives à CG+ amas
Un traitement par daptomycine est initié.
L'identification retrouve un SARM (CMI dapto = 0,25 mg/L).

Réalisez-vous une ETT ?

A. Oui, dès que possible

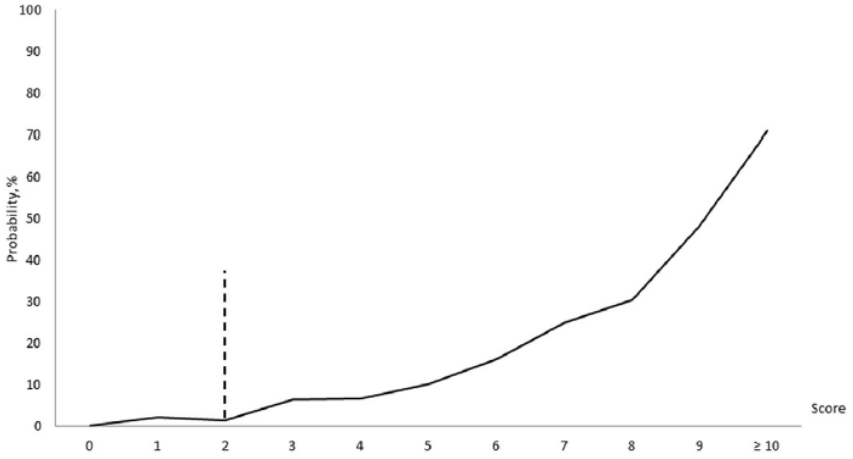
B. Oui, plutôt à J7 de la bactériémie

C. Non, sauf si les hémocultures restent positivent après 48h

D. Non car l'infection sur dispositif intravasculaire nosocomiale est faiblement associée au risque d'EI

E. Non, car une ETT normale sur TAVI n'éliminera pas une EI

Bactériémie à *S. aureus* : bilan minimum



	Weight
Cerebral or peripheral emboli	5
Meningitis	5
Permanent intracardiac device or previous IE	4
Pre-existing native valve disease	3
Intravenous drug use	4
Persistent bacteremia	3
Vertebral osteomyelitis	2
Community or non nosocomial health care associated acquisition	2
Severe sepsis or shock >48h	1
C-reactive protein >190 mg/L	1

Table 4 Performance score for IE in 2008 patients with *Staphylococcus aureus* bacteremia, VIRSTA Study.

VIRSTA score	Sensitivity (CI 95%)	Specificity (CI 95%)	Positive predictive value (CI 95%)	Negative predictive value (CI 95%)
0 versus ≥1	99.3 (99.2; 99.3)	18.5 (17.3; 19.6)	13.1 (12.1; 14.2)	99.5 (99.5; 99.6)
≤1 versus ≥2	97.2 (96.1; 98.7)	32.2 (30.8; 33.5)	15.1 (13.9; 16.2)	98.9 (98.4; 99.5)
≤2 versus ≥3	95.8 (94.3; 97.8)	44.2 (42.6; 45.6)	17.6 (16.2; 18.9)	98.8 (98.4; 99.4)

Tubiana *et al.*, Journal of Infection 2016

Le patient est resté subfébrile pendant 4 jours
L'ETT est réalisée à J7 et montre une végétation de 5 mm sur la valve aortique, sans fuite sévère
Les hémocultures n'ont pas été contrôlées
RCP endocardite : traitement médical

Quel traitement médicale proposez-vous ?

A. Poursuite daptomycine seule

B. Daptomycine + rifampicine

C. Daptomycine + gentamicine

D. Daptomycine + rifampicine + gentamicine

E. Daptomycine + vancomycine

ESC 2023 :

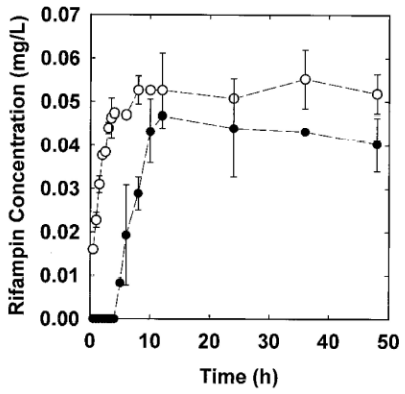
IE caused by methicillin-resistant staphylococci			
In patients with NVE due to methicillin-resistant staphylococci, vancomycin is recommended for 4–6 weeks using the following doses:		I	B
Adult antibiotic dosage and route			
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses		
Paediatric antibiotic dosage and route			
Vancomycin	30 mg/kg/day i.v. in 2–3 equally divided doses		
In patients with PVE due to methicillin-resistant staphylococci, vancomycin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:		I	B
Adult antibiotic dosage and route			
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses		
Rifampin	900–1200 mg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
Paediatric antibiotic dosage and route			
Vancomycin	30 mg/kg/day i.v. in 2–3 equally divided doses		
Rifampin	20 mg/kg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

Rifampicine : activité anti-biofilm

TABLE 5. Number of staphylococcus isolates susceptible to single antibiotics

Drug[a]	*S. epidermidis* (*n* = 17)				MSSA (*n* = 11)				MRSA (*n* = 12)			
	Planktonic		Biofilm		Planktonic		Biofilm		Planktonic		Biofilm	
	Inhibit	Kill	Inhibit	Kill	Inhibit	Kill	Inhibit	Kill	Inhibit	Kill	Inhibit	Kill
LZD	17	0	0	0	11	0	0	0	12	0	1	0
RIF	16	8	1	8	11	3	1	2	10	0	3	5
CFZ	9	1	0	0	11	3	3	0	1	0	0	0
OXA	0	0	0	0	11	2	1	0	0	0	0	0
VAN	17	7	2	0	11	1	2	0	12	1	4	0
GEN	5	4	0	0	4	2	0	0	4	1	0	0
AZM	4	0	0	0	8	0	0	0	1	0	0	0
CIP	0	0	0	0	7	4	1	0	2	1	0	0
FA	14	0	1	1	11	1	0	0	9	0	3	1

Saginur *et al*. AAC 2005



○ Sans biofilm
• Avec biofilm

Zheng *et al*. AAC 2002

TABLE 2. Eradication of adherent bacteria of two isogenic strains of *S. epidermidis* in an in vitro and in an in vivo model

Drug	No. of sterile beads/total no. of beads studied			
	In vitro model		In vivo model	
	RP62A	M7	RP62A	M7
Amikacin	0/25	0/25	0/24	6/24[a]
Levofloxacin	9/25	21/25[a]	1/24	8/24[a]
Rifampin	22/25	25/25	8/24	18/24[a]
Teicoplanin	0/25	0/25	0/24	5/24[a]

[a] The statistical significance of the eradication rate between the two strains was determined, and the difference was significant ($P < 0.05$).

Schwank *et al*. AAC 1994

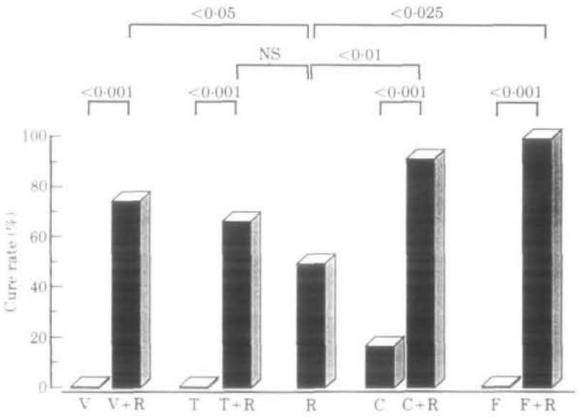


Table II. Minimum bactericidal concentration (MBC) of *S. aureus* ATCC 29213 in different growth phases

Antibiotic	Phases of bacterial growth logarithmic[a] (mg/L)	stationary[b] (mg/L)	Fold increase
Vancomycin	3·4	263	77·4
Teicoplanin	1·9	94	49·5
Ciprofloxacin	0·75	125	167
Fleroxacin	5·0	333	66·6
Rifampicin	0·44	3·4	7·7

[a]Incubation in Mueller-Hinton broth.
[b]Incubation in phosphate buffered saline supplemented with 1% glucose and 4% Mueller-Hinton broth.

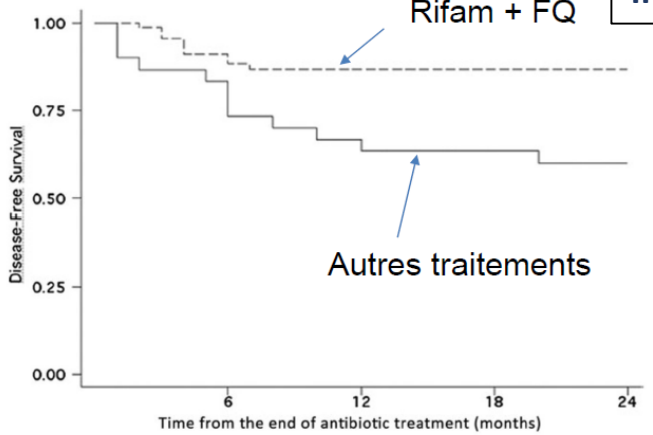
Zimmerli *et al*. JAC 1994

Rifampicine : activité anti-biofilm

OUI

Rétrospectif

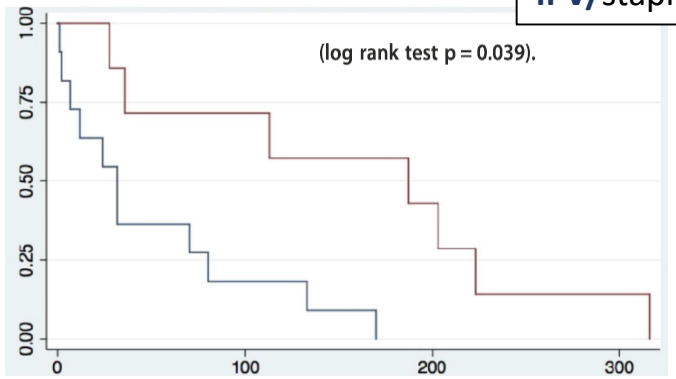
IPJ/SA



Senneville *et al.* CID 2011

Prospectif, non interventionnel

IPV/staph spp.

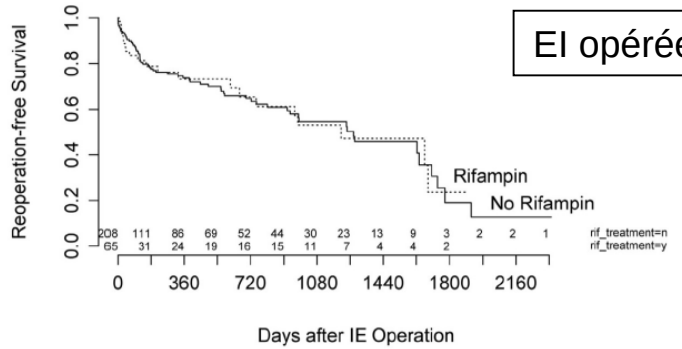


Legout *et al.* 2014

Rétrospectif, score de propension

NON

EI opérée



EI/staph spp.

Shrestha *et al.* 2014

Rétrospectif

PVEI opérée

Table 2. Outcomes of 180 episodes of staphylococcal prosthetic valve endocarditis treated with, or without, rifampin

Variable	Total (n=180)	Rifampin-based combination (n=101)	No rifampin (n=79)	Odd-Ratio (CI 95%)	*P* Value
Mortality					
In-hospital mortality	42 (23.6)	26 (25.7)	16 (20.3)	1.4 (0.67-2.77)	.49
Six-month mortality	58 (32.6)	36 (35.6)	22 (27.8)	1.4 (0.76-2.72)	.34
One-year mortality	63 (35.4)	38 (37.6)	25 (31.6)	1.2 (0.66-2.28)	.62
Relapse	13 (7.3)	6 (5.9)	7 (8.9)	0.64 (0.21-2.02)	.65
Vitamin K antagonist imbalance during endocarditis	21 (33.9)	15 (42.9)	6 (22.2)	2.63 (0.85-8.11)	.15
Bleeding complication	23 (12.9)	13 (12.8)	10 (12.7)	1.02 (0.42-2.46)	.85
Length of stay, days	37 ± 17.6	42.3 ± 18.6	31.3 ± 14.0	-	<.0001

Le Bot *et al.* 2020

Le patient est traité par daptomycine monothérapie.

Les hémocultures sont recontrôlées, et reviennent toujours positives au même germe…

Que proposez-vous ?

A. Relai par vancomycine

B. Refaire une CMI daptomycine

C. Daptomycine + ceftaroline

D. Daptomycine + rifampicine

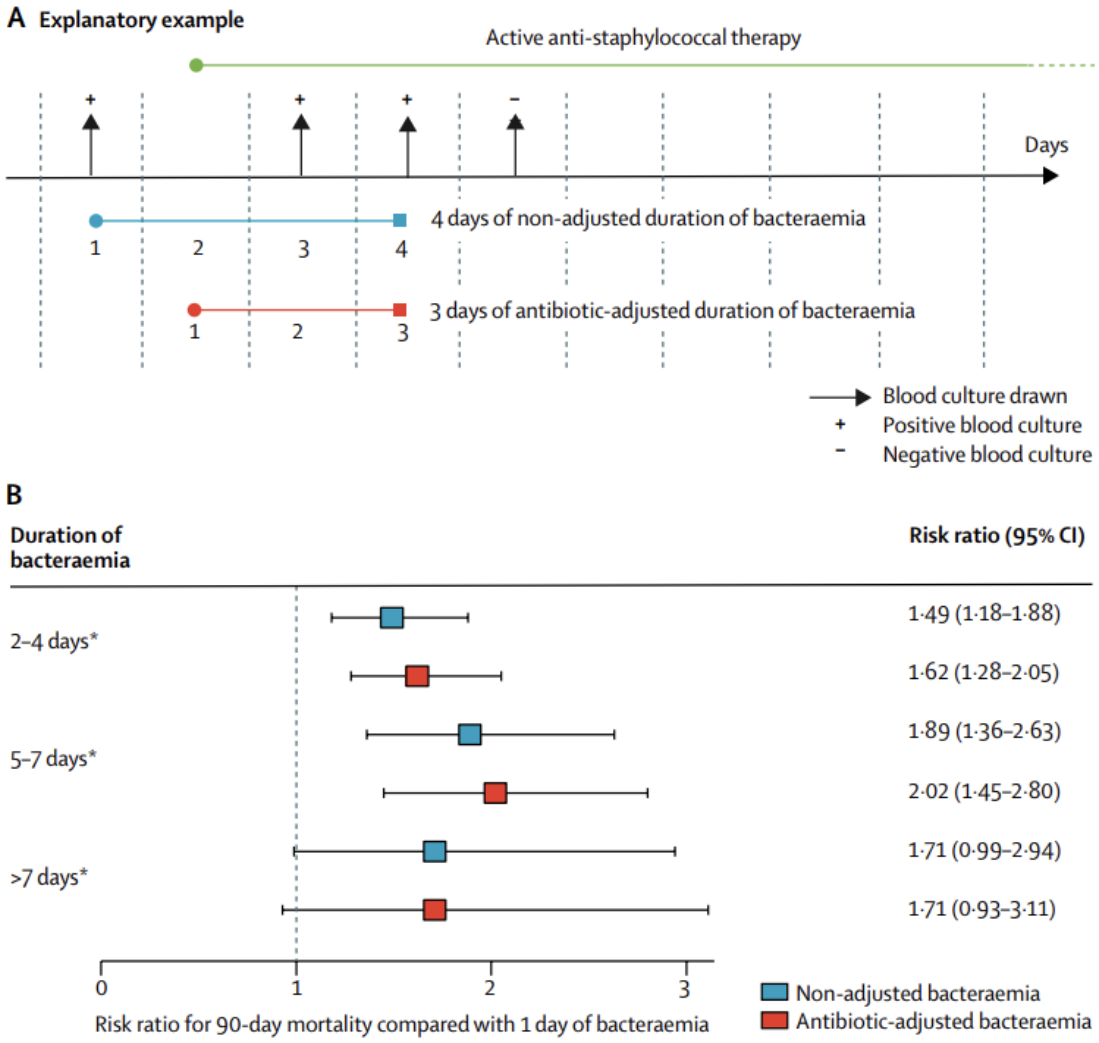
E. Refaire une ETT

F. Faire un TDM TAP IV+

G. Faire un pet-TDM

Critères pronostics de la bactériémie : durée sous ATB

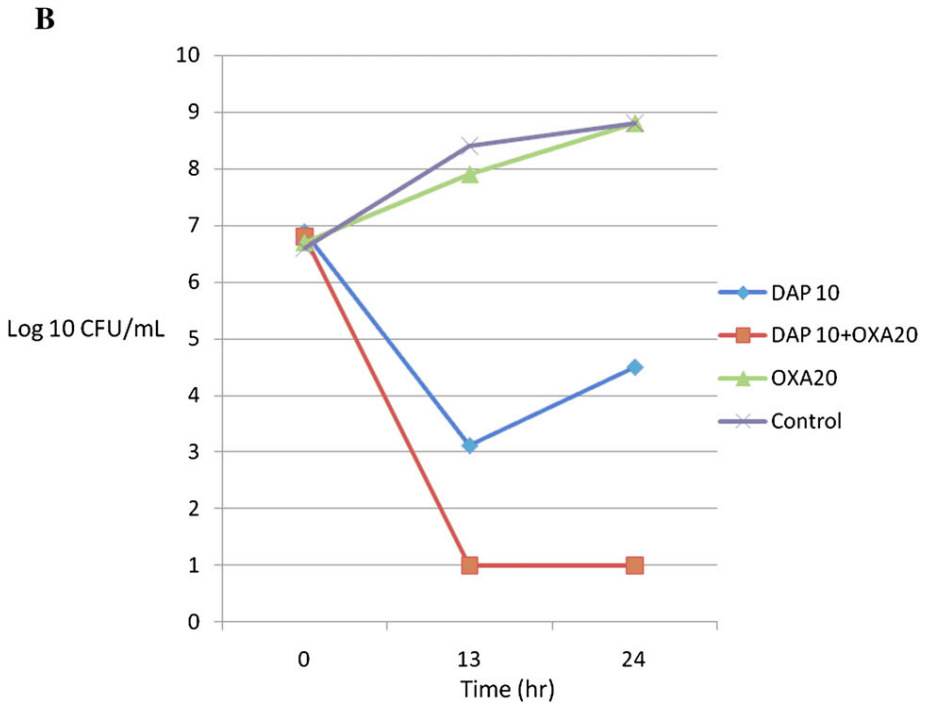
❑ Bactériémie >24h sous ATB adaptée : excès de mortalité.

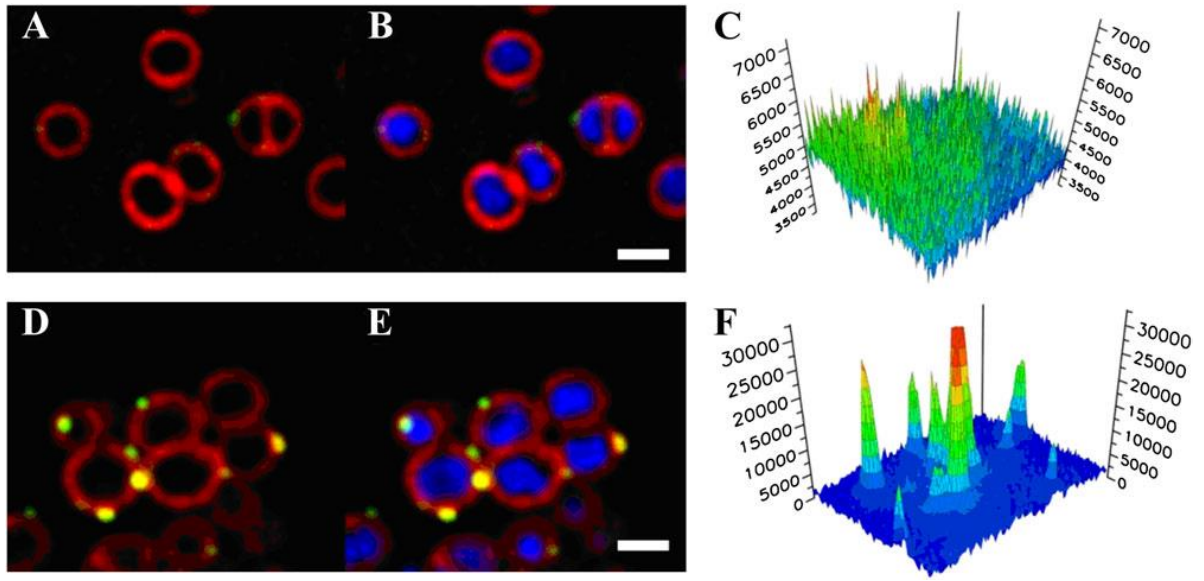


Hc+>/=J2 : surmortalité

Khuel *et al.* 2021

Daptomycine + BL : des promesses





MRSA strain
DPT non susceptible

Dhand *et al*. CID 2011

Daptomycine + BL : des promesses

	Overall (N = 229)	Daptomycin Monotherapy (n = 157)	Daptomycin Plus β-Lactam (n = 72)	*P*
Median (IQR) time to negative blood culture from index culture,[a] hours	113 (73, 168)	116 (80, 181)	106 (63, 156)	.498
Persistent bacteremia (positive blood cultures ≥7 days after blood culture collection),[a] n (%)	55 (27.9)	41 (27.5)	14 (19.4)	.193
Median (IQR) time to negative blood culture after starting daptomycin,[b] hours	64 (31, 125)	66 (35, 136)	56 (23, 102)	.639
Positive blood cultures ≥5 days after starting daptomycin,[b] n (%)	50 (27.5)	38 (31.7)	12 (19.4)	.078
Median (IQR) length of inpatient admission, days	15 (11, 24)	14 (11, 21)	16 (12, 28)	.228
Composite clinical failure, n (%)				
60-day mortality and/or 60-day recurrence	52 (22.7)	43 (27.4)	9 (12.5)	.013
60-day mortality	31 (13.5)	24 (15.3)	7 (9.7)	.253
30-day mortality	23 (10.0)	18 (11.5)	5 (6.9)	.351
60-day recurrence	27 (11.8)	23 (14.6)	4 (5.6)	.50
30-day recurrence	12 (5.2)	11 (7.0)	1 (1.4)	.110
Median (IQR) time to recurrence,[c] days	42 (13, 54)	42 (9, 55)	42 (18, 53)	1.00
Acute kidney injury,[d] n (%)	10 (5.9)	3 (2.9)[e]	7 (10.8)[f]	.046
Clostridium difficile–associated diarrhea, n (%)	6 (2.6)	2 (1.3)	4 (5.6)	.080
Creatinine phosphokinase elevation, n (%)	10 (4.4)	7 (4.5)	3 (4.2)	1.00

Rétrospectif

Bactériémie : DPT (2nd agent) +/- BL (>40% empirique)

Céphalosporine : FEP >40%, ceftaroline < 10%

Jorgensen *et al.* CID 2020

Daptomycine + BL : non confirmé sur méta-analyse

Adjuvant β-Lactam Therapy Combined with Vancomycin or Daptomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia: a Systematic Review and Meta-analysis

Chunjiang Wang,[a] Chao Ye,[b] Linglong Liao,[c] Zhaohui Wang,[b] Ying Hu,[b] Chao Deng,[d] Liang Liu[e]

Three randomized controlled trials and 12 retrospective cohort studies were identified, totaling 2,594 patients. Combination treatment significantly reduced the risk of clinical failure (risk ratio [RR] = 0.80; 95% confidence interval [CI], 0.66 to 0.96; $P = 0.02$; $I^2 = 39\%$), bacteremia recurrence (RR = 0.66; 95% CI, 0.50 to 0.86; $P = 0.002$; $I^2 = 0\%$), and persistent bacteremia (RR = 0.65; 95% CI, 0.55 to 0.76; $P < 0.00001$; $I^2 = 0\%$) and shortened the duration of bacteremia (standardized mean difference [SMD] = −0.37; 95% CI, −0.48 to −0.25; $P < 0.00001$; $I^2 = 0\%$). There was no significant difference in the risk of crude mortality, nephrotoxicity, or thrombocytopenia between groups

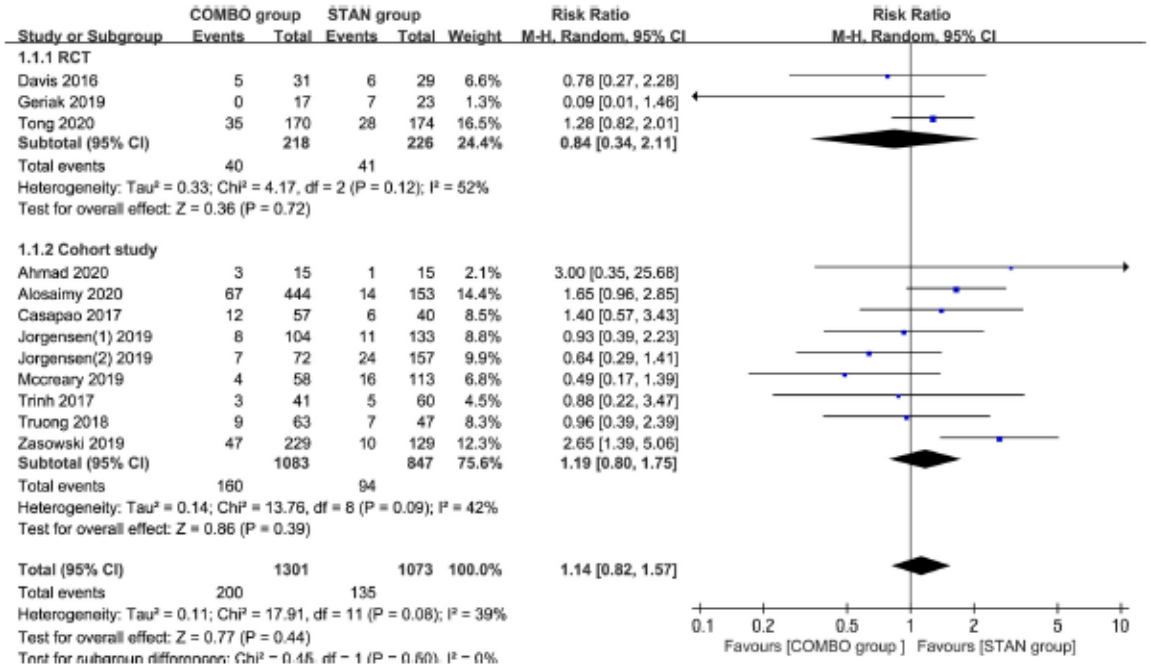


FIG 2 Forest plot of the risk ratio (RR) for crude mortality in patients with MRSA bacteremia.

Wang *et al. AAC* 2020

Daptomycine + ceftaroline : séduisant *in vitro*

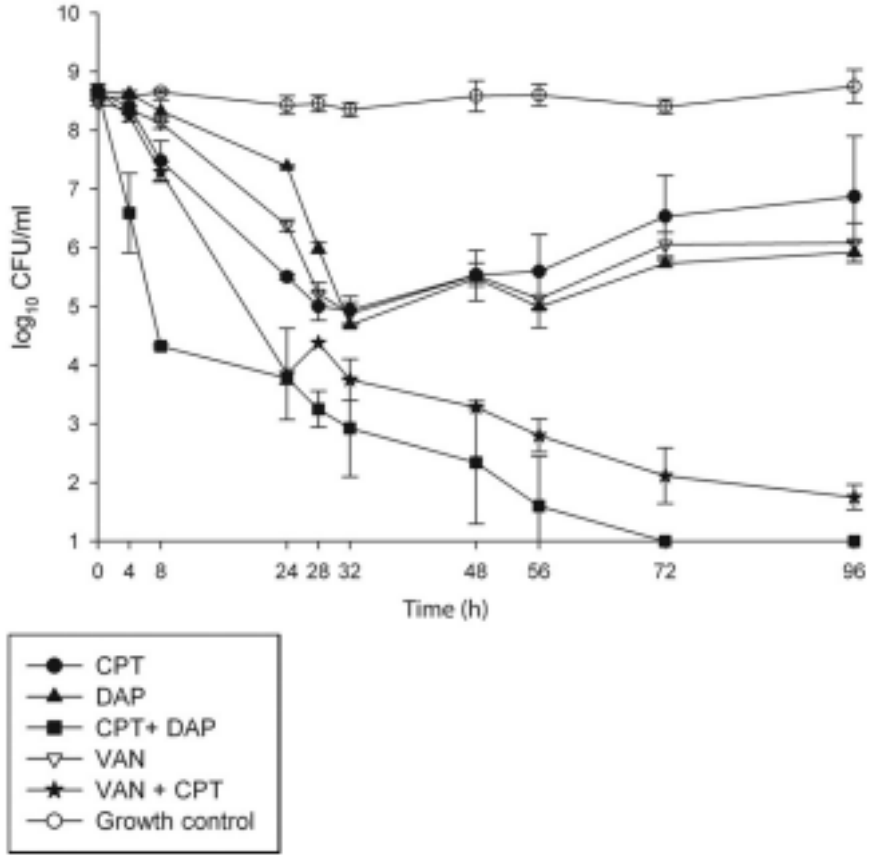
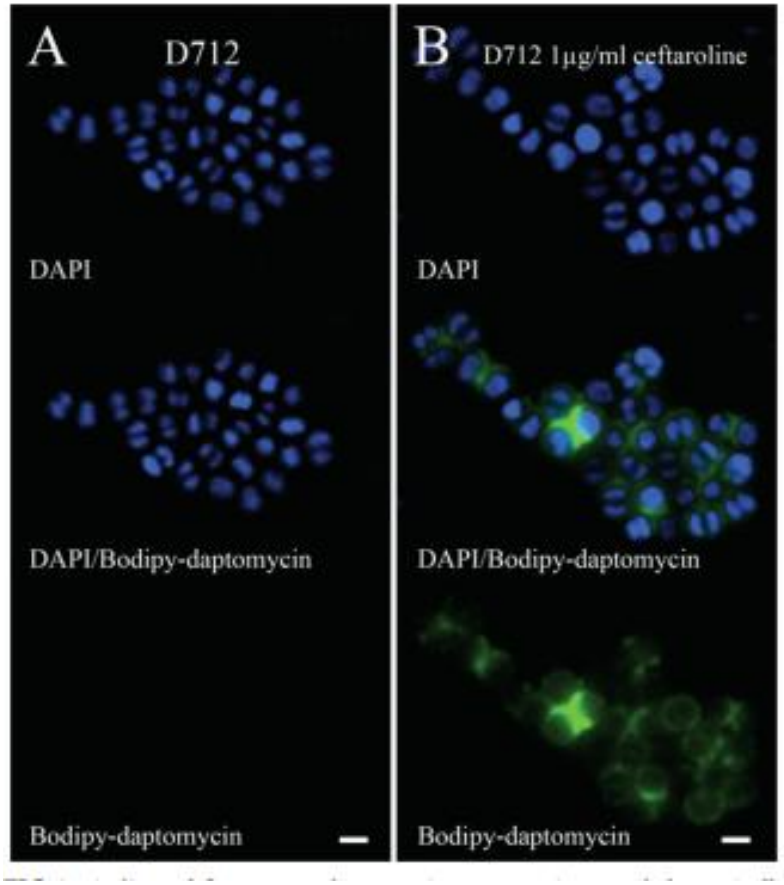


FIG 1 Activity of CPT, DAP, and VAN alone and in combination against D712 (A) and D592 (B). The error bars indicate SD.



Werth *et al.* AAC 2011

Daptomycine + ceftaroline : en traitement de sauvetage

Combination ceftaroline and daptomycin salvage therapy for complicated methicillin-resistant *Staphylococcus aureus* bacteraemia compared with standard of care ☆

Tanner M. Johnson [a,b], Kyle C. Molina [a,b], Matthew A. Miller [a,b], Tyree H. Kiser [a,b], Misha Huang [c,d], Scott W. Mueller [a,b,*]

[a] *Department of Pharmacy, University of Colorado Hospital, Aurora, CO, USA*
[b] *Department of Clinical Pharmacy, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO, USA*
[c] *Department of Medicine–Infectious Diseases, University of Colorado Hospital, Aurora, CO, USA*
[d] *Division of Infectious Diseases, University of Colorado School of Medicine, Aurora, CO, USA*

Table 3
Effectiveness outcomes.

Outcome	SoC (control) (n = 30)	DAP+CPT (n =30)	P-Value
Clinical failure	13 (43)	6 (20)	0.052
MRSA-related death within 60 days	4 (13)	6 (20)	0.49
Recurrence within 60 days	9 (30)	0	<0.01
All-cause death within 90 days	7 (23)	8 (27)	0.77
Total duration of bacteraemia (days)	5 (4–8)	9 (7–11)	0.01
Time to blood culture clearance on final antibiotic regimen (days)	5 (3–6)	4 (2–5)	0.08
Time to defervescence (h)	102 (27–350)	121 (48–221)	0.93
Time to WBC normalisation (days)	6 (4–18)	13 (10–16)	0.14
60-day hospital-free days	37 (0–46)	34 (2–38)	0.37

SoC, standard of care; DAP, daptomycin; CPT, ceftaroline; MRSA, methicillin-resistant *Staphylococcus aureus*; WBC, white blood cell.
NOTE: All values are presented as n (%) or median (interquartile range). Percentages are of patients for whom data were available.

Rétrospectif monocentrique …

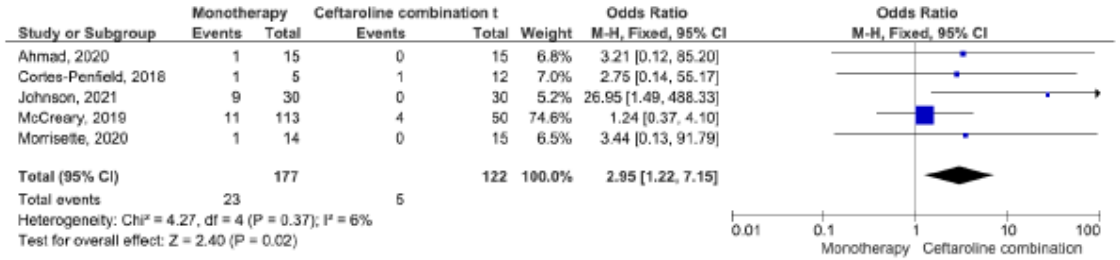
Johnson et *et al.* IJAA 2021

Daptomycine + ceftaroline : efficacité non confirmée en méta-analyse

Comparing the Outcomes of Ceftaroline plus Vancomycin or Daptomycin Combination Therapy versus Vancomycin or Daptomycin Monotherapy in Adults with Methicillin-Resistant *Staphylococcus aureus* Bacteremia—A Meta-Analysis

Chienhsiu Huang [1,*], Ihung Chen [1] and Lichen Lin [2]

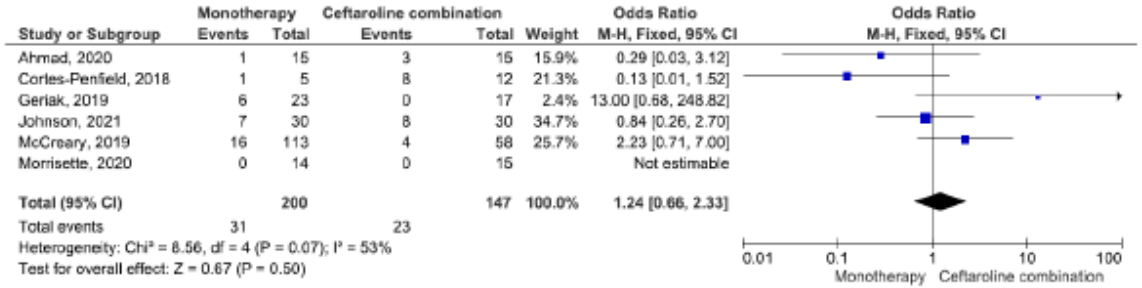
Récurrence



Study or Subgroup	Monotherapy Events	Monotherapy Total	Ceftaroline combination t Events	Ceftaroline combination t Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ahmad, 2020	1	15	0	15	6.8%	3.21 [0.12, 85.20]
Cortes-Penfield, 2018	1	5	1	12	7.0%	2.75 [0.14, 55.17]
Johnson, 2021	9	30	0	30	5.2%	26.95 [1.49, 488.33]
McCreary, 2019	11	113	4	50	74.6%	1.24 [0.37, 4.10]
Morrisette, 2020	1	14	0	15	6.5%	3.44 [0.13, 91.79]
Total (95% CI)		**177**		**122**	**100.0%**	**2.95 [1.22, 7.15]**
Total events	23		5			

Heterogeneity: Chi² = 4.27, df = 4 (P = 0.37); I² = 6%
Test for overall effect: Z = 2.40 (P = 0.02)

Mortalité



Study or Subgroup	Monotherapy Events	Monotherapy Total	Ceftaroline combination Events	Ceftaroline combination Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ahmad, 2020	1	15	3	15	15.9%	0.29 [0.03, 3.12]
Cortes-Penfield, 2018	1	5	8	12	21.3%	0.13 [0.01, 1.52]
Geriak, 2019	6	23	0	17	2.4%	13.00 [0.58, 248.82]
Johnson, 2021	7	30	8	30	34.7%	0.84 [0.26, 2.70]
McCreary, 2019	16	113	4	58	25.7%	2.23 [0.71, 7.00]
Morrisette, 2020	0	14	0	15		Not estimable
Total (95% CI)		**200**		**147**	**100.0%**	**1.24 [0.66, 2.33]**
Total events	31		23			

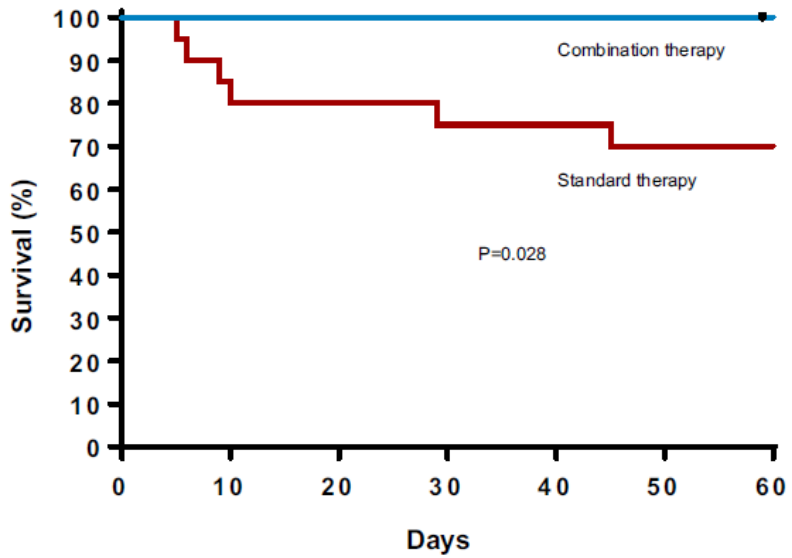
Heterogeneity: Chi² = 8.56, df = 4 (P = 0.07); I² = 53%
Test for overall effect: Z = 0.67 (P = 0.50)

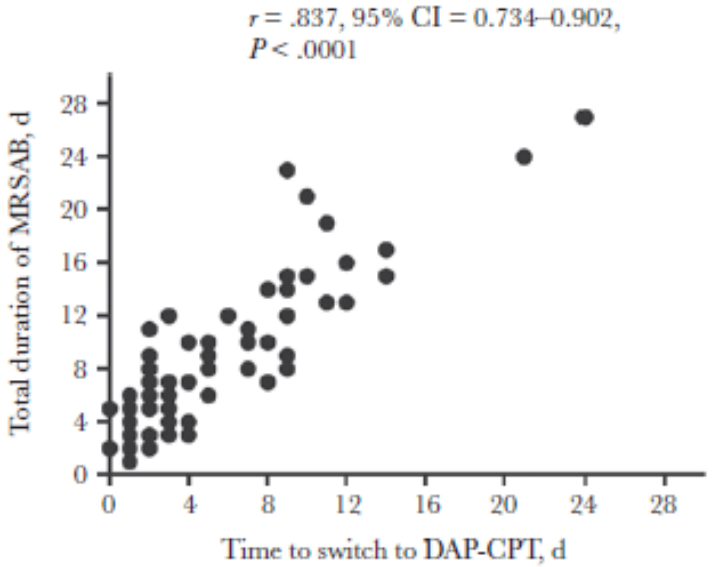
Huang et *et al.* Antibiotics 2022

Daptomycine + ceftaroline : arrêt précoce pour efficacité …

Multicenter Cohort of Patients With Methicillin-Resistant *Staphylococcus aureus* Bacteremia Receiving Daptomycin Plus Ceftaroline Compared With Other MRSA Treatments

ıycin plus Ceftaroline in MRSA Bacteremia





Prospectif
Bithérapie précoce (<72h)

Geriak *et al.* 2019 AAC

Mc Creary *et al.* 2020

Daptomycine + ceftaroline : en résumé

Pas de bénéfice évident sur mortalité
→Intérêt études bien menées sur introduction précoce (<72h)

Bénéfice sur durée bactériémie/récurrence
→ Dans l'attente du source control

Cas clinique

L'antibiothérapie est adaptée par daptomycine + ceftaroline.
Les CMI sont à 0,25 et 0,125 respectivement. Les hémocultures sont stérilisées. L'ETT est stable
Le pet-TDM retrouve un aspect de spondylodiscite T12-L1 avec un volumineux abcès du psoas gauche (11x7x5cm)
Le patient est récusé d'un drainage radiologique devant les comorbidités et l'amélioration clinique.
Décision de maintien de l'antibiothérapie 6 semaines
Le patient présente une dégradation subaiguë de son état respiratoire à J22 d'antibiothérapie efficace
PCR grippe/COVID/VRS négative
Auscultation : quelques crépitants
Radiologie : infiltrat mal systématisé, bilatéraux

Quel diagnostic évoquez-vous ?

A. Un embole septique

B. Une EP avec infarctus pulmonaire

C. Une surinfection

D. Une pneumonie d'inhalation

E. Une cause médicamenteuse

antibiotics

MDPI

Communication

Risk Factors of Daptomycin-Induced Eosinophilic Pneumonia in a Population with Osteoarticular Infection

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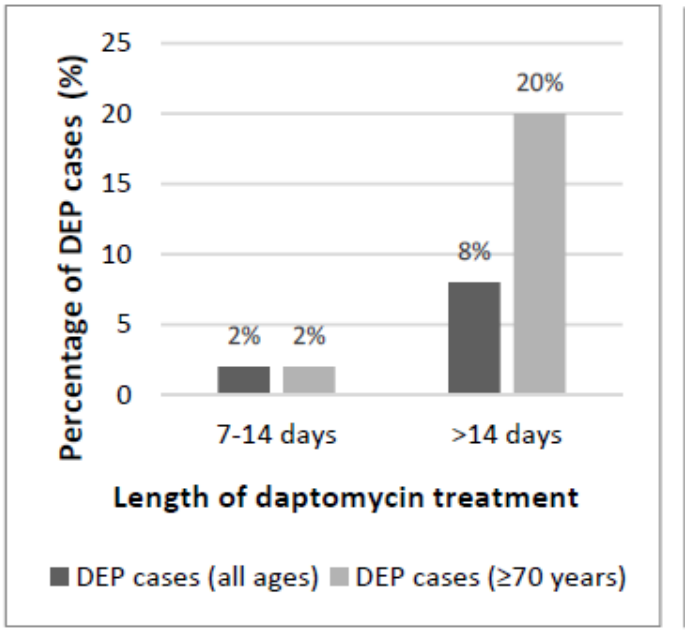

Abstract: Background: Daptomycin-induced eosinophilic pneumonia (DEP) is a rare but severe adverse effect and the risk factors are unknown. The aim of this study was to determine risk factors for DEP. Methods: A retrospective cohort study was performed at the Bone and Joint Infection Unit of the Hospital Universitari Bellvitge (January 2014–December 2018). To identify risk factors for DEP, cases were divided into two groups: those who developed DEP and those without DEP. Results: Among the whole cohort (n = 229) we identified 11 DEP cases (4.8%) and this percentage almost doubled in the subgroup of patients ≥70 years (8.1%). The risk factors for DEP were age ≥70 years (HR 10.19, 95%CI 1.28–80.93), therapy >14 days (7.71, 1.98–30.09) and total cumulative dose of daptomycin ≥10 g (5.30, 1.14–24.66). Conclusions: Clinicians should monitor cumulative daptomycin dosage to minimize DEP risk, and be cautious particularly in older patients when the total dose of daptomycin exceeds 10 g.