Points importants du traitement médical d'une endocardite infectieuse

Cours de DES national - Mercredi 25 mars 2026

Dr Raphaël LECOMTE

Maladies Infectieuses et Tropicales

CHU de Nantes

Quelles recommandations?

AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Baddour *et al.* Circulation 2015

ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–95
https://doi.org/10.1093/eurheartj/ehad193

ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

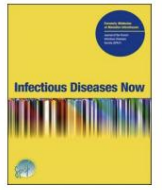
Delgado *et al.* Eur Heart J 2023

ELSEVIER

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now



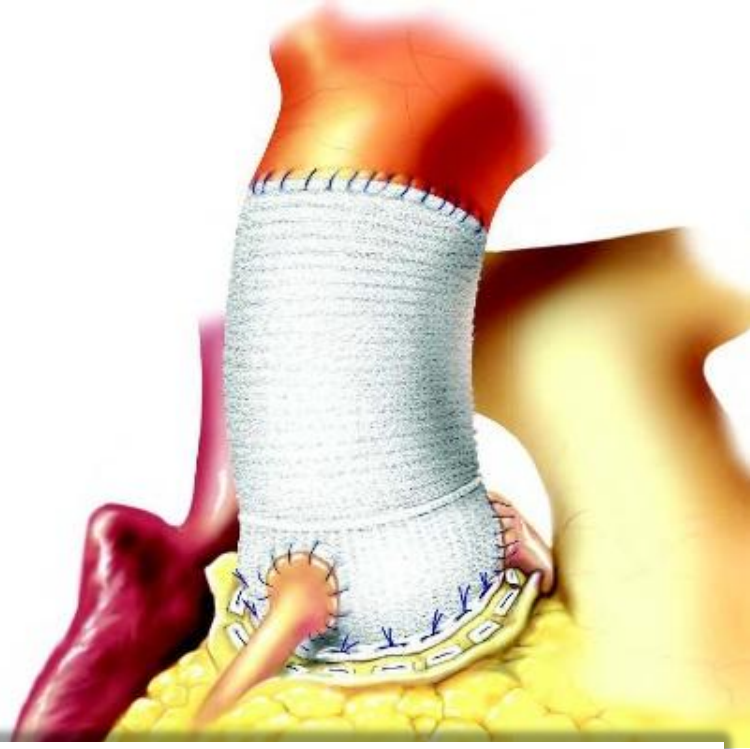
Guidelines

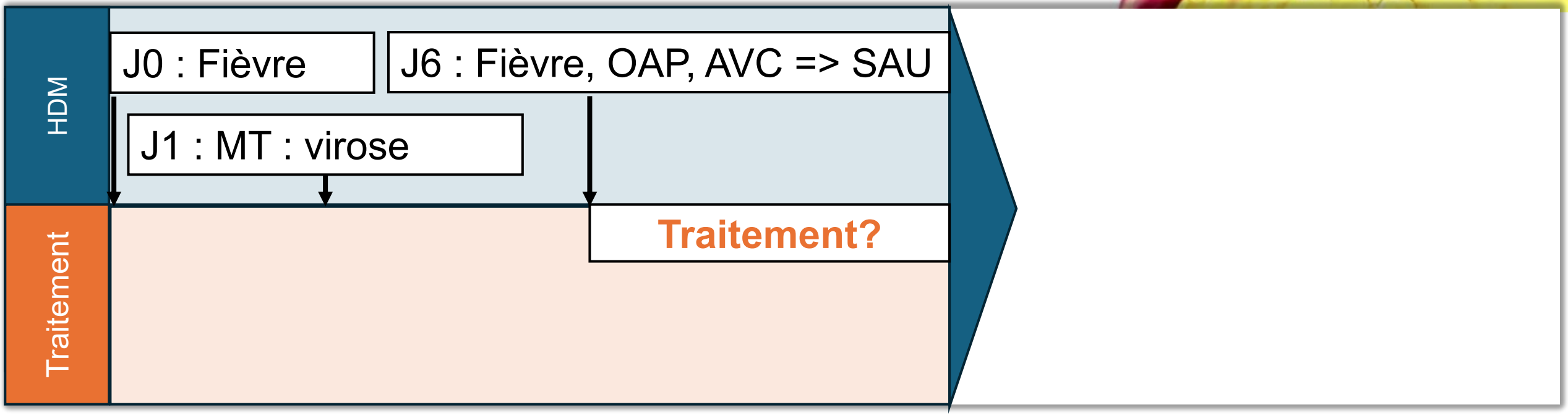
Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

Vincent Le Moing[a,*], Éric Bonnet[b], Vincent Cattoir[c,d,e], Catherine Chirouze[f], Laurène Deconinck[g], Xavier Duval[h], Bruno Hoen[f], Nahéma Issa[i], Raphaël Lecomte[j,k], Pierre Tattevin[l], Asmaa Tazi[m,n], François Vandenesch[o,p], Christophe Strady[q]

M. G, 69 ans

- Bioprothèse aortique avec procédure de Bentall en 2011.
- Antécédent d'endocardite à *Steptococcus infantarius* en 2013
- Résection d'un polype sigmoïde en 2013

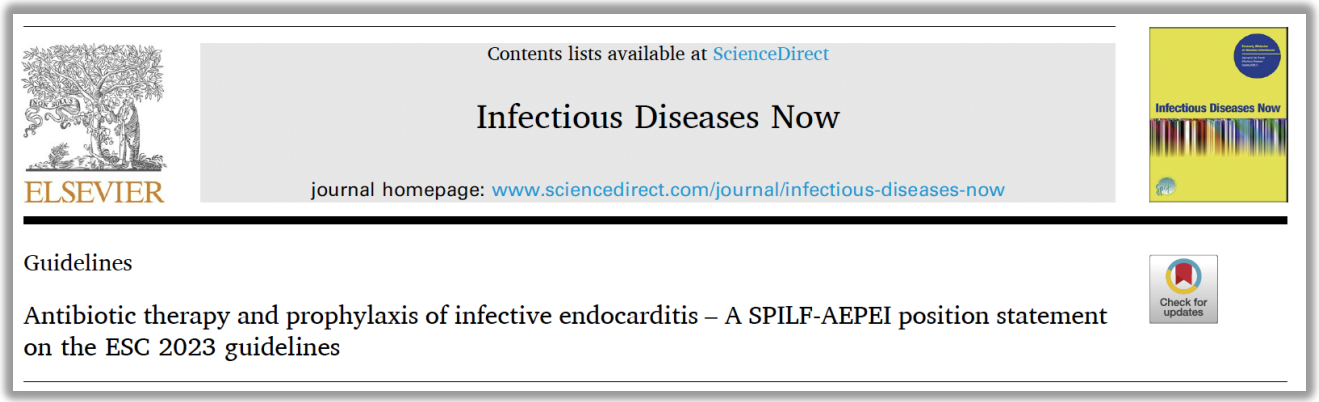




Question 1 : Introduisez-vous un traitement antibiotique?

- Oui
- Non

Quand débuter un traitement en urgence?



Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

Guideline

Empirical antimicrobial treatment of suspected IE is recommended in each of the following situations:

- Acute onset with rapid progression of symptoms over the last week
- Large vegetation (>10 mm)
- Sepsis
- Before surgery when emergency valve surgery is indicated.

In all other situations, antibiotic treatment may be deferred until the results of blood cultures are available.

Quand débuter un traitement en urgence?

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

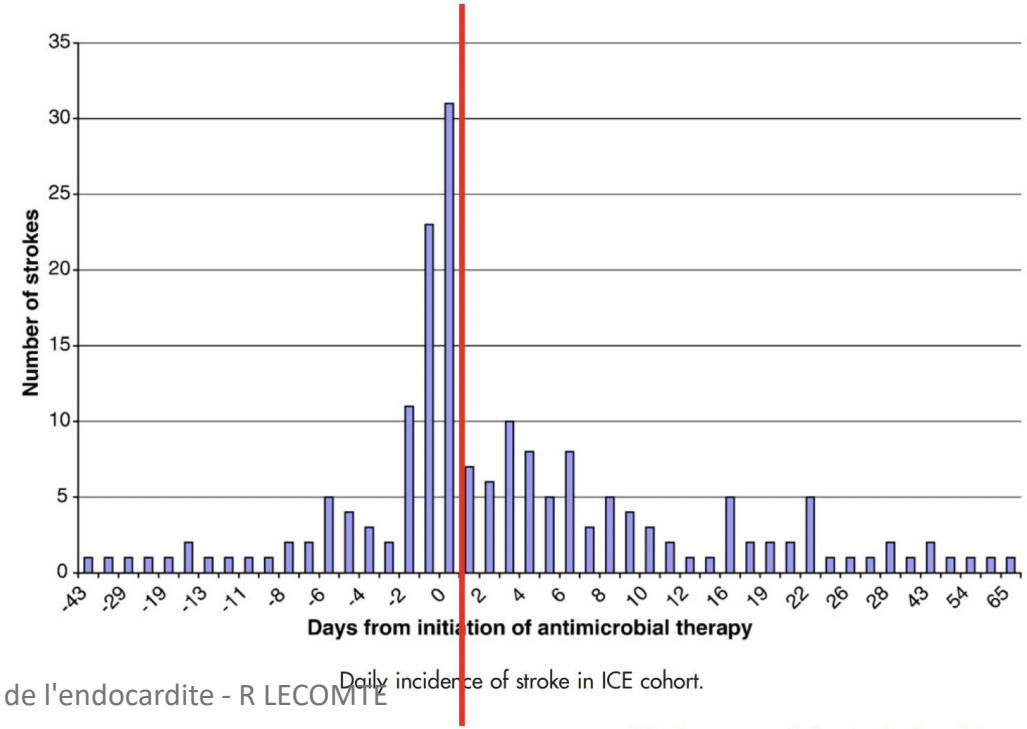
Guideline

Empirical antimicrobial treatment of suspected IE is recommended in each of the following situations:

- Acute onset with rapid progression of symptoms over the last week
- Large vegetation (>10 mm)
- Sepsis
- Before surgery when emergency valve surgery is indicated.

In all other situations, antibiotic treatment may be deferred until the results of blood cultures are available.

The relationship between the initiation of antimicrobial therapy and the incidence of stroke in infective endocarditis: An analysis from the ICE Prospective Cohort Study (ICE-PCS)



Daily incidence of stroke in ICE cohort.

Dickerman SA et al. Am Heart J 2007

Quand débuter un traitement en urgence?

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

Guideline

Empirical antimicrobial treatment of suspected IE is recommended in each of the following situations:

- Acute onset with rapid progression of symptoms over the last week
- Large vegetation (>10 mm)
- Sepsis
- Before surgery when emergency valve surgery is indicated.

In all other situations, antibiotic treatment may be deferred until the results of blood cultures are available.

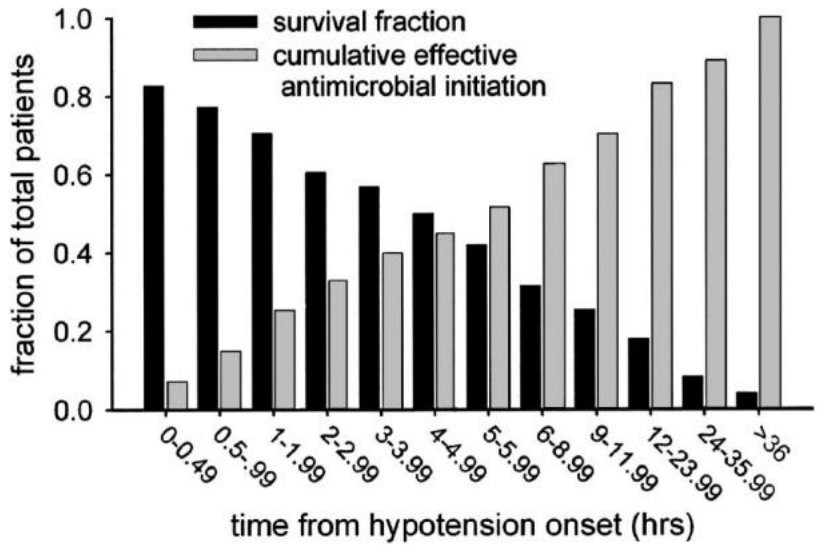


Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

Chaque heure de retard d'introduction de l'ATB est associée à une augmentation de la mortalité de 7,6%

Kumar *et al.* Critical care med. 2006

Question 2 : quel traitement proposez-vous en probabiliste?

- Amoxicilline + Céfazoline + Gentamicine
- Amoxicilline + Céfazoline
- Amoxicilline + Daptomycine + Gentamicine
- Amoxicilline + Daptomycine
- Vancomycine + Gentamicine
- Vancomycine

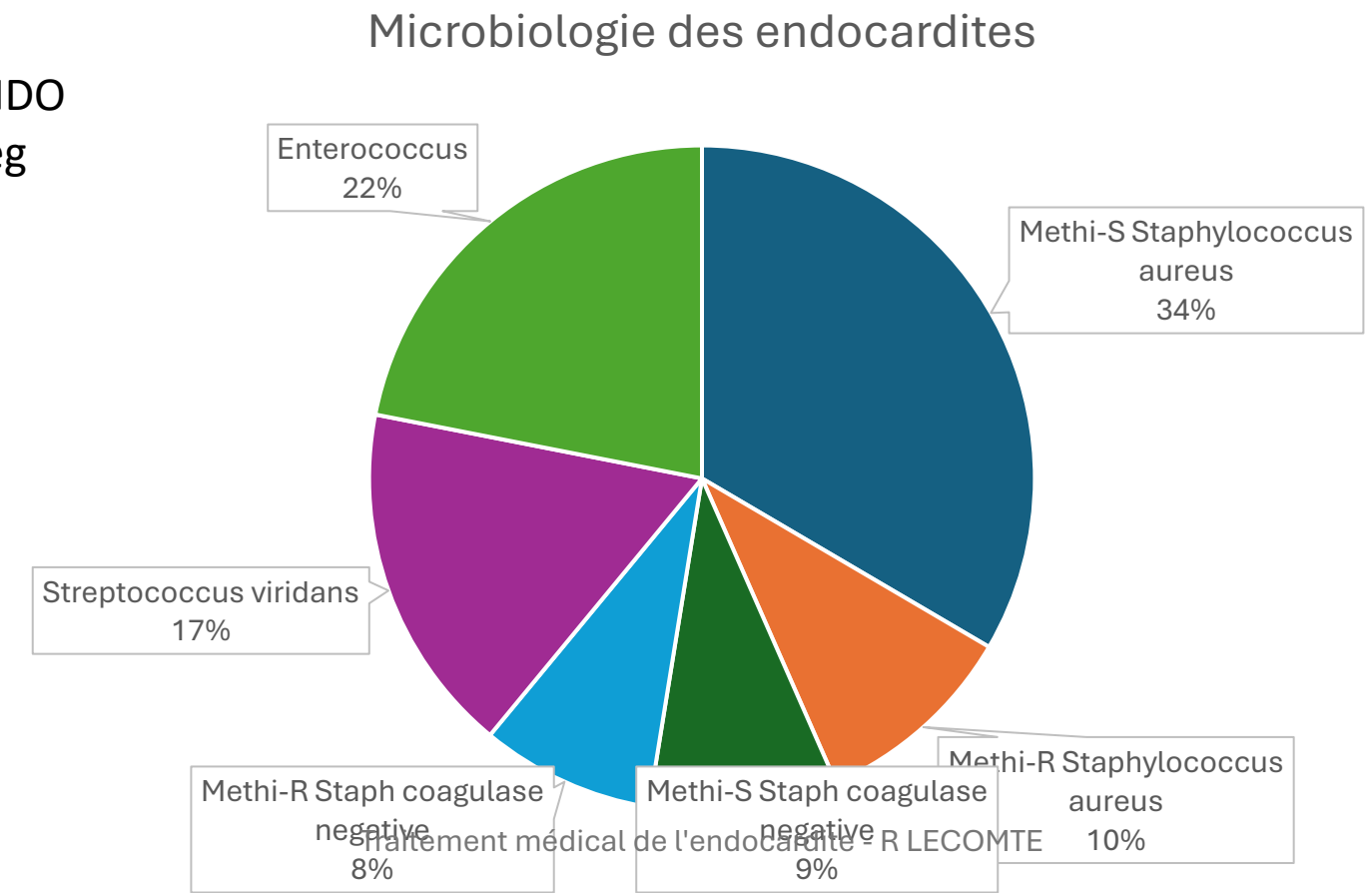
Question 2 : quel traitement proposez-vous en probabiliste?

- Amoxicilline + Céfazoline + Gentamicine
- **Amoxicilline + Céfazoline**
- Amoxicilline + Daptomycine + Gentamicine
- Amoxicilline + Daptomycine
- Vancomycine + Gentamicine
- Vancomycine

Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study

Gilbert Habib [1,2]*, Paola Anna Erba [3,4], Bernard Iung [5], Erwan Donal[6],

NB : cohorte EURO ENDO
Avec 20% d'EI à Hc Neg



Habib *et al.* Eur Heart J 2019

Definition, clinical profile, microbiological spectrum, and prognostic factors of early-onset prosthetic valve endocarditis

Javier López[1]*, Ana Revilla[1], Isidre Vilacosta[2], Eduardo Villacorta[1], Carlos González-Juanatey[3], Itziar Gómez[1], María Jesús Rollán[4], and José Alberto San Román[1]

[1]Instituto de Ciencias del Corazón (ICICOR), Hospital Clínico Universitario, C/Ramón y Cajal 3, 47005 Valladolid, Spain; [2]Hospital Clínico San Carlos, Madrid, Spain; [3]Complejo Hospitalario Xeral Calde, Lugo, Spain; and [4]Hospital Universitario Río Hortega, Valladolid, Spain

- 172 PVE
- Pas de différence entre < 2 mois et 2-12 mois.
- En revanche, cutt of de 1 an pertinent:
  - SCN 37 vs. 18%, P . 0.005)
  - Streptocoques viridans (18 vs. 1%, P . 0.001).
  - Résistance à la méticilline des SCN (77 vs. 30%, P . 0.004).

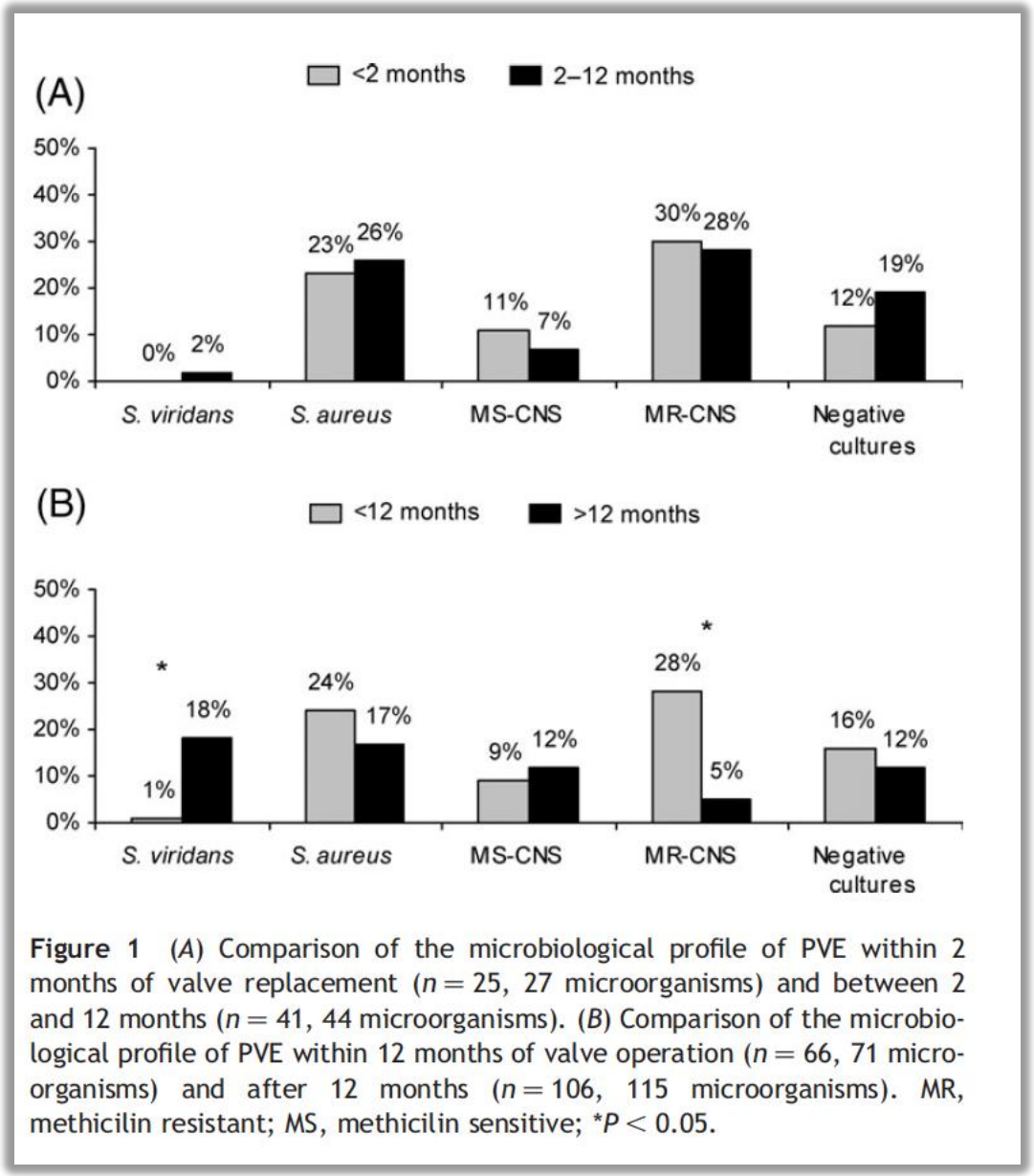


Figure 1 (*A*) Comparison of the microbiological profile of PVE within 2 months of valve replacement ($n = 25$, 27 microorganisms) and between 2 and 12 months ($n = 41$, 44 microorganisms). (*B*) Comparison of the microbiological profile of PVE within 12 months of valve operation ($n = 66$, 71 microorganisms) and after 12 months ($n = 106$, 115 microorganisms). MR, methicilin resistant; MS, methicilin sensitive; $^*P < 0.05$.

J. Lopez *et al.* Eur Heart J 2007

Quelle bétalactamine?

- Etude rétrospective
- **Bactériémies** à SAMS
- Analyse du traitement probabiliste
- N= 541

ORIGINAL ARTICLE INFECTIOUS DISEASES

Are all beta-lactams similarly effective in the treatment of methicillin-sensitive *Staphylococcus aureus* bacteraemia?

M. Paul[1,2], N. Zemer-Wassercug[1], O. Talker[1], Y. Lishtzinsky[1], B. Lev[3], Z. Samra[3,2], L. Leibovici[4,2] and J. Bishara[1,2]

1) *Unit of Infectious Diseases, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel,* 2) *Sacker Faculty of Medicine, Tel-Aviv University, Ramat-Aviv, Israel,* 3) *Microbiology Laboratory Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel and* 4) *Medicine E, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel*

TABLE 2. Multivariable logistic regression analysis for 30-day mortality: empirical antibiotic treatment[a]

Variable[b]	OR, 95% CI *n* = 541 patients, deaths = 202	p-value
Empirical antibiotic treatment		
Oxacillin/cefazolin	Reference	
Cefuroxime	1.98 (0.98–4.01)	0.058
Ceftriaxone/cefotaxime	2.24 (1.23–4.08)	0.008
Beta-lactam-beta-lactamase	2.68 (1.23–5.85)	0.013
Other beta-lactams	0.81 (0.35–1.9)	0.629
Age (per 1 year increment)	1.04 (1.02–1.06)	<0.001
Female sex	1.69 (1.08–2.63)	0.021
Poor functional capacity (bedridden)	1.73 (1.02–2.93)	0.041
Malignancy	1.89 (1.15–3.09)	0.012
Shock at onset	5.61 (2.75–11.45)	<0.001
Urea (per 1 mg/dL increment)	1.01 (1.007–1.016)	<0.001
Albumin (per 1 mg/dL increment)	0.54 (0.38–0.78)	0.001
Thrombocytes (per 1 K/μL increment)	0.996 (0.994–0.998)	<0.001
Mechanical ventilation	Not retained in final model	0.078
Skin/soft tissue source of infection		0.111

Paul et al. CMI 2011

Quelle bétalactamine?

ORIGINAL ARTICLE INFECTIOUS DISEASES

Are all beta-lactams similarly effective in the treatment of methicillin-sensitive *Staphylococcus aureus* bacteraemia?

M. Paul[1,2], N. Zemer-Wassercug[1], O. Talker[1], Y. Lishtzinsky[1], B. Lev[3], Z. Samra[3,2], L. Leibovici[4,2] and J. Bishara[1,2]

1) Unit of Infectious Diseases, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel, 2) Sacker Faculty of Medicine, Tel-Aviv University, Ramat-Aviv, Israel, 3) Microbiology Laboratory Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel and 4) Medicine E, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel

- Etude rétrospective
- **B**actériémies à SAMS
- A
- N

Empirical antibiotic treatment		
Oxacillin/cefazolin	Reference	
Cefuroxime	1.98 (0.98–4.01)	0.058
Ceftriaxone/cefotaxime	2.24 (1.23–4.08)	0.008
Beta-lactam-beta-lactamase	2.68 (1.23–5.85)	0.013
Other beta-lactams	0.81 (0.35–1.9)	0.629

Paul *et al.* CMI 2011

Choix de la bétalactamine : des données dans l'endocardite?

- Analyse post-hoc d'une cohorte prospective
- Monocentrique CHU de Nantes
- 208 patients
- 2 groupes:
  - Référence
  - Autre
- Critère de jugement : probabilité de stérilisation de la bactériémie par jour de traitement

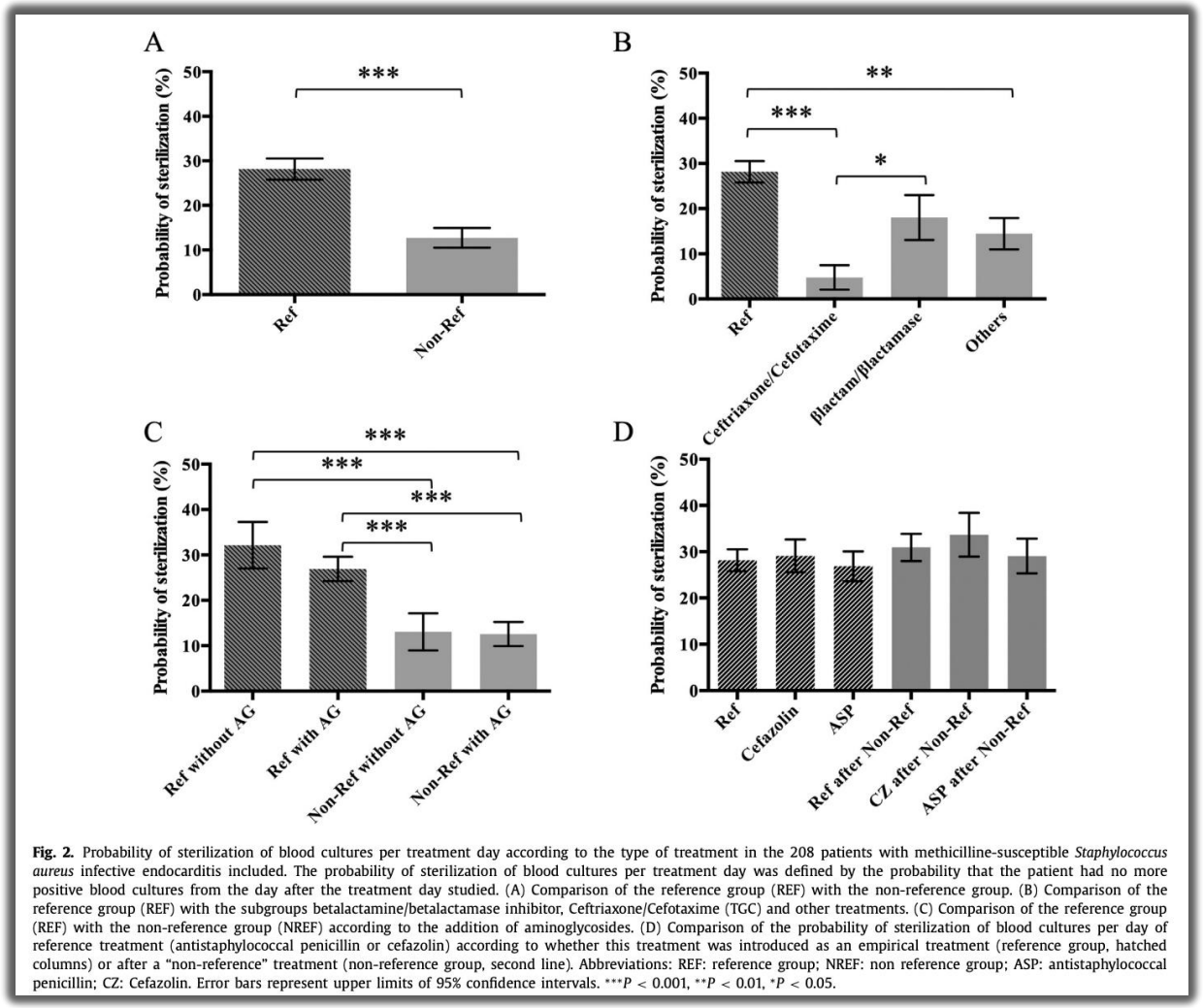
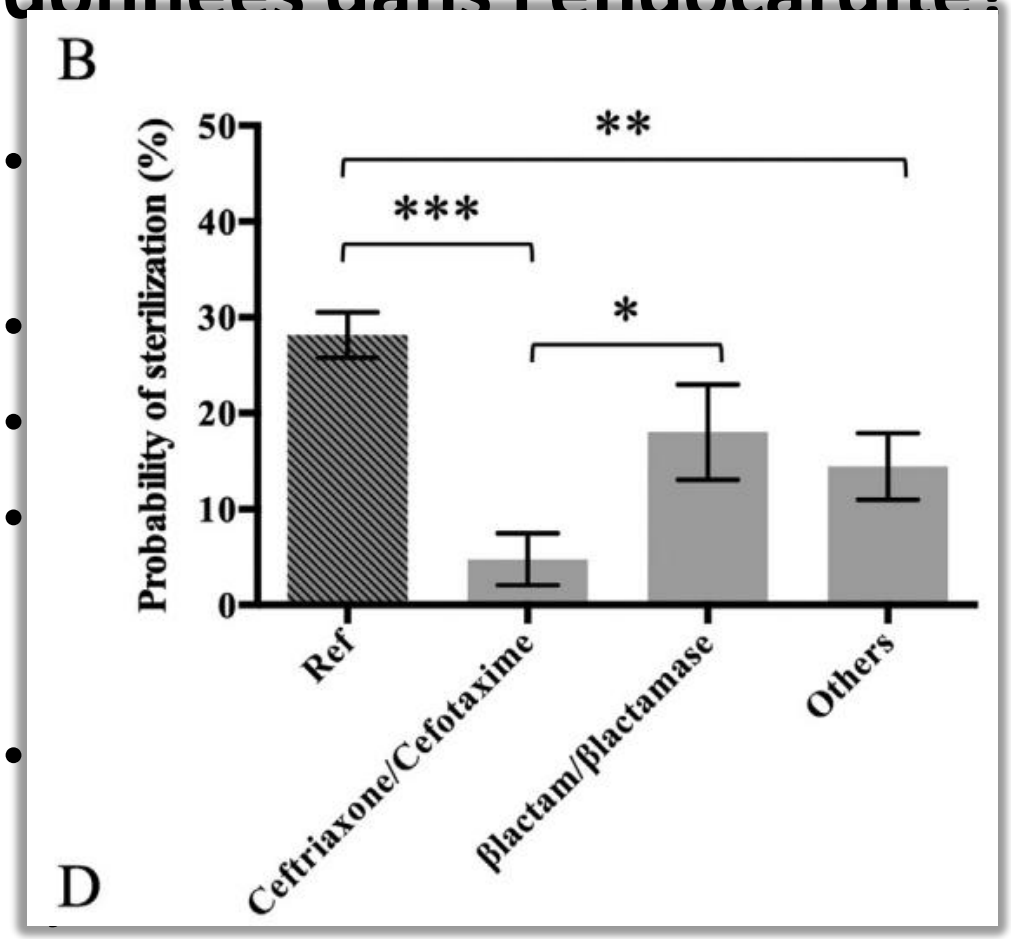
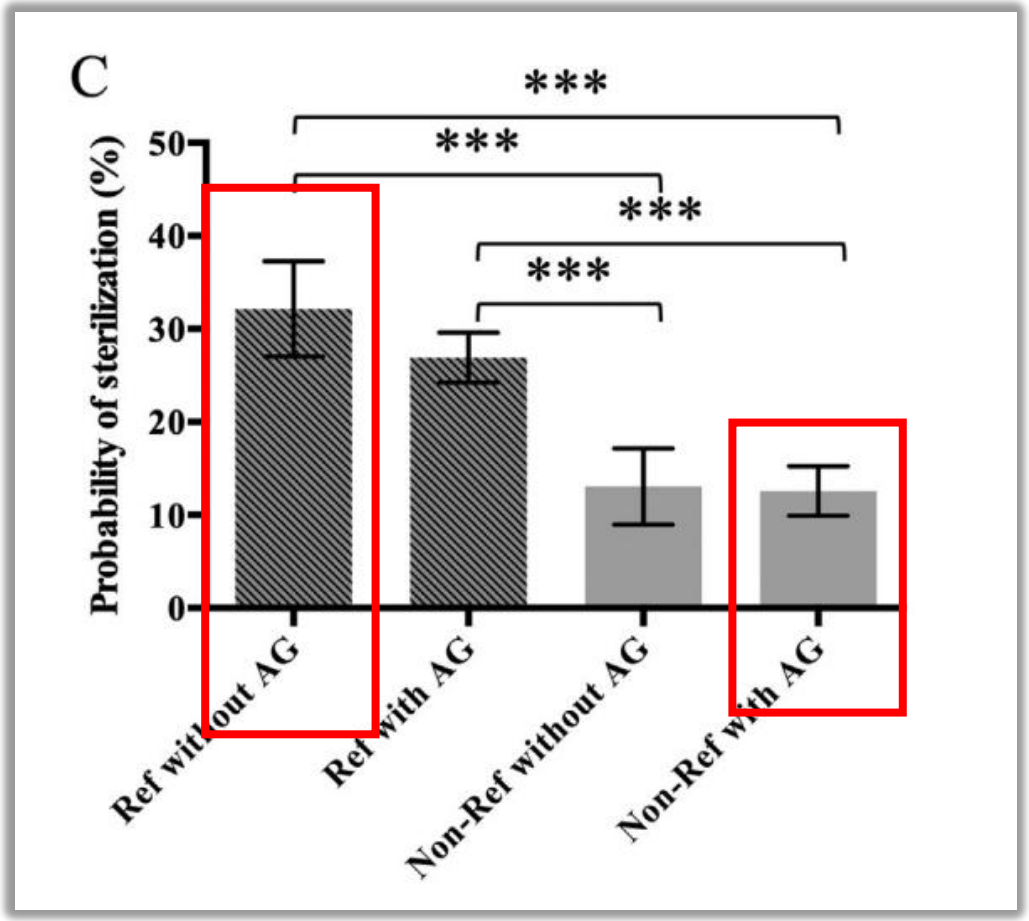


Fig. 2. Probability of sterilization of blood cultures per treatment day according to the type of treatment in the 208 patients with methicilline-susceptible *Staphylococcus aureus* infective endocarditis included. The probability of sterilization of blood cultures per treatment day was defined by the probability that the patient had no more positive blood cultures from the day after the treatment day studied. (A) Comparison of the reference group (REF) with the non-reference group. (B) Comparison of the reference group (REF) with the subgroups betalactamine/betalactamase inhibitor, Ceftriaxone/Cefotaxime (TGC) and other treatments. (C) Comparison of the reference group (REF) with the non-reference group (NREF) according to the addition of aminoglycosides. (D) Comparison of the probability of sterilization of blood cultures per day of reference treatment (antistaphylococcal penicillin or cefazolin) according to whether this treatment was introduced as an empirical treatment (reference group, hatched columns) or after a "non-reference" treatment (non-reference group, second line). Abbreviations: REF: reference group; NREF: non reference group; ASP: antistaphylococcal penicillin; CZ: Cefazolin. Error bars represent upper limits of 95% confidence intervals. $^{***}P < 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$.

Lecomte *et al.* IJID 2024

Choix de la bétalactamine : des données dans l'endocardite?



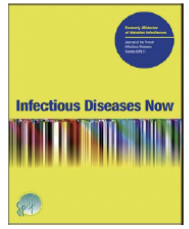


Lecomte *et al.* IJID 2024

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now



Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

For native valve IE and late-onset prosthetic valve IE (i.e., symptoms onset > 1 year post-valve implantation), preferred empirical treatment may be.

– amoxicillin (200 mg/kg/day) + cefazolin (100 mg/kg/day)
– combined with gentamicin (5 mg/kg/day) only in patients with sepsis

or (if allergy to β-lactams).

– vancomycin (30 mg/kg/day, continuous infusion after a loading dose).

Pourquoi amoxicilline + céfazoline?

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

Nathan Peiffer-Smadja[1,2]†, Elena Guillotel[3]†, David Luque-Paz[3], Naouale Maataoui[2,4], F.-Xavier Lescure[1,2] and Vincent Cattoir [3,5,6]*

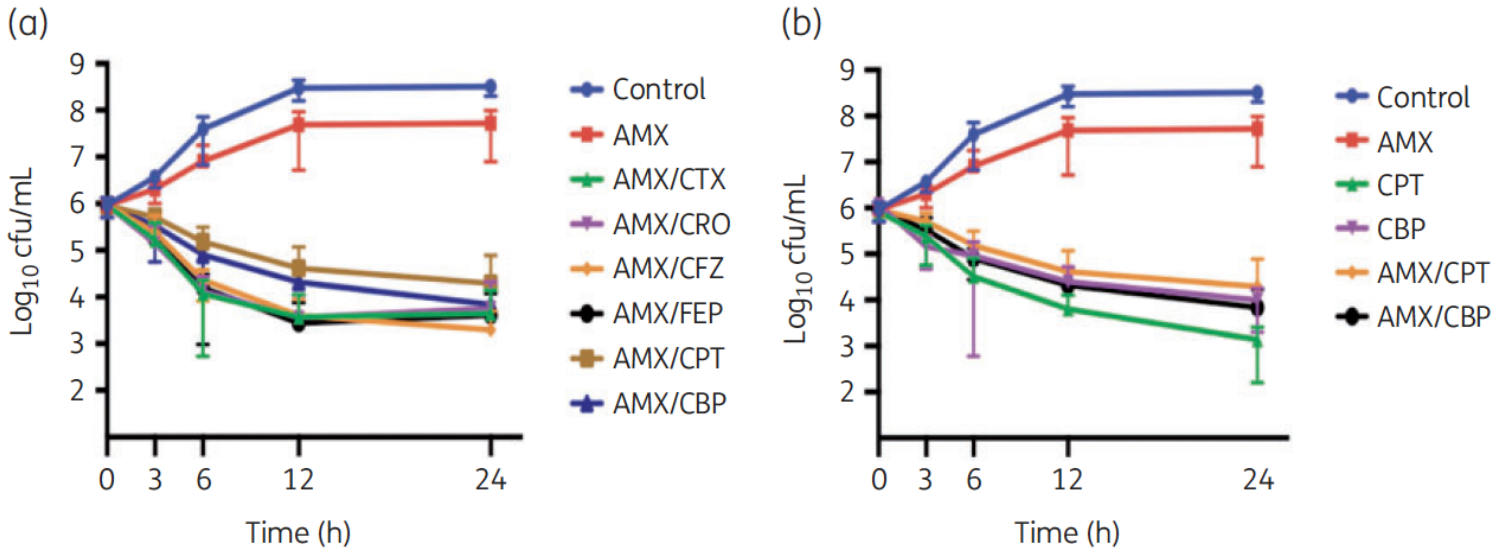


Figure 1. Mean time–kill curves of amoxicillin alone and in combination with different cephalosporins (a), and of amoxicillin, ceftaroline, ceftobiprole, amoxicillin/ceftaroline and amoxicillin/ceftobiprole (b) for the 12 studied *E. faecalis* strains. Error bars represent SEMs of triplicate experiments for the 12 strains. AMX, amoxicillin; CTX, cefotaxime; CRO, ceftriaxone; CFZ, cefazolin; FEP, cefepime; CPT, ceftaroline; CBP, ceftobiprole. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

The combinations amoxicillin/cefazolin, amoxicillin/cefotaxime, amoxicillin/ceftriaxone and amoxicillin/cefepime were synergistic at 12 and 24 h against 12/12 strains and amoxicillin/ceftobiprole and amoxicillin/ceftaroline against 10/12 strains.

Question 3 : Si la suspiçion forte d’endocardite était survenue dans les 12 mois après la chirurgie de bentall, quel traitement auriez-vous proposé en probabiliste?

- Amoxicilline + Céfazoline
- Amoxicilline + Daptomycine
- Céfépime + Daptomycine
- Vancomycine

En cas de PVE dans l'année qui suit la pose?

Early-onset prosthetic valve endocarditis definition revisited: Prospective study and literature review

Rinaldo Focaccia Siciliano[a,*], Bruno Azevedo Randi[a], Danielle Menosi Gualandro[b], Roney Orismar Sampaio[c], Márcio Sommer Bittencourt[d], Christian Emmanuel da Silva Pelaes[a], Alfredo José Mansur[d], Pablo Maria Alberto Pomerantzeff[e], Flávio Tarasoutchi[c], Tânia Mara Varejão Strabelli[a]

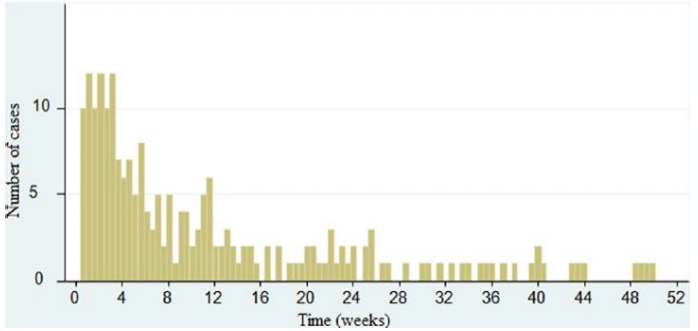


Figure 1. Distribution of 172 cases of early-onset prosthetic valve endocarditis within the first year of valve replacement.

Table 1
Distribution of the microorganisms identified in 138 early-onset prosthetic valve endocarditis cases, by sensitivity profile.[a]

Microorganism	0–120 days	121–365 days	Uncorrected *p*-value	Hochberg corrected *p*-value
Sensitive CoNS	12.1% (13/107)	5.88% (2/34)	0.36	0.9
MSSA	3.7% (4/107)	11.7% (4/34)	0.10	0.5
Sensitive *Enterococcus spp*	7.48% (8/107)	5.88% (2/34)	1.00	1.0
Sensitive GNB	7.48% (8/107)	2.94% (1/34)	0.45	0.9
Streptococcus spp	1.87% (2/107)	23.5% (8/34)	<0.001	0.007
Fungi	2.80% (3/107)	17.6% (6/34)	0.007	0.042
HACEK	0% (0/107)	2.94% (1/34)	0.25	0.9
Resistant microorganisms	64.4% (69/107)	32.3% (11/34)	0.001	0.007
Resistant CoNS[b]	37.3% (40/107)	26.4% (9/34)		
MRSA	13.0% (14/107)	0% (0/34)		
Resistant *Enterococcus spp*[c]	8.41% (9/107)	2.94% (1/34)		
ESBL-producing GNB[d]	5.60% (6/107)	2.94% (1/34)		

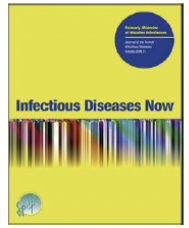
CoNS, coagulase-negative staphylococci; MSSA, methicillin-sensitive *Staphylococcus aureus*; GNB, Gram-negative bacilli; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended-spectrum beta-lactamase.

[a] Culture-negative cases are excluded from this Table Some cases had more than one microorganism isolated.
[b] Methicillin-resistant CoNS.
[c] Ampicillin-resistant *Enterococcus spp*.
[d] ESBL-producing GNB, of which none were carbapenemase-producing.

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now



Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

- En cas d'EI sur prothèse dans l'année qui suit la pose de prothèse:

For early-onset prosthetic valve IE (i.e., symptoms onset < 1 year post-valve implantation), preferred empirical treatment may be.

– daptomycin (12 mg/kg/day), or vancomycin (30 mg/kg/day, continuous infusion after a loading dose)
– combined with cefepime (2 g IV/8h)
– combined with gentamicin (5 mg/kg/day) only in patients with sepsis

Empirical treatment must be adapted as soon as reliable microbiological documentation is obtained.

Question 3 : Si la suspiçion forte d'endocardite était survenue dans les 12 mois après la chirurgie de bentall, quel traitement auriez-vous proposé en probabiliste?

- Amoxicilline + Céfazoline
- Amoxicilline + Daptomycine
- **Céfépime + Daptomycine**
- Vancomycine

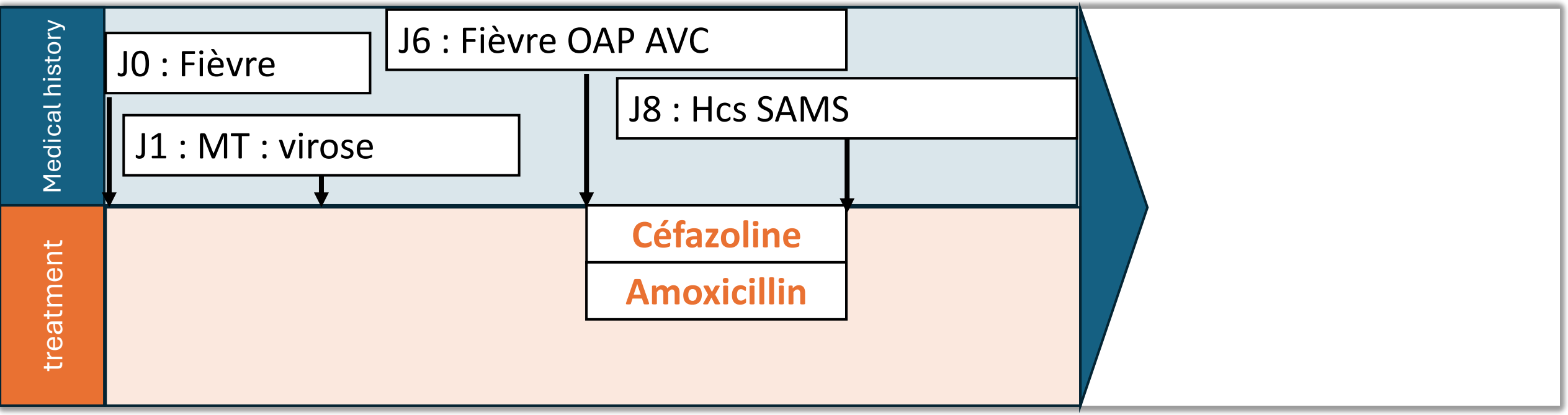
Take-home messages

Probabiliste:

- Viser le SAMS+++ et couverture strepto entérocoque
- Amoxicilline Céfazoline
- Cut off de 1 an PVE
- CEF DPC PVE < 1 an

M. G, 69 year-old man

- J8 : 3 hémocultures positives à SAMS multi-sensible.



Question 3 : quelle est votre conduire à tenir concernant la bétalactamine

1. Maintien céfazoline
2. Switch pour cloxacilline
3. Maintien céfazoline mais switch en cas de suspiçion d’échec

Pénicilline M ou céfazoline?

- Les pénicillines du groupe M :
  - Traitement de référence
  - Mais effets indésirables fréquents
- La céfazoline :
  - Mieux tolérée
  - Mais risque d'effet inoculum

Table 2. Premature Antimicrobial Discontinuation and Drug-Emergent Events Stratified by Treatment Group[a]

Event	Nafcillin (n = 366)	Cefazolin (n = 119)	*P* Value
PAD	124 (33.8)	8 (6.7)	<.001
DEEs[a]	114 (31.1)	14 (11.7)	<.001
Rash	51 (13.9)	5 (4.2)	.002
Renal impairment	42 (11.4)	4 (3.3)	.006
Liver abnormalities	30 (8.1)	2 (1.6)	.01
Neutropenia	31 (8.4)	4 (3.3)	.06
Clostridium difficile colitis	9 (2.4)	1 (0.8)	.46

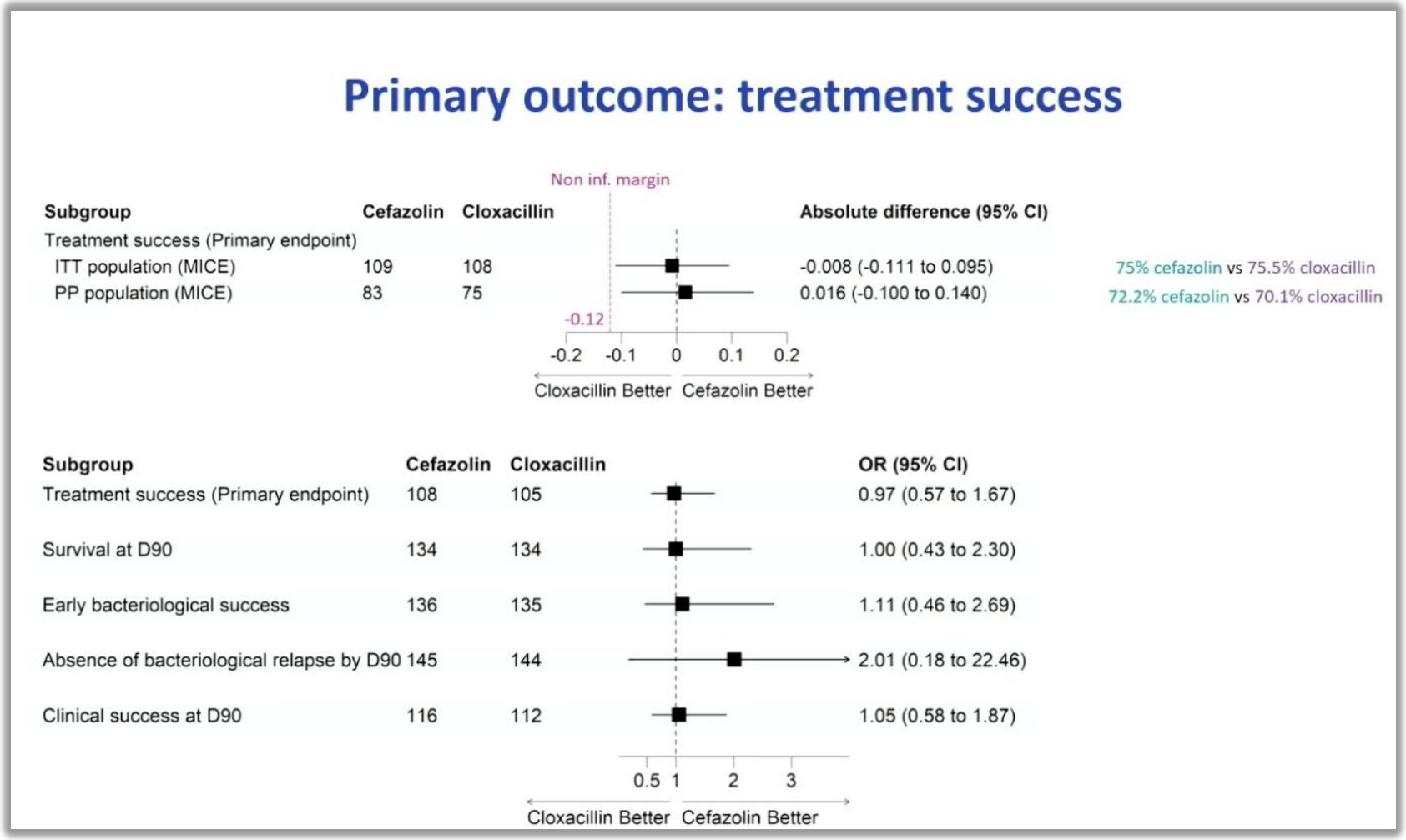
Data are presented as No. (%).

Abbreviations: DEEs, drug-emergent events; PAD, premature antimicrobial discontinuation.

[a] Represents unique patients experiencing drug-related adverse events (DRAEs); each patient could experience >1 DRAE. DRAEs were defined as follows: renal impairment, an increase in serum creatinine of >0.5 mg/dL or 50% increase from baseline; liver abnormalities, alanine aminotransferase >100μ/L; neutropenia, neutrophil count <1000/μL.

Youngest et al. CID 2014. *Nannini et al. CID 2003. Kernodle JID 1989*

Etude CloCeBa



Session ECCMID 2025 « The Trial Run: recent trials on *S. aureus* bacteraemia management »

Xavier Lescure *et al.*

Etude SNAP

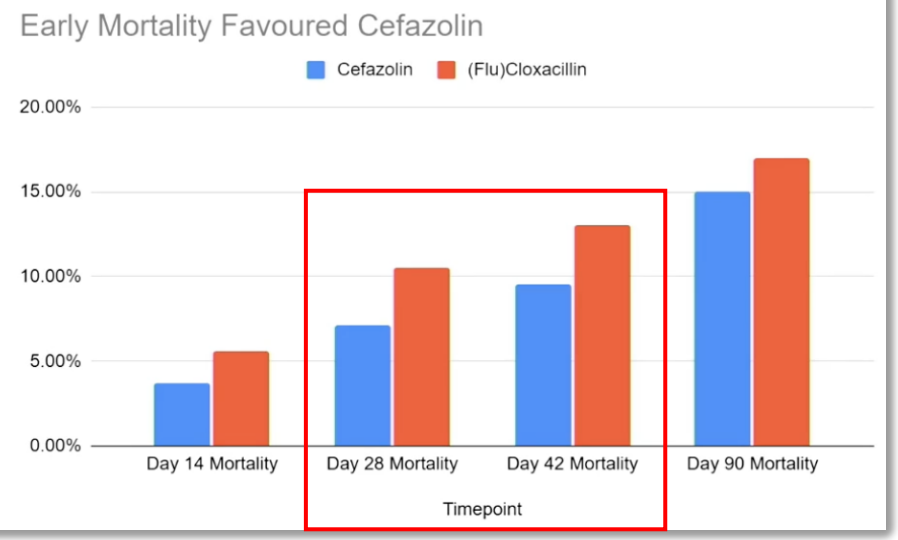
Primary outcome

	(Flu)cloxacillin (n=670)	Cefazolin (n=671)
All-cause mortality at 90 days		
Yes	109 (17.0)	97 (15.0)
Missing	28 (4.2)	26 (3.9)

Adjusted odds ratio (median, 95% CrI)	0.81 (0.59, 1.12)
Non-inferiority, Pr(OR<1.2):	0.9922
Superiority, Pr(OR<1.0):	0.8978

Key core secondary outcomes

Mortality time point	OR cefazolin vs (flu)cloxacillin	Prob OR<1 (superiority)
14 days	0.67	0.9411
28 days	0.61	0.9919
42 days	0.66	0.9887



Session ECCMID 2025 « The Trial Run: recent trials on *S. aureus* bacteraemia management »
Joshua Paul Davis *et al.*

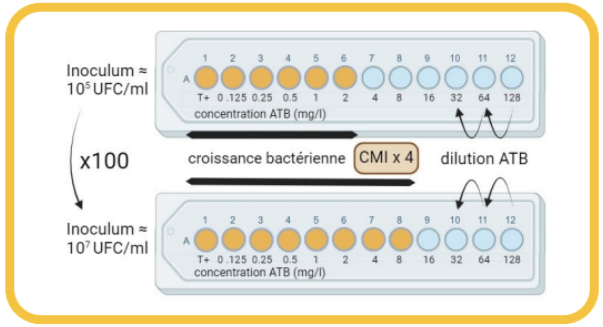
Bactériémies et endocardites

COL01-02

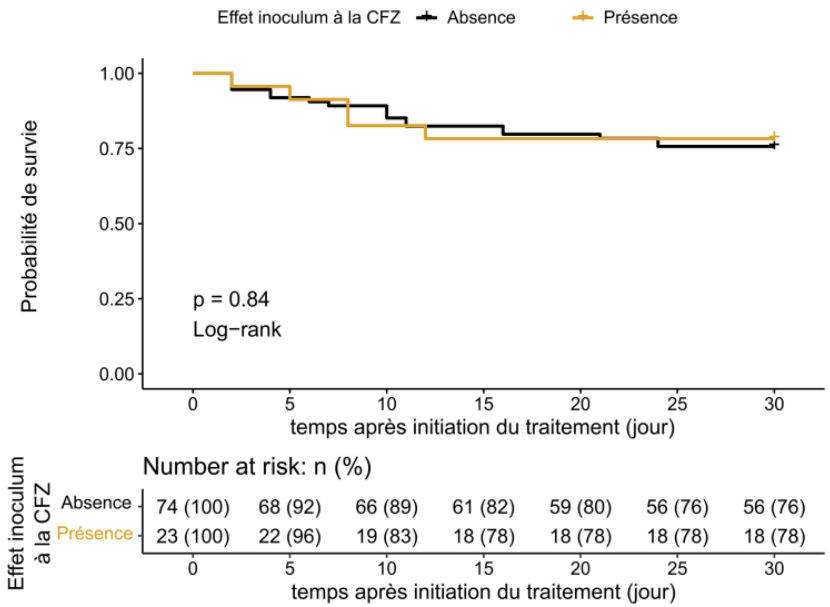
Impact de blaZ dans le traitement des endocardites infectieuses à *Staphylococcus aureus* sensible à la méticilline : une preuve clinique de l'effet inoculum.

B. Jean [1], M. Crolle [1], P. Tattevin [2], A. Le bot [2], D. Luque Paz [2], F. Guerin [2], L. Armand [3], Y. Yazdanpanah [3], C. Massip [1], P. Delobel [1]

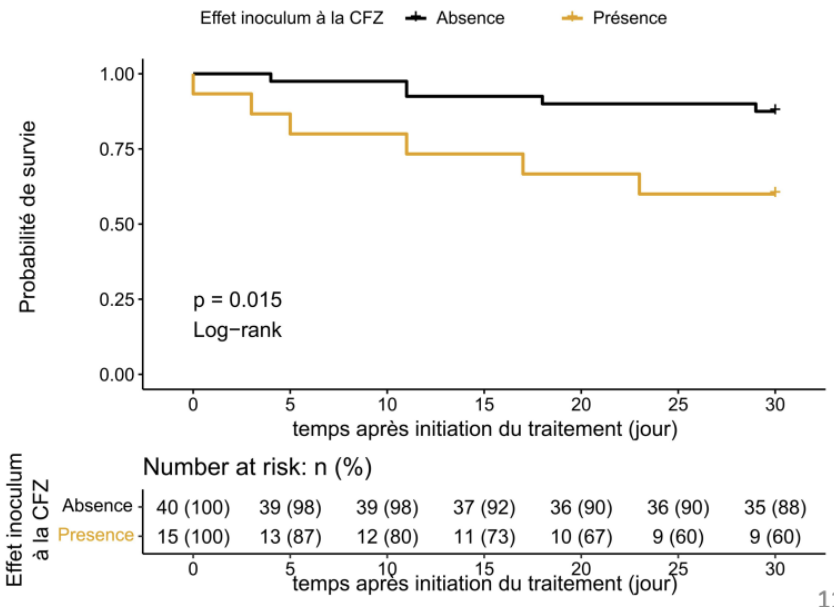
effet inoculum à la CFZ



PAS



CFZ



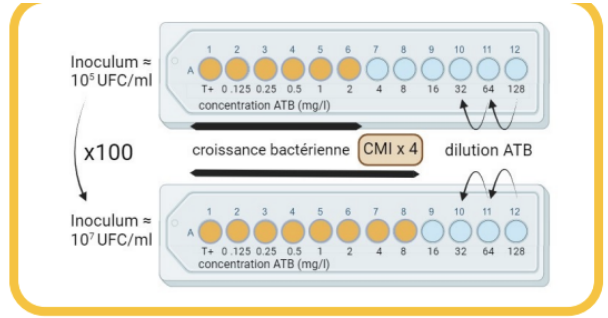
Bactériémies et endocardites

COL01-02

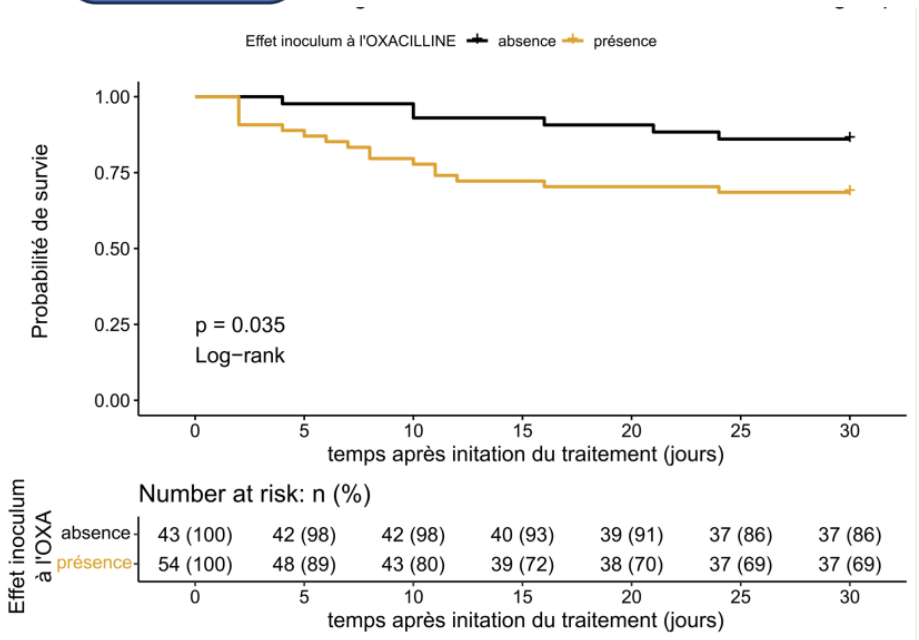
Impact de blaZ dans le traitement des endocardites infectieuses à *Staphylococcus aureus* sensible à la méticilline : une preuve clinique de l'effet inoculum.

B. Jean [1], M. Crolle [1], P. Tattevin [2], A. Le bot [2], D. Luque Paz [2], F. Guerin [2], L. Armand [3], Y. Yazdanpanah [3], C. Massip [1], P. Delobel [1]

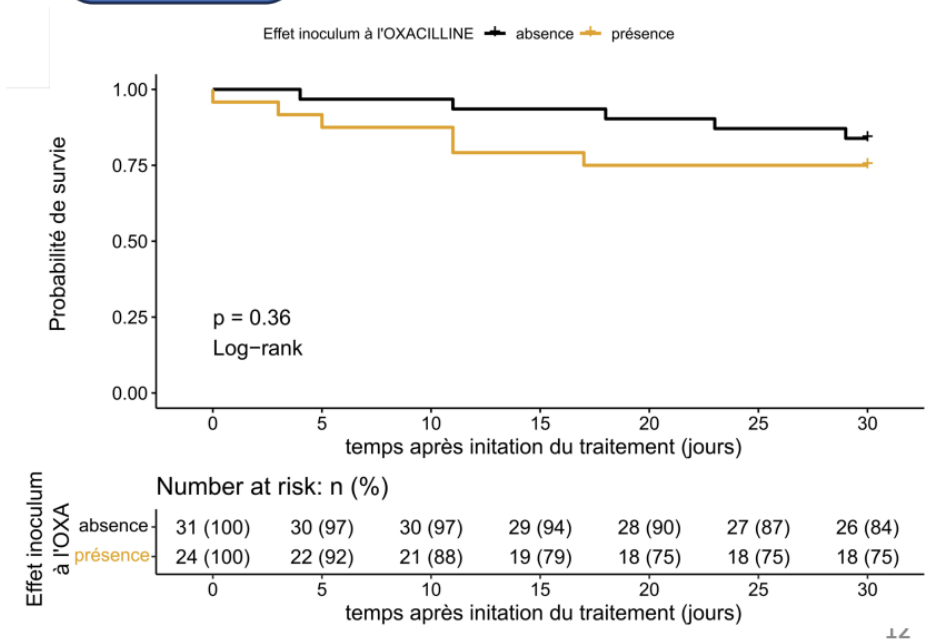
effet inoculum à l'OXA



PAS



CFZ



Recommandations SPILF:

One concern with cefazolin is that some strains have an "inoculum effect" that may be associated with clinical failure [25]. However, a recent retrospective study showed that an inoculum effect can also be observed with oxacillin and that this effect is a risk factor for one-month mortality in IE [26]. There is currently no method of assessing inoculum effect. in routine clinical microbiology practice In case of suspected failure, it may be prudent to switch to the alternative.

Table 5
Recommendations for antibiotic treatment for staphylococcal NVE.

Situation	Regimen	Comments	Duration
Methicillin-susceptible staphylococci			
Without allergy to β-lactams	Cefazolin or(Cl)oxacillin	Preferred option in case of meningitis.	
			Left-sided NVE
Early or non-severe late allergy to penicillin	Cefazolin		4-week treatment if i) apyrexia obtained during the first few days of treatment and ii) blood cultures negative by day 3 6 weeks in other cases
Late severe allergy to penicillin	Daptomycin with fosfomycin		Right-sided NVE 2-week treatment if i) apyrexia obtained during the first few days of treatment and ii) blood cultures negative by day 3 4 weeks in other cases

Question 3 : quelle est votre conduire à tenir concernant la bétalactamine

1. Maintien céfazoline
2. Switch pour cloxacilline
3. **Maintien céfazoline mais switch en cas de suspiçion d’échec**

Take-home messages

Probabiliste:

- Viser le SAMS+++ et couverture strepto entérocoque
- Amoxicilline Céfazoline
- Cut off de 1 an PVE
- CEF DPC PVE < 1 an

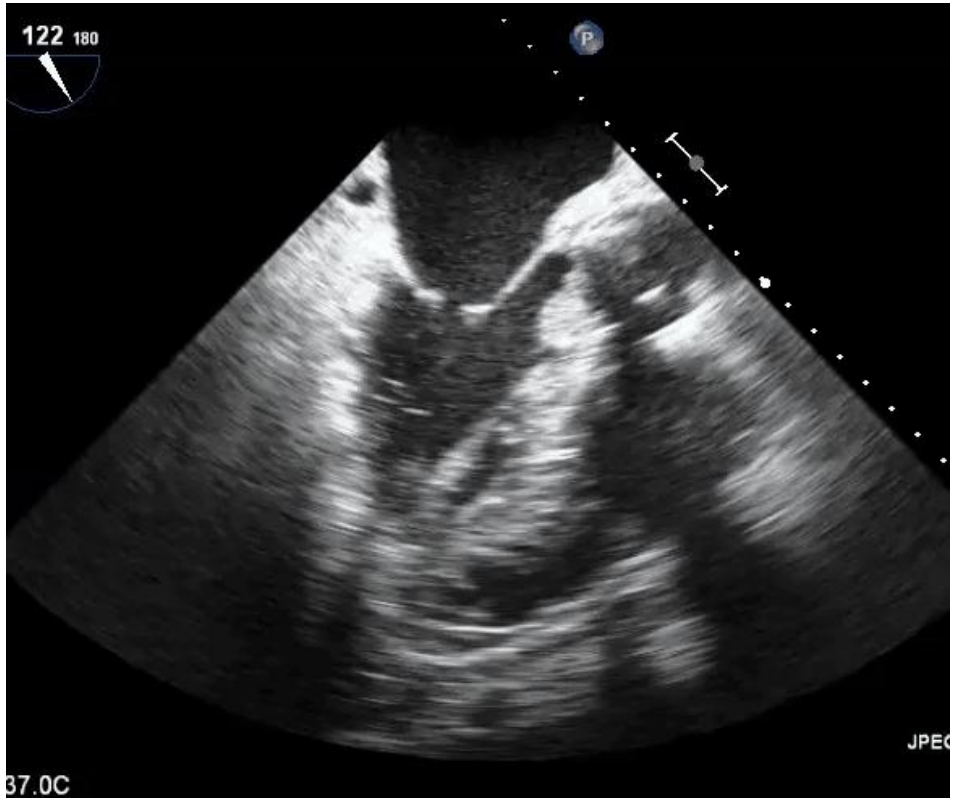
Bétalactamines:

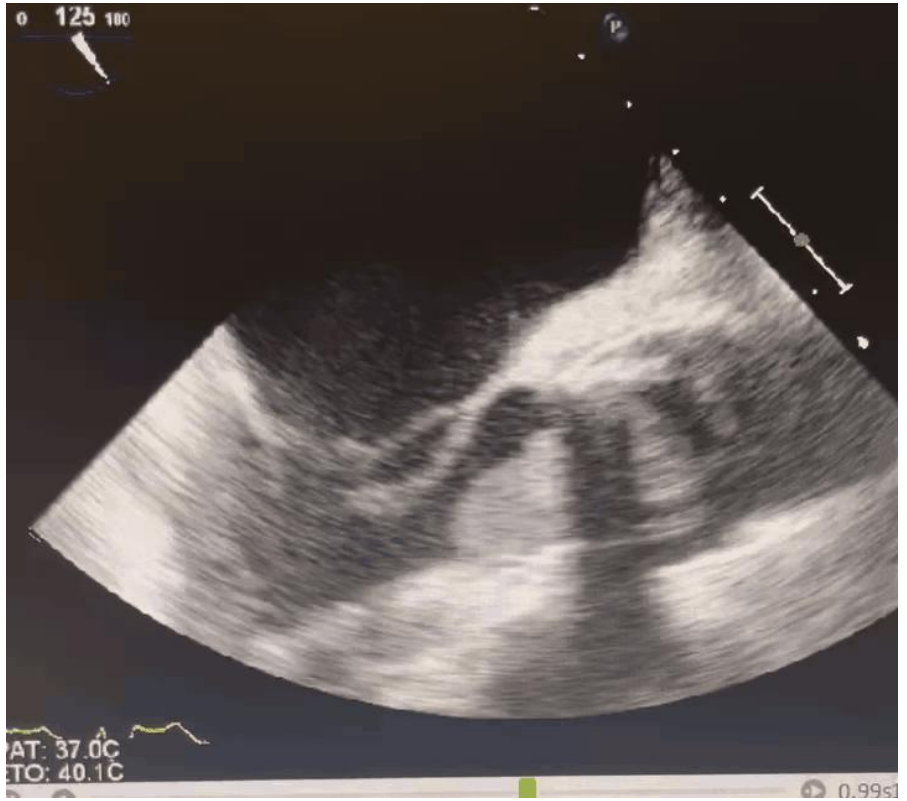
- Privilégier ASP et Céfazoline+++
- Y compris:
  - En probabiliste
  - en cas de bithérapie avec aminoside
- Switch en cas d’échec

M. G, 69 ans

ETT/ETO réalisé en urgence:

- végétation de 23 mm sur la valve prothétique aortique
- Insuffisance aortique massive

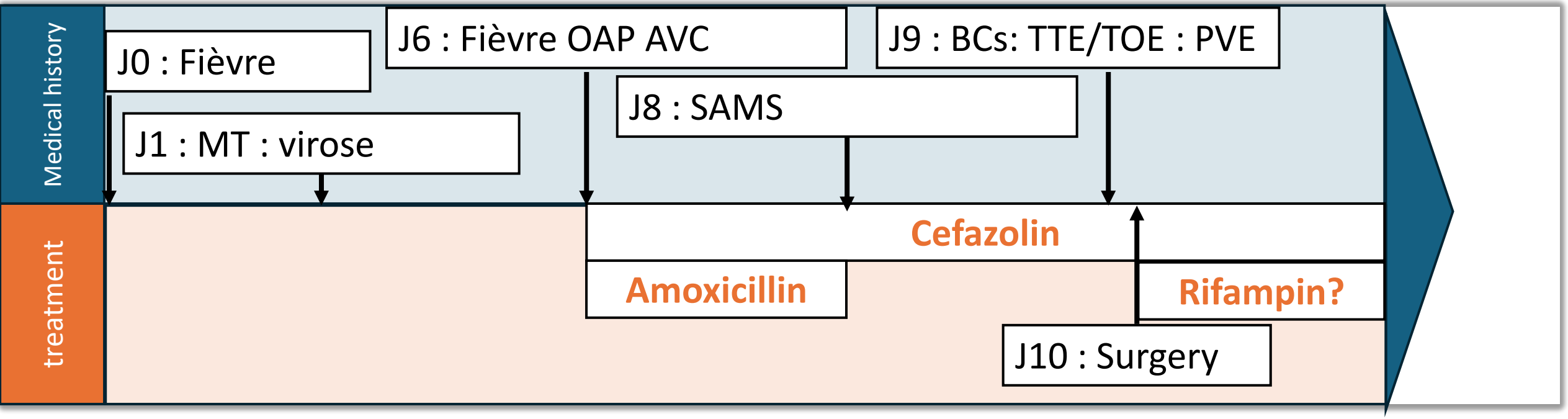




M. G, 69 year-old man

- Chirurgie

Emergency[d] surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary oedema or cardiogenic shock.[420,423,424,429,476,477]	I	B



Question 4 : après chirurgie et une fois l'inoculum contrôlé, ajoutez vous de la rifampicine?

- Oui
- Non

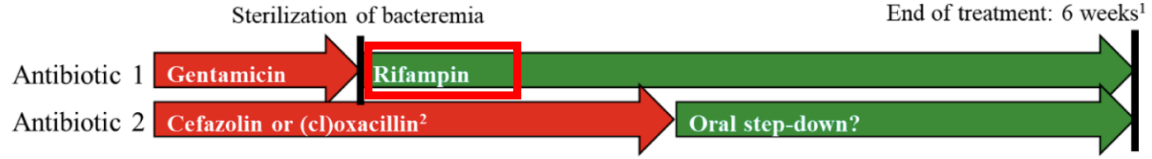
Recommandations : PVE à staphylocoques

Endocarditis Involving a Prosthetic Valve or Other Prosthetic Material Caused by Staphylococci (Table view)

Regimen	Dose* and Route	Duration, wk	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin	12 g/24 h IV in 6 equally divided doses	≥6	*Class I; Level of Evidence B*	Vancomycin should be used in patients with immediate-type hypersensitivity reactions to β-lactam antibiotics (see Table 5 for dosing guidelines); cefazolin may be substituted for nafcillin or oxacillin in patients with non–immediate-type hypersensitivity reactions to penicillins.
Plus				
Rifampin	900 mg per 24 h IV or orally in 3 equally divided doses	≥6		
Plus				
Gentamicin†	3 mg/kg per 24 h IV or IM in 2 or 3 equally divided doses	2		

In patients with PVE due to methicillin-susceptible staphylococci, (flu)cloxacillin or cefazolin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:[264,314,316–318,320]			
Adult antibiotic dosage and route			
(Flu)cloxacillin[c]	12 g/day i.v. in 4–6 doses	I	B
Cefazolin	6 g/day i.v. in 3 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

Treatment of methicillin-susceptible staphylococcal prosthetic valve endocarditis



[1]6 weeks after the first day of effective therapy: negative blood culture in the case of initial positive blood culture or day of surgery if valve cultures are positive.
[2]The choice of cefazolin *vs* (cl)oxacillin should follow the same rules than for NVE

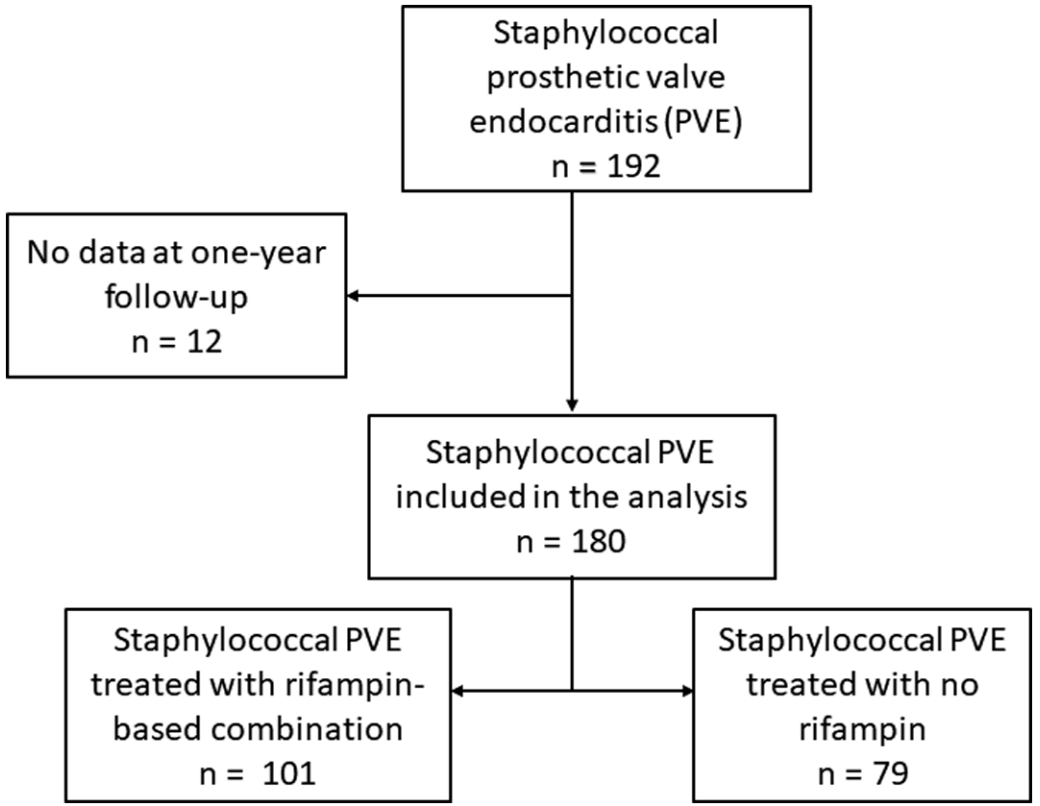
Baddour Circulation 2015, Delgado Eur Heart J 2023, Le Moing ID now 2025

Is Rifampin Use Associated With Better Outcome in Staphylococcal Prosthetic Valve Endocarditis? A Multicenter Retrospective Study

Clinical Infectious Diseases

MAJOR ARTICLE

- Observational study
- Staphylococcal PVE
- 2000-2018
- 3 centers : Brest Nantes Rennes
- Primary outcome : 1 year all caused mortality



56.1% of patients were treated with rifampicin

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)	Odds Ratio (95% CI)	*P* Value
Mortality					
In-hospital mortality	42 (23.6)	26 (25.7)	16 (20.3)	1.4 (.67–2.77)	.49
6-month mortality	58 (32.6)	36 (35.6)	22 (27.8)	1.4 (.76–2.72)	.34
1-year mortality	63 (35.4)	38 (37.6)	25 (31.6)	1.2 (.66–2.28)	.62
Relapse	13 (7.3)	6 (5.9)	7 (8.9)	.64 (.21–2.02)	.65
Vitamin K antagonist imbalance during endocarditis	21 (33.9)	15 (42.9)	6 (22.2)	2.63 (.85–8.11)	.15
Bleeding complication	23 (12.9)	13 (12.8)	10 (12.7)	1.02 (.42–2.46)	.85
Length of stay, days	37 ± 17.6	42.3 ± 18.6	31.3 ± 14.0	…	<.0001

Quantitative variables are expressed as mean ± standard deviation; qualitative variables are expressed by numbers (%).

Abbreviation: CI, confidence interval.

	Univariate				Multivariate	
Variable	Dead During the 1-year Follow-up (n = 63)	Alive at 1 year (n = 117)	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Definite endocarditis (modified Duke criteria)	57 (90.5)	92 (78.6)	2.38 (.91–6.19)	.11	7.15 (1.47–34.77)	.018
Cerebral emboli	27 (42.9)	26 (22.2)	2.62 (1.35–5.19)	.006	2.95 (1.30–6.70)	.009
Staphylococcus aureus	45 (71.4)	69 (59.0)	1.74 (.90–3.36)	.14		
Methicillin-resistant *S. aureus*	9 (14.3)	8 (6.8)	2.27 (.83–6.22)	.17	6.04 (1.34–27.26)	.019
Bleeding complication	6 (9.5)	12 (10.3)	.92 (.33–2.59)	.92		
Rifampin treatment	38 (60.3)	63 (53.8)	1.30 (.70–2.42)	.50	.90 (.38–2.11)	.81

Quantitative variables are expressed as mean ± standard deviation or median (interquartile range) as appropriate; qualitative variables are expressed by numbers (%).

A benefit in patient with non operated PVE?

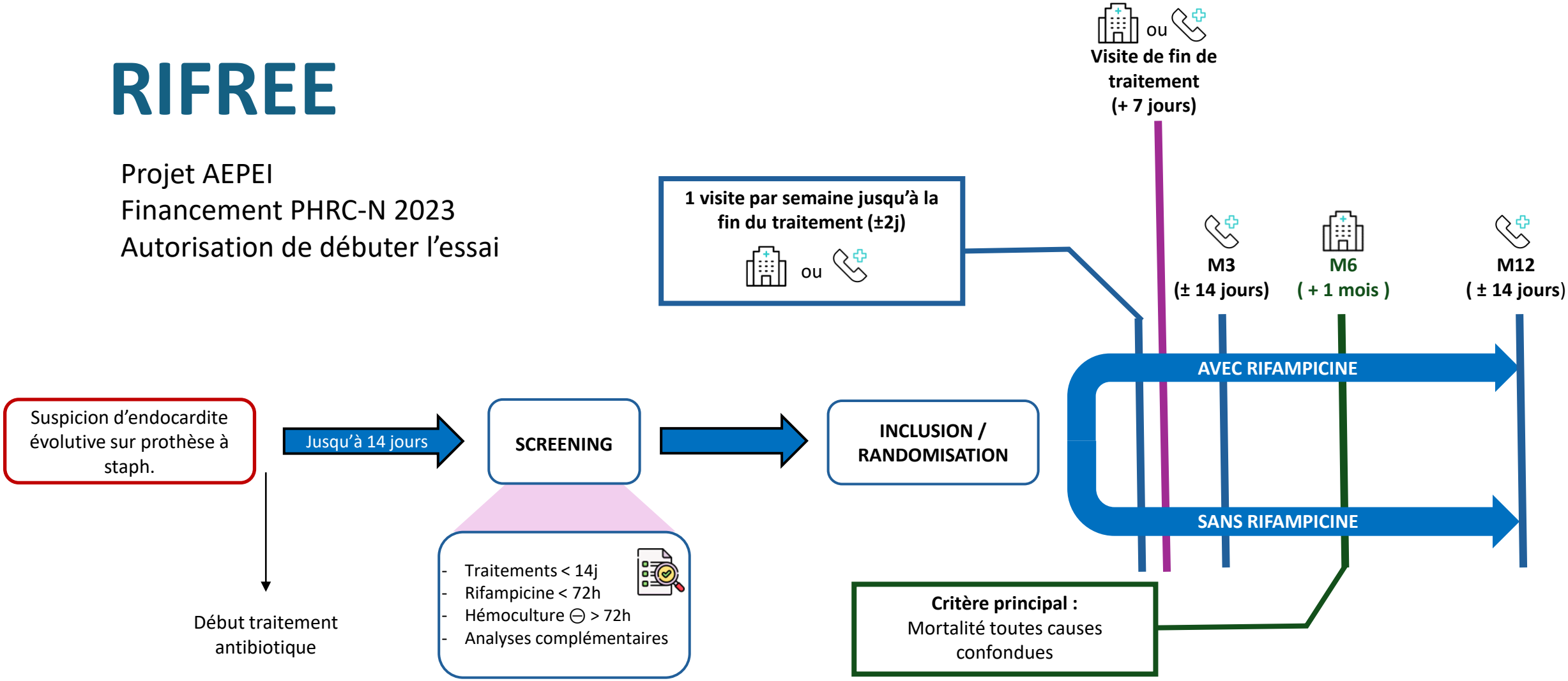
Supplementary table 4. Univariate analysis of outcomes in 128 patients with staphylococci prosthetic valve endocarditis without valve surgery

Variable	Total (n=128)	Rifampin-based combination (n=66)	No rifampin (n=62)	Odd-Ratio (CI 95%)	*P* Value
Mortality					
In-hospital mortality	29 (22.7)	18 (27.3)	11 (17.7)	1.73 (0.74-4.06)	.28
One-month mortality	37 (28.9)	21 (31.8)	16 (25.8)	1.34 (0.62-2.90)	.58
Three-month mortality	39 (30.5)	23 (34.8)	16 (25.8)	1.54 (0.72-3.29)	.36
Six-month mortality	44 (34.4)	27 (40.9)	17 (27.4)	1.83 (0.87-3.85)	.16
One-year mortality	49 (38.3)	29 (43.9)	20 (32.3)	1.65 (0.80-3.39)	.24
Relapse	12 (9.4)	6 (9.0)	6 (9.7)	0.93 (0.28-3.07)	.93
Vitamin K antagonist imbalance during endocarditis	16 (12.5)	11 (16.7)	5 (8.6)	2.3 (0.74-7.00)	.23
Bleeding complication	15 (11.7)	7 (10.6)	8 (12.9)	0.80 (0.27-2.36)	.90
Length of stay, days	35.2 ± 17.1	39.7 ± 18.9	30 4 ± 13.6	-	.007

Quantitative variables are expressed as mean +/- standard deviation, qualitative variables are expressed by numbers (%)

RIFREE

Projet AEPEI
Financement PHRC-N 2023
Autorisation de débuter l'essai



Contents lists available at ScienceDirect

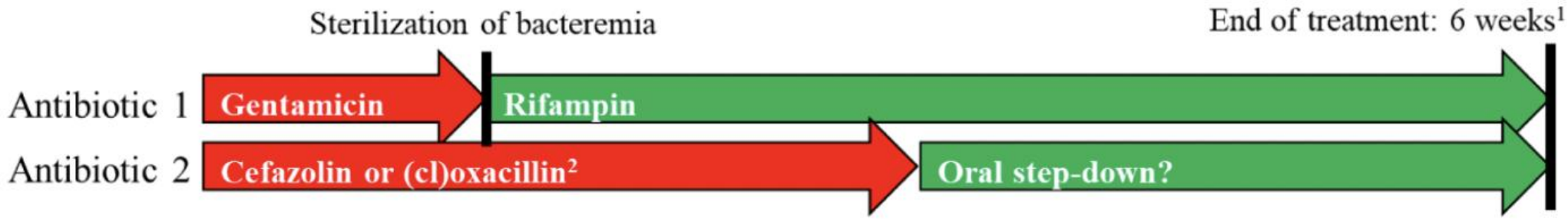
Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

Treatment of methicillin-susceptible staphylococcal prosthetic valve endocarditis



[1]6 weeks after the first day of effective therapy: negative blood culture in the case of initial positive blood culture or day of surgery if valve cultures are positive.
[2]The choice of cefazolin *vs* (cl)oxacillin should follow the same rules than for NVE

Table 1
Duration (in weeks) of aminoglycoside treatment for the most frequent aetiologies of infective endocarditis

	European guideline (ESC 2015)	American guidelines (AHA 2015)	Proposal (this review)
***Staphylococcus* spp.**			
Native valve	0	0	0
Prosthetic valve	2	2	<1 (until BC are negative or surgery) followed by rifampicin initiation

Lebeaux *et al.* Clin microbiol infect 2020

Take-home messages

Probabiliste:

- Viser le SAMS+++ et couverture strepto entérocoque
- Amoxicilline Céfazoline
- Cut off de 1 an PVE
- CEF DPC PVE < 1 an

Bétalactamines:

- Privilégier ASP et Céfazoline+++
- Y compris:
  - En probabiliste
  - en cas de bithérapie avec aminoside
- Switch en cas d'échec

Rifampicine:

- Uniquement PVE
- Recommandée en l'absence de contre-indication en attendant l'essai RIFREE
- Attendre la stérilisation de la bactériémie avant de l'introduire

Question 8 : quel traitement auriez-vous introduit en cas de résistance à la méticilline et en l'absence de signe de sepsis?

- Vancomycine
- Vancomycine gentamicine
- Daptomycine
- Daptomycine gentamicine
- Daptomycine ceftaroline
- Daptomycine ceftaroline gentamicine

Quel traitement en cas de résistance à la méticilline?

- Etude de non-infériorité en 2006
- Bactériémie et endocardite/SAMS et SARM
- Essai randomisé:
  - 120 patients : Dapto seule
  - 115 patients traitements standard (ASP/VAN + Genta)
- CJP : succès thérapeutique à J42

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 17, 2006 VOL. 355 NO. 7

Daptomycin versus Standard Therapy for Bacteremia and Endocarditis Caused by *Staphylococcus aureus*

Table 2. Outcomes 42 Days after the End of Therapy, According to Prespecified Diagnostic Categories.

Criteria	Daptomycin	Standard Therapy	Absolute Difference in Success Rates
	no. of patients/total no. (%)		*% (95% CI)**
Overall success (intention to treat)	53/124 (42.7)	48/122 (39.3)	3.4 (–8.9 to 15.7)
Overall success (modified intention to treat)	53/120 (44.2)	48/115 (41.7)†	2.4 (–10.2 to 15.1)
Success according to methicillin susceptibility of *Staphylococcus aureus*‡			
MSSA	33/74 (44.6)	34/70 (48.6)	–4.0 (–20.3 to 12.3)
MRSA	20/45 (44.4)	14/44 (31.8)	12.6 (–7.4 to 32.6)

Fowler *et al.* NEJM 2006

Si CMI à la vancomycine > 1 mg/L

Early Use of Daptomycin Versus Vancomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia With Vancomycin Minimum Inhibitory Concentration >1 mg/L: A Matched Cohort Study

Kyle P. Murray,[1] Jing J. Zhao,[1] Susan L. Davis,[3] Ravina Kullar,[3] Keith S. Kaye,[2] Paul Lephart,[4] and Michael J. Rybak[1,2,3]

- Etude cas contrôle daptomycine *vs.* Vancomycine
- Bactériémie à SARM avec CMI Vanco > 1 mg/L
- CJP composite: échec clinique (mortalité à J30 et/ou bactériémie supérieure à 7 jours)

Table 2. Patient Outcomes

	DAP (n = 85)	VAN (n = 85)	*P* Value
Clinical failure[a]	17 (20.0%)	41 (48.2%)	<.001
Mortality at 30 d	3 (3.5%)	11 (12.9%)	.047
Persistent bacteremia	16 (18.8%)	36 (42.4%)	.001
Duration of bacteremia, d[b]	3 (2–5)	5 (3–8)	.003
Length of stay, d[b]	11 (8–18)	12 (8–17)	.532
Duration of treatment, d[b]	10 (8–17)	9 (6–16)	.324
Recurrence of MRSA bacteremia within 30 d[c]	0 (0.0%)	3 (4.1%)	.104
Readmission within 30 d[c]	16 (19.5%)	19 (25.3%)	.381
Total hospital charges, 2011 US dollars	$95 244 ($60 637–$156 020)	$86 504 ($48 030–$183 008)	0.643
Total medication charges, 2011 US dollars	$26 841 ($16 820–$39 659)	$15 848 ($7988–$29 240)	<0.001
Total laboratory charges, 2011 US dollars	$9235 ($6332–$14 456)	$10 276 ($5827–$17 206)	0.857

Murray *et al.* Clin Infect Dis 2013

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy
CLINICAL THERAPEUTICS
October 2016 Volume 60 Issue 10
https://doi-org.proxy.insermbiblio.inist.fr/10.1128/aac.00227-16

Quelle que soit la CMI?

- Etude de cohorte
- Bactériémies à SARM
- 2010-2015 USA
- Score de propension
- CJP : mortalité J30 et/ou bactériémie persistante à J7 et/ou modification du traitement

Daptomycin Improves Outcomes Regardless of Vancomycin MIC in a Propensity-Matched Analysis of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

TABLE 1 Baseline demographics and clinical characteristics[a] (Table view)

	Result for patients receiving:		
Characteristic	VAN (n = 131)	DAP (n = 131)	P value
Median (IQR) age (yr)	57.0 (46.0–70.0)	56.0 (43.0–61.0)	0.095
Median (IQR) Pitt bacteremia score	3 (2–3)	3 (2–3)	0.933
Median (IQR) baseline CR_{CL} (ml/min)	61.6 (37.9–84.0)	60.4 (40.3–82.5)	0.885
No. (%) of patients with:			
AKI on admission	45 (34.4)	44 (33.6)	0.896
History of DM	43 (32.8)	50 (38.2)	0.366
HIV/AIDS	9 (6.9)	10 (7.6)	0.812
CHD	22 (16.8)	20 (15.3)	0.736
i.v. drug use	34 (26.0)	35 (26.7)	0.888
CKD (not HD)	16 (12.2)	24 (18.3)	0.169
Liver disease	21 (16.0)	30 (22.9)	0.160
Antibiotic use in past 30 days	33 (25.2)	27 (20.6)	0.262
Vancomycin use in past 30 days	12 (9.2)	7 (5.3)	0.341
Hospitalization in past year	66 (50.4)	65 (49.6)	0.902
Surgery in past 30 days	5 (3.8)	14 (10.7)	0.032
MRSA infection in past year	7 (5.3)	16 (12.2)	0.049
No. (%) of patients with the following primary site of infection:			0.572
Bone/joint	27 (20.6)	38 (29.0)	
Skin/soft tissue	33 (25.2)	30 (22.9)	
Deep abscess	14 (10.7)	14 (10.7)	
Infective endocarditis	23 (17.6)	25 (19.1)	
i.v. catheter	15 (11.5)	10 (7.6)	
Other	19 (14.5)	14 (10.7)	

[a] AKI, acute kidney injury; DAP, daptomycin; DM, diabetes mellitus; CHD, congestive heart disease; CKD, chronic kidney disease; CR_{CL}, creatinine clearance; HD, hemodialysis; IQR, interquartile range; VAN, vancomycin.

Claeys *et al.* AAC 2016

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy
CLINICAL THERAPEUTICS
October 2016 Volume 60 Issue 10
https://doi-org.proxy.insermbiblio.inist.fr/10.1128/aac.00227-16

Quelle que soit la CMI?

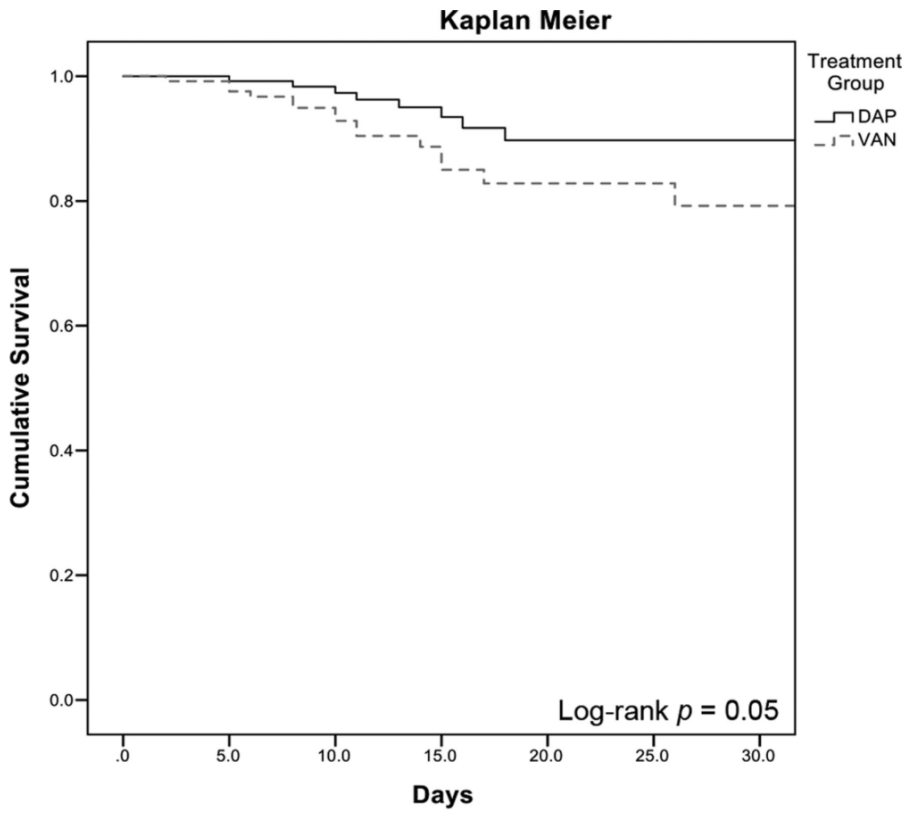


FIG 2 Kaplan-Meier analysis of probability of 30-day survival for vancomycin-treated versus daptomycin-treated patients.

Daptomycin Improves Outcomes Regardless of Vancomycin MIC in a Propensity-Matched Analysis of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

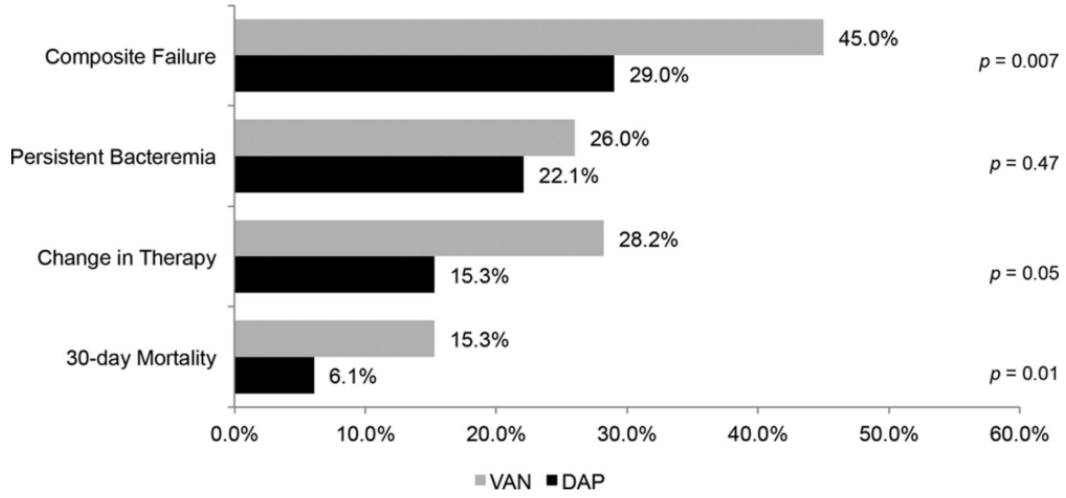


FIG 1 Clinical failure by treatment group. VAN, vancomycin; DAP, daptomycin.

9% de néphrotoxicité dans le groupe vanco
1,5% d'élévation de CPK dans le groupe DPC

Claeys *et al.* AAC 2016

Quel traitement en cas de résistance à la méticilline?

- Etude de non-infériorité en 2006
- Essai random
  - 120 patient
  - 115 patient (ASP/VAN +
- CJP : succès t

Therapy for Bacteremia
y Staphylococcus aureus

Pour 6 des 19 échecs sous daptomycine : augmentation des CMI (d'un facteur 4 minimum)
Que des patients ayant des bactériémies compliquées

o Prespecified Diagnostic Categories.

cin	Standard Therapy	Absolute Difference in Success Rates
patients/total no. (%)		*% (95% CI)**
2.7)	48/122 (39.3)	3.4 (–8.9 to 15.7)
4.2)	48/115 (41.7)†	2.4 (–10.2 to 15.1)
4.6)	34/70 (48.6)	–4.0 (–20.3 to 12.3)
4.4)	14/44 (31.8)	12.6 (–7.4 to 32.6)

Fowler *et al.* NEJM 2006

Comment protéger la daptomycine?

High-Dose Daptomycin plus Fosfomycin Is Safe and Effective in Treating Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* Endocarditis

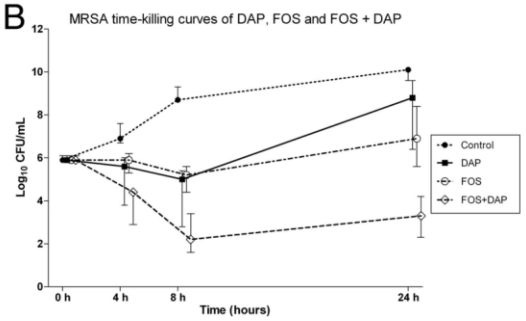


FIG 1 Time-kill curves of fosfomycin (FOS), daptomycin (DAP), and FOS plus DAP for 7 MSSA (A) and 7 MRSA (B) strains. Each result is expressed as a median and the interquartile range. Antibiotic concentrations were tested at the MIC, except for 2 MSSA strains (1112 and P7), where DAP was tested at 0.5 times the MIC.

Clinical Data on Daptomycin plus Ceftaroline versus Standard of Care Monotherapy in the Treatment of Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Matthew Geriak[a], Fadi Haddad[b], Khulood Rizvi[c], Warren Rose[d], Ravina Kullar[e], Kerry LaPlante[f], Marie Yu[b], Logan Vasina[a], Krista Ouellette[a], Marcus Zervos[c], Victor Nizet[f], George Sakoulas[a,g]

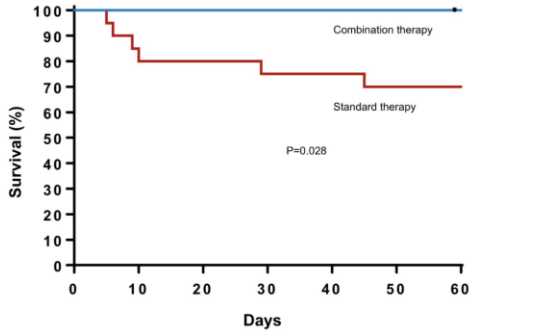


FIG 1 Survival analysis of patients receiving daptomycin plus ceftaroline compared with those receiving standard of care in a prospective randomized study. Day 0 represents the day of first positive blood culture. Significance of mortality difference at 30 days ($P = 0.048$) and 60 days ($P = 0.028$).

- Et à posologie plus élevée que dans l'étude de Fowler: 10 mg/kg/J

METHODS

We randomly assigned 124 patients with *S. aureus* bacteremia with or without endocarditis to receive 6 mg of daptomycin intravenously per kilogram of body weight

Recommandation SPILF 2025

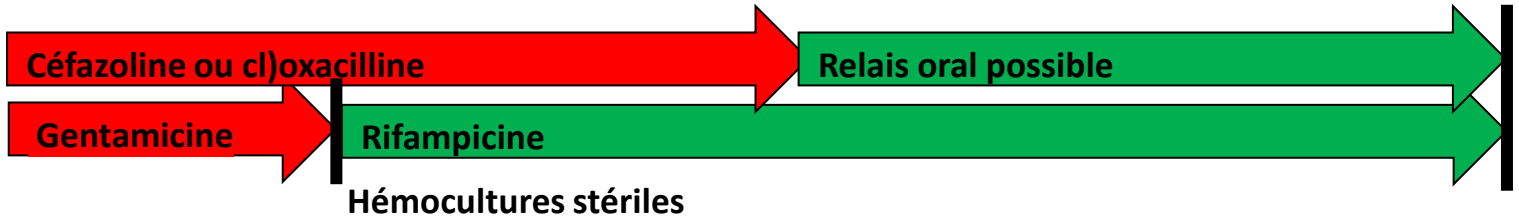
Methicillin-resistant staphylococci		
Without allergy to β-lactams	Daptomycin with ceftaroline or Daptomycin with fosfomycin	Duration of the combination therapy: as long as the bacteremia lasts and for a maximum of 7 days from the 1st negative blood culture.
Late severe allergy to penicillin or allergy to cephalosporins	Daptomycin with fosfomycin	
	or Vancomycin	If vancomycin MIC ≤ 1 mg/L.

Guidelines (see Table 5):

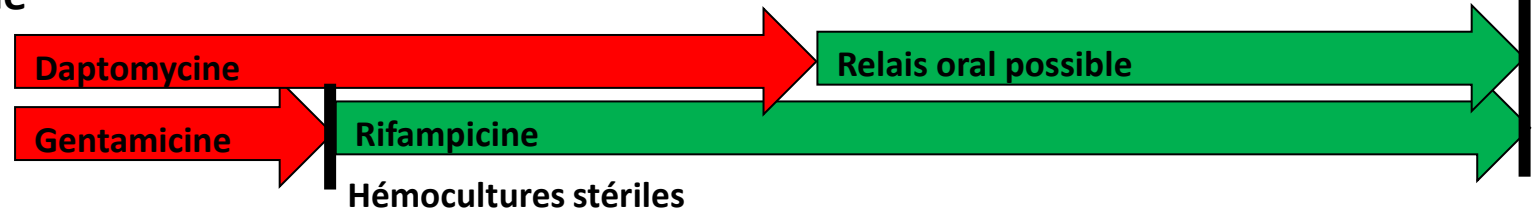
- As a first-line treatment, a dual therapy: daptomycin with another antibiotic.
  - o Daptomycin should be prescribed at 10 mg/kg/day, with monitoring for toxicity (rhabdomyolysis, eosinophil pneumonia).
  - o The "best" companion to daptomycin appears to be ceftaroline. Fosfomycin may also be used.
  - o The duration of dual therapy is unknown, but we suggest at least as long as the bacteremia persists and for a maximum of 7 days from the first negative blood culture.
  - o In the event of persistent bacteremia on daptomycin, it is wise to monitor the daptomycin MIC (risk of daptomycin-resistant mutant selection).
- Although vancomycin is the oldest and most "validated" option, it should be considered essentially as an alternative, for example to the combination of daptomycin and ceftaroline in case of late severe allergy to penicillin, provided that vancomycin MIC is ≤ 1 mg/L. Serum drug levels and renal function must be monitored.

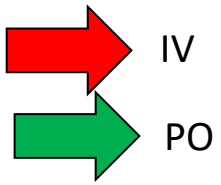
Antibiothérapie des EI staphylococciques sur valves prothétiques

Staphylocoque sensible à la méticilline — **6 semaines ***



Staphylocoque résistant à la méticilline ou allergie grave aux Béta-Lactamines si staphylocoque sensible à la méticilline — **6 semaines ***





* Durée de 6 semaines / 1ère hémoculture négative ou du jour de la chirurgie si les cultures de valve sont positives

Entérocoques

13-18% des endocardites infectieuses

Incidence en augmentation

Sujets agés/Tavi

Habib Eur Hear J 2019; Fernandez-Hidalgo Future microbiol 2020;
Olmos J Am Coll Cadiol 2017; Chirouza Clin Microbiol Infect 2013; Khan Plos One 2020

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

Nuria Fernández-Hidalgo,[1] Benito Almirante,[1] Joan Gavaldà,[1] Mercè Gurgui,[2] Carmen Peña,[3] Arístides de Alarcón,[4] Josefa Ruiz,[5] Isidre Vilacosta,[6] Miguel Montejo,[7] Nuria Vallejo,[8] Francisco López-Medrano,[9] Antonio Plata,[10] Javier López,[11] Carmen Hidalgo-Tenorio,[12] Juan Gálvez,[13] Carmen Sáez,[14] José Manuel Lomas,[15] Marco Falcone,[18] Javier de la Torre,[16] Xavier Martínez-Lacasa,[17] and Albert Pahissa[1]

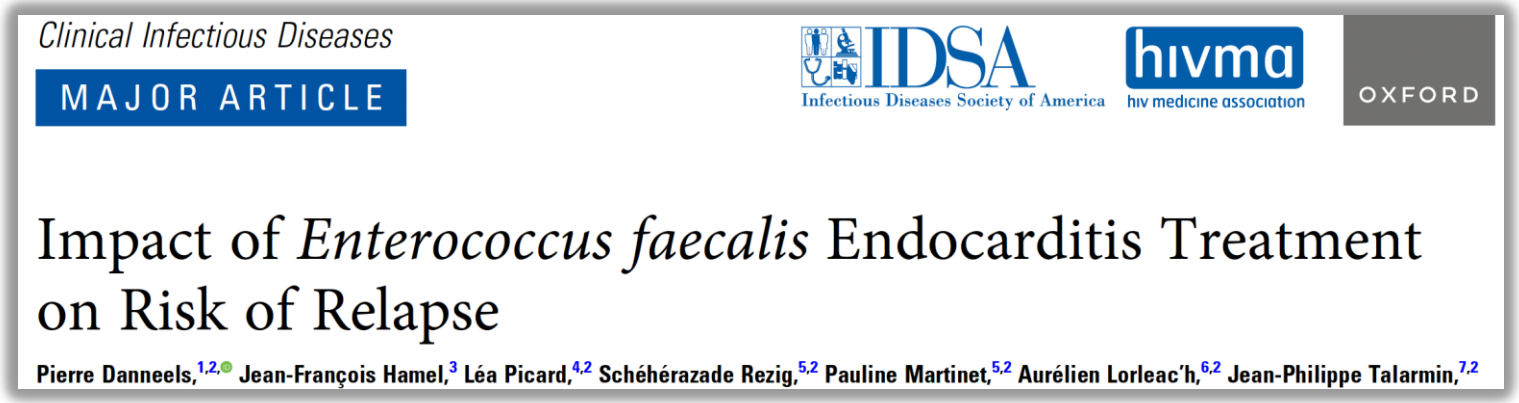
Table 3. Outcomes of 246 Episodes of *Enterococcus faecalis* Infective Endocarditis Treated With Ampicillin Plus Ceftriaxone or Ampicillin Plus Gentamicin

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Failures			
Death during treatment	35 (22%)	18 (21%)	0.81
Death during 3-mo follow-up	13 (8%)	6 (7%)	0.72
Adverse effects requiring treatment withdrawal	2 (1%)	22 (25%)	<0.001
Treatment failure requiring change of antimicrobials	2 (1%)	2 (2%)	0.54
Relapse	3/124 (3%)	3/69[a] (4%)	0.67

[a] These patients had received 28, 26, and 42 days of ampicillin plus gentamicin, respectively.

Table 2. Treatment and In-Hospital Mortality According to Antimicrobial Combination in 246 Episodes of *Enterococcus faecalis* Infective Endocarditis Treated With Ampicillin Plus Ceftriaxone or Ampicillin Plus Gentamicin

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Duration of antimicrobial treatment, d, median (IQR)			
Overall, in survivors	42 (39–46)	42 (35–44)	.122
Days until surgery	11 (6–22)	9 (3–22)	.34
Adverse events			
Overall	14 (9%)	38 (44%)	<.001
Overall obliging to withdraw treatment	2 (1%)	22 (25%)	<.001
Drug stopped due to rash/fever	1 (0.6%)	0	.46
Drug stopped due to leukopenia	1 (0.6%)	0	.46
Drug stopped due to new renal failure	0	20 (23%)	<.001
Drug stopped due to vestibular toxicity	0	2 (2%)	.055



- Objectif: évaluer l'impact du traitement sur les rechutes.
- Design:
  - Etude rétrospective multicentrique
  - 14 hôpitaux français
  - Diagnostic d'EI à E faecalis entre 2015 et 2019
  - Critère de jugement principal : rechute à 1 an

- Définition:
  - Rechutes: Hc même germe < 1 an
  - Réinfection: Hc même germe > 1 an
  - Traitement:
    - AG Amoxicilline gentamicine
    - AC amoxicilline ceftriaxone
    - AG/AC traitement séquentiel
    - A amoxicilline

Danneels *et al.* CID 2022

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Impact of *Enterococcus faecalis* Endocarditis Treatment on Risk of Relapse

Pierre Danneels,[1,2] Jean-François Hamel,[3] Léa Picard,[4,2] Schéhérazade Rezig,[5,2] Pauline Martinet,[5,2] Aurélien Lorleac'h,[6,2] Jean-Philippe Talarmin,[7,2]

- 279 patients
- Age médian 74 ans
- 42% PVE
- 32% de chirurgie
- Traitement:
  - AC 41%
  - AG 30%
  - AC/AG 23%
  - A 3%
- AC : plus agés, plus comorbides, plus d'IRC (p<0.01)

Variable	Total (n = 279)	A-G Combination (n = 83)	A-C Combination (n = 114)	A-G/A-C Combinations (n = 63)	Amoxicillin (n = 9)	Other Treatment (n = 10)
Demographic features and underlying conditions						
Age, y	74 [66–83]	71 [61–79]	78 [67–86]	73 [67–79]	71 [67–81]	81.5 [74–85]
Gender, male	221 (79.2)	70 (84.3)	86 (75.4)	51 (81.0)	5 (55.6)	9 (90.0)
Type of IE and underlying cardiac condition						
Native valve IE	162 (58.1)	52 (62.7)	67 (58.8)	31 (49.2)	6 (66.7)	6 (60.0)
Prosthetic valve IE	117 (41.9)	31 (37.3)	47 (41.2)	32 (50.8)	3 (33.3)	4 (40.0)
TAVI	35 (12.5)	5 (6.0)	22 (19.3)	5 (7.9)	1 (11.1)	2 (20.0)
ICD	55 (19.7)	12 (14.5)	24 (21.1)	16 (25.4)	0 (0.0)	3 (30.0)
Previous endocarditis	23 (8.2)	6 (7.2)	9 (7.9)	7 (11.1)	1 (11.1)	0 (0.0)
Duration of symptoms before diagnosis, d	10 [2–30]	9 [1–30]	14 [3–33]	12 [7–30]	3 [1–8]	14.5 [7–30]
Clinical complication	216 (77.4)	60 (72.3)	90 (78.9)	53 (84.1)	5 (55.6)	8 (80.0)
Acute heart failure	116 (41.6)	24 (28.9)	54 (47.4)	31 (49.2)	3 (33.3)	4 (40.0)
Heart conduction disturbance	21 (7.5)	8 (9.6)	7 (6.1)	6 (9.5)	0 (0.0)	0 (0.0)
Acute kidney injury	83 (29.7)	15 (18.1)	35 (30.7)	27 (42.9)	1 (11.1)	5 (50.0)
Systemic embolic event	140 (50.2)	41 (49.4)	56 (49.1)	34 (54.0)	3 (33.3)	6 (60.0)
Vertebral osteomyelitis	36 (12.9)	7 (8.4)	20 (17.5)	5 (7.9)	1 (11.1)	3 (30.0)
CNS embolism	63 (22.6)	24 (28.9)	20 (17.5)	18 (28.6)	0 (0.0)	1 (10.0)
Bleeding	30 (10.8)	7 (8.4)	8 (7.0)	11 (17.5)	0 (0.0)	4 (40.0)
Echocardiographic findings						
TEE performed	214 (76.7)	72 (86.7)	81 (71.1)	50 (79.4)	6 (66.7)	5 (50.0)
Vegetation	222 (79.6)	72 (86.7)	82 (71.9)	53 (84.1)	8 (88.9)	7 (70.0)
Aortic	141 (50.5)	51 (61.4)	44 (38.6)	34 (54.0)	7 (77.8)	5 (50.0)
Mitral	100 (35.8)	29 (34.9)	43 (37.7)	25 (39.7)	1 (11.1)	2 (20.0)
Tricuspid	14 (5.0)	2 (2.4)	9 (7.9)	2 (3.2)	1 (11.1)	0 (0.0)
Pulmonary	2 (0.7)	1 (1.2)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Multivalvular	33 (11.8)	11 (13.3)	13 (11.4)	8 (12.7)	1 (11.1)	0 (0.0)
ICD lead associated endocarditis	15 (5.4)	5 (6.0)	5 (4.4)	5 (7.9)	0 (0.0)	0 (0.0)

Danneels *et al.* CID 2022

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Impact of *Enterococcus faecalis* Endocarditis Treatment on Risk of Relapse

Pierre Danneels,[1,2] Jean-François Hamel,[3] Léa Picard,[4,2] Schéhérazade Rezig,[5,2] Pauline Martinet,[5,2] Aurélien Lorleac'h,[6,2] Jean-Philippe Talarmin,[7,2]

- 26,5% de mortalité
- 9,3% de rechute (15,7% si on inclut les patients non décédés et ayant des données de suivi à un an).
- Monothérapie par amoxicilline significativement associé à un risque de rechute
- Tendance pour un meilleur résultat avec le traitement séquentiel

Table 3. Outcome of 279 Cases of Endocarditis Due to *E. faecalis* According to the Treatment Received and Those Who Received a Complete Treatment

Outcome	Total (n = 279)	A-G combination (n = 83)	A-C combination (n = 114)	A-G/A-C combinations (n = 63)	Amoxicillin (n = 9)	Other treatment (n = 10)
All patients						
Mortality						
At the end of treatment	41 (14.7)	8 (9.6)	19 (16.7)	9 (14.3)	3 (33.3)	2 (20.0)
At 6 m	65 (23.3)	11 (13.3)	36 (31.6)	13 (20.6)	3 (33.3)	2 (20.0)
At 1 y	74 (26.5)	15 (18.1)	37 (32.5)	16 (25.4)	3 (33.3)	3 (30.0)
Relapse						
At 6 m	22 (7.9)	9 (10.8)	10 (8.8)	1 (1.6)	2 (22.2)	0 (0.0)
At 1 y	26 (9.3)	9 (10.8)	12 (10.5)	2 (3.2)	3 (33.3)	0 (0.0)
All relapses	28 (10.0)	9 (10.8)	13 (11.4)	2 (3.2)	3 (33.3)	1 (10.0)
Patients with complete treatment						
Mortality						
At the end of treatment	33/193 (17.1)	6/49 (12.2)	17/85 (20.0)	9/52 (17.3)	1/6 (16.7)	…
At 6 m	48/193 (24.9)	7/49 (14.3)	28/85 (32.9)	12/52 (23.1)	1/6 (16.7)	…
At 1 y	53/193 (27.5)	10/49 (20.4)	29/85 (34.1)	13/52 (25.0)	1/6 (16.7)	…
Relapse						…
At 6 m	16/193 (8.3)	4/49 (8.2)	9/85 (10.6)	1/52 (1.9)	2/6 (33.3)	…
At 1 y	19/193 (9.8)	4/49 (8.2)	10/85 (11.8)	2/52 (3.8)	3/6 (50.0)	…
All relapses	19/193 (9.8)	4/49 (8.2)	10/85 (11.8)	2/52 (3.8)	3/6 (50.0)	…

Qualitative variables are expressed by no. (%). Percentages were calculated with all patients in the column as the denominator, except for variables with missing data, for which the number of patients with available data is mentioned.
Abbreviation: *E. faecalis*, *Enterococcus faecalis*.

Danneels *et al.* CID 2022

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Impact of *Enterococcus faecalis* Endocarditis Treatment on Risk of Relapse

Pierre Danneels,[1,2] Jean-François Hamel,[3] Léa Picard,[4,2] Schéhérazade Rezig,[5,2] Pauline Martinet,[5,2] Aurélien Lorleac'h,[6,2] Jean-Philippe Talarmin,[7,2]

Caractéristiques des rechutes:

- Tardives
- Cultures positives
- Souvent asymptomatiques

Devenir:

- Mortalité 28,6%
- 27% d'antibiothérapie suppressive
- 11% de rechutes

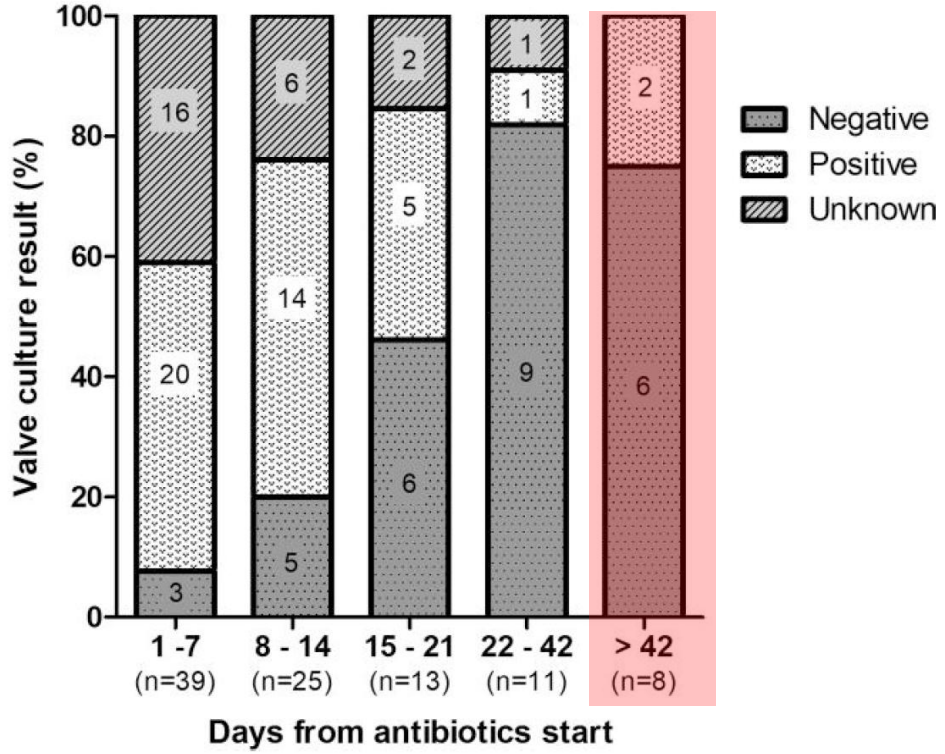


Figure 1. Valve culture result according to the time between the start of antibiotics and surgery.

Table 4. Characteristics, Management, and Outcome of 28 Patients Who Experienced Relapse

Characteristics	Value n = 28
Time from EFIE diagnosis to relapse	
<3 m	10 (35.7)
3–6 m	12 (42.9)
6–12 m	4 (14.3)
12–24 m	1 (3.6)
>24 m	1 (3.6)
Presentation at relapse diagnosis	
Asymptomatic	8/27 (29.6)
Systematic blood culture control	6/27 (22.2)
Delayed surgery with positive valve culture	2/27 (7.4)
Symptomatic	19/27 (70.4)
Fever/sepsis	19/27 (70.4)
Cardiac failure	5/27 (18.5)
Systemic embolic event	7/27 (25.9)
Management of relapse	
Surgery	7 (25.0)
Antibiotic treatment	
A-C	12/26 (46.2)
A-G	5/26 (19.2)
A-G/A-C	4/26 (15.4)
Glycopeptide	4/26 (15.4)
Suppressive antibiotic therapy	7/26 (26.9)
Outcome of relapse	
Endocarditis-related death	8 (28.6)
Cure	20 (71.4)
Relapse	3 (10.7)

All results are no. of patients/no. of patients with available data (%). Percentages were calculated with all patients in the column as the denominator, except for variables with missing data, for which the number of patients with available data is mentioned.
Abbreviation: EFIE, *Enterococcus faecalis* infective endocarditis.

Danneels *et al.* CID 2022

Therapeutic Issues in Relapsing *Enterococcus faecalis* Endocarditis

Guillermo Cuervo,[1] Carlos Báguena,[2] Jaume Llopis,[3] Juan M. Pericàs,[4] Anders Dahl,[5] Vivian Chu,[6] and José M. Miró[1,a]

[1]Department of Infectious Diseases, Hospital Clinic—IDIBAPS, University of Barcelona, Barcelona, Spain;

« In our opinion, the finding from Danneels and colleagues' work that has a greater potential to influence clinical practice is not related to antibiotic treatment but rather to cardiac surgery. »

=> 1 rechute sur les 90 patients opérés (traitement par une monothérapie d'amoxicilline contre 25 sur les 189 parmi les patients non opérés (P=.01).

Table 1. Comparison of Relapse Rates Between Different National and International Multicentric Cohorts

Cohort	Antibiotic Treatment	Overall Relapse Rate, n/Total N (%; 95% CI)	Relapse/No Surgery, n/Total N (%; 95% CI)	Relapse/Surgery Performed, n/Total N (%; 95% CI)	*P*
French cohort [1]	A + G	9/83 (10.84%; 4.15–17.53)[a]	20/172 (11.63%; 6.84–16.42)	0/98 (.00%; .00–.04)	.001
	A + C	10/114 (8.77%; 3.58–13.96)[a]			
	A + G → A + C	1/63 (1.59%; .00–4.67)[a]			
Danish cohort [4]	A + G[b]	5/84 (5.95%; .89–11.01)[c]	4/55 (7.27%; .41–14.14)	1/29 (3.45%; .00–10.09)	.481
Spanish cohort [5]	A + G or A + C	16/468 (3.42%; 1.77–5.07)[a]	13/276 (4.71%; 2.21–7.21)	3/192 (1.56%; .00–3.32)	.066
ICE cohort[d]	A + G or A + C	13/852 (1.52%; .70–2.35)[a]	11/512 (2.15%; .89–3.40)	2/340 (.59%; .00–1.40)	.069

Abbreviations: A, amoxicillin/ampicillin; C, ceftriaxone; CI, confidence interval; G, gentamicin; ICE, International Collaboration on Endocarditis.

[a]Six-month relapse.

[b]Two different gentamicin regimens

[c]One-year relapse.

[d]Unpublished data.

NB: 17% de rechute dans les PVE à entérocoques non opérés (Lecomte *et al.* CID 2021)

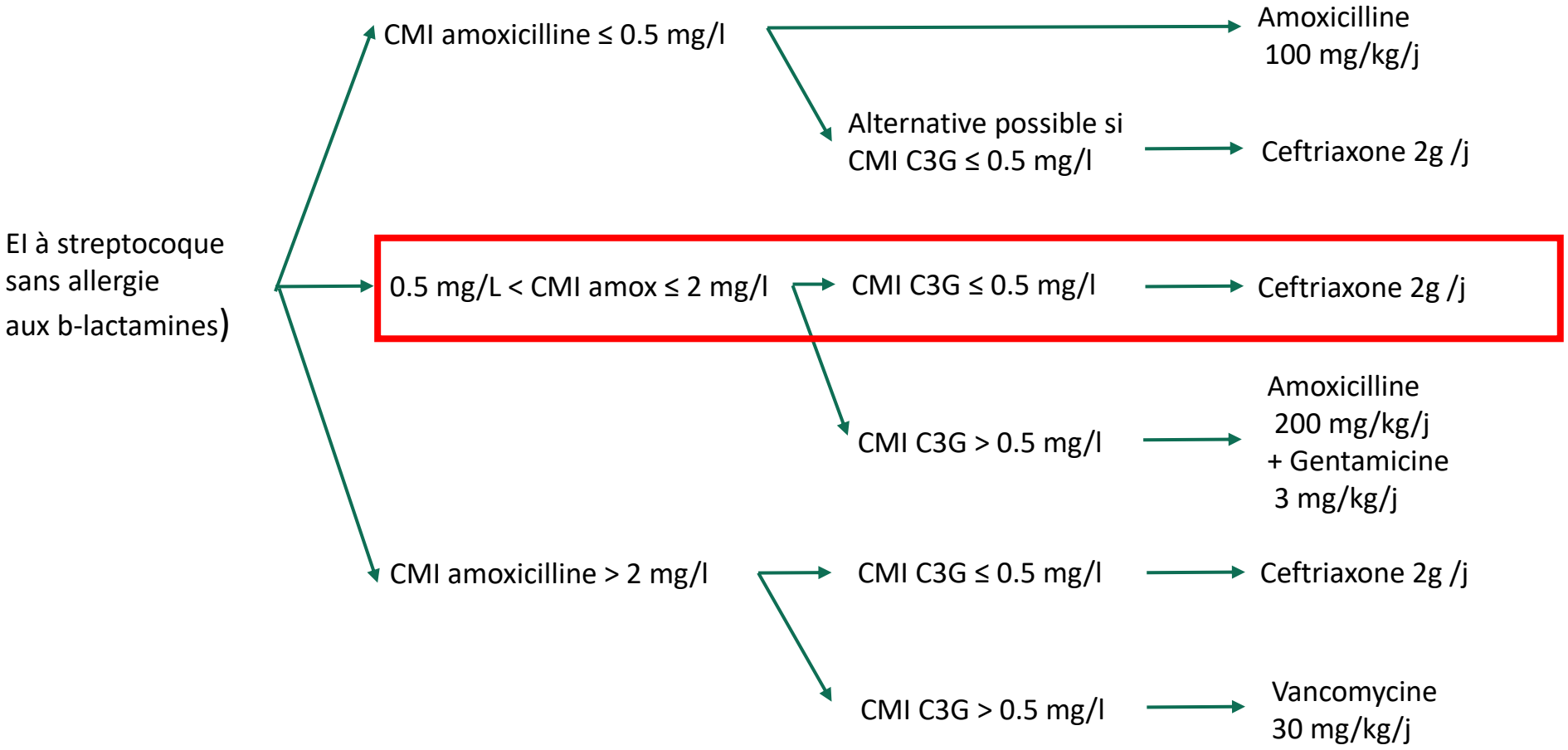
Antibiothérapie des EI à entérocoques

Enterococcus faecalis		
	Schéma d'antibiothérapie par voie IV	Durée
Sans allergie aux béta-lactamines	Amoxicilline + ceftriaxone	6S/6S
Allergie aux pénicillines	Daptomycine *+/- Ceftaroline Vancomycine + gentamicine	6S 6S /2S
***Enterococcus faecium* sans haut niveau de résistance aux aminosides**		
Quelle que soit la sensibilité à l'amoxicilline	Vancomycine + gentamicine	6S/2S

* Si CMI $\leq$ 2 mg/l

Traitement des endocardites à streptocoques

Antibiothérapie EI à streptocoque



Take-home messages

Probabiliste:

- Viser le SAMS+++ et couverture strepto entérocoque
- Amoxicilline Céfazoline
- Cut off de 1 an PVE
- CEF DPC PVE < 1 an

Bétalactamines:

- Privilégier ASP et Céfazoline+++
- Y compris:
  - En probabiliste
  - en cas de bithérapie avec aminoside
- Switch en cas d'échec

Rifampicine:

- Uniquement PVE
- Recommandée en l'absence de contre-indication en attendant l'essai RIFREE
- Attendre la stérilisation de la bactériémie avant de l'introduire

Résistance à la méticilline:

- Daptomycine recommandée en première intention
- Forte posologie (10 mg/kg)
- Surveillance CPK/éosino
- Bithérapie ceftaroline ou fosfomycine pendant 7 jours

Entérocoque/strepto:

- Amoxicilline + Ceftriaxone
- Peu de certitudes:
  - Ceftriaxone 2g ou 4g?
  - Pas de comparaison face à face des 2 traitements historiques.
- Strepto : importance CMI amox

Le relai per os

POET Study

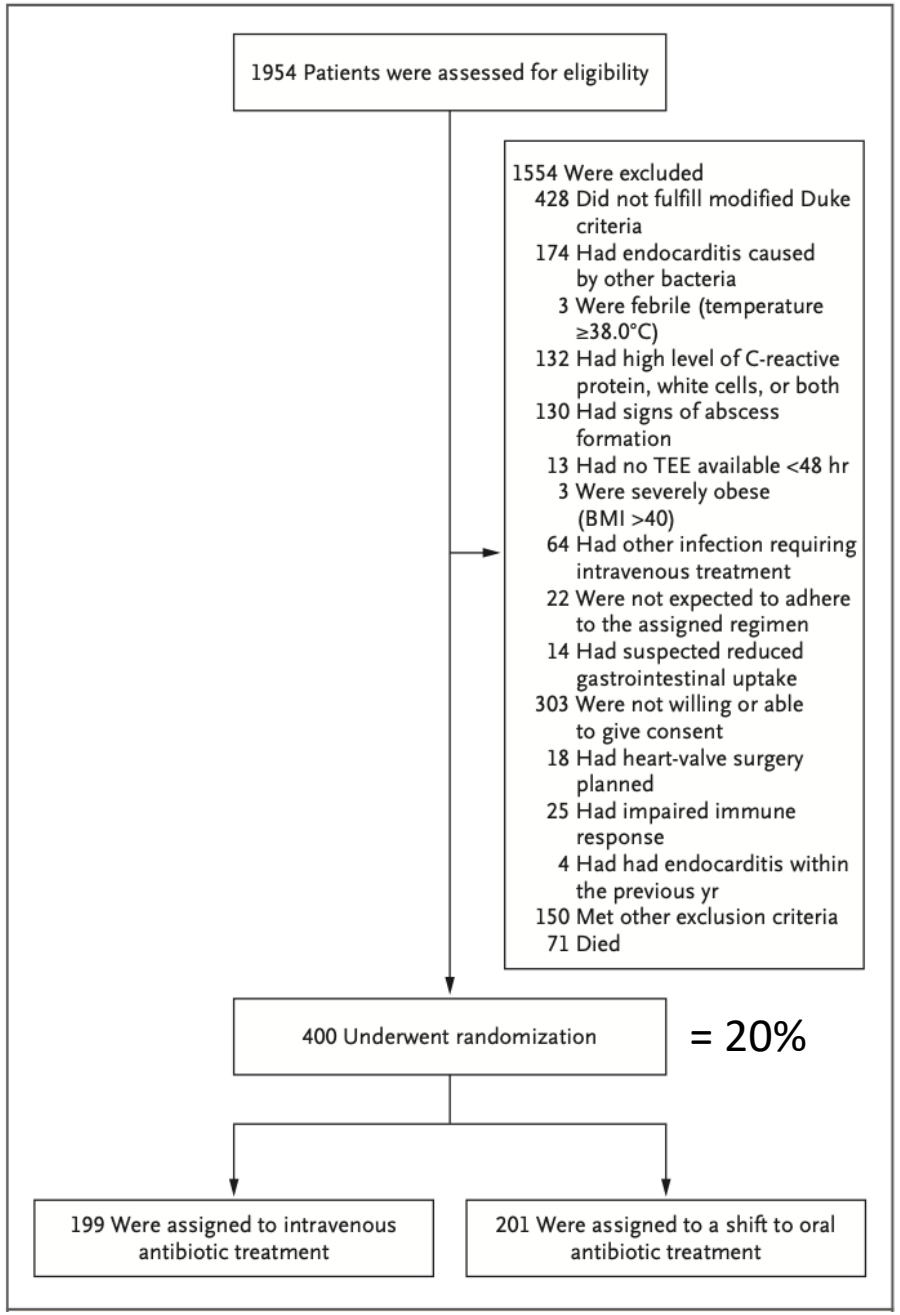
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

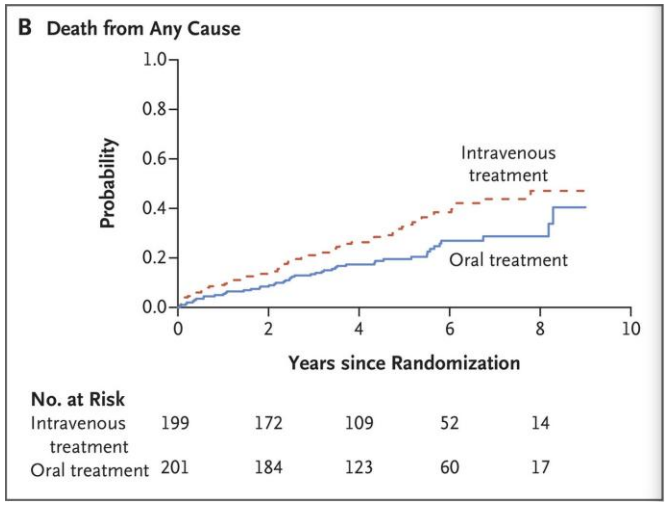
- RCT danois
- EI du cœur gauche à CG+
- Au moins 10 jours IV
- Stabilité clinique et ETO systématique



POET Study

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (–1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (–3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (–2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (–3.1 to 3.1)	0.97 (0.28 to 3.33)

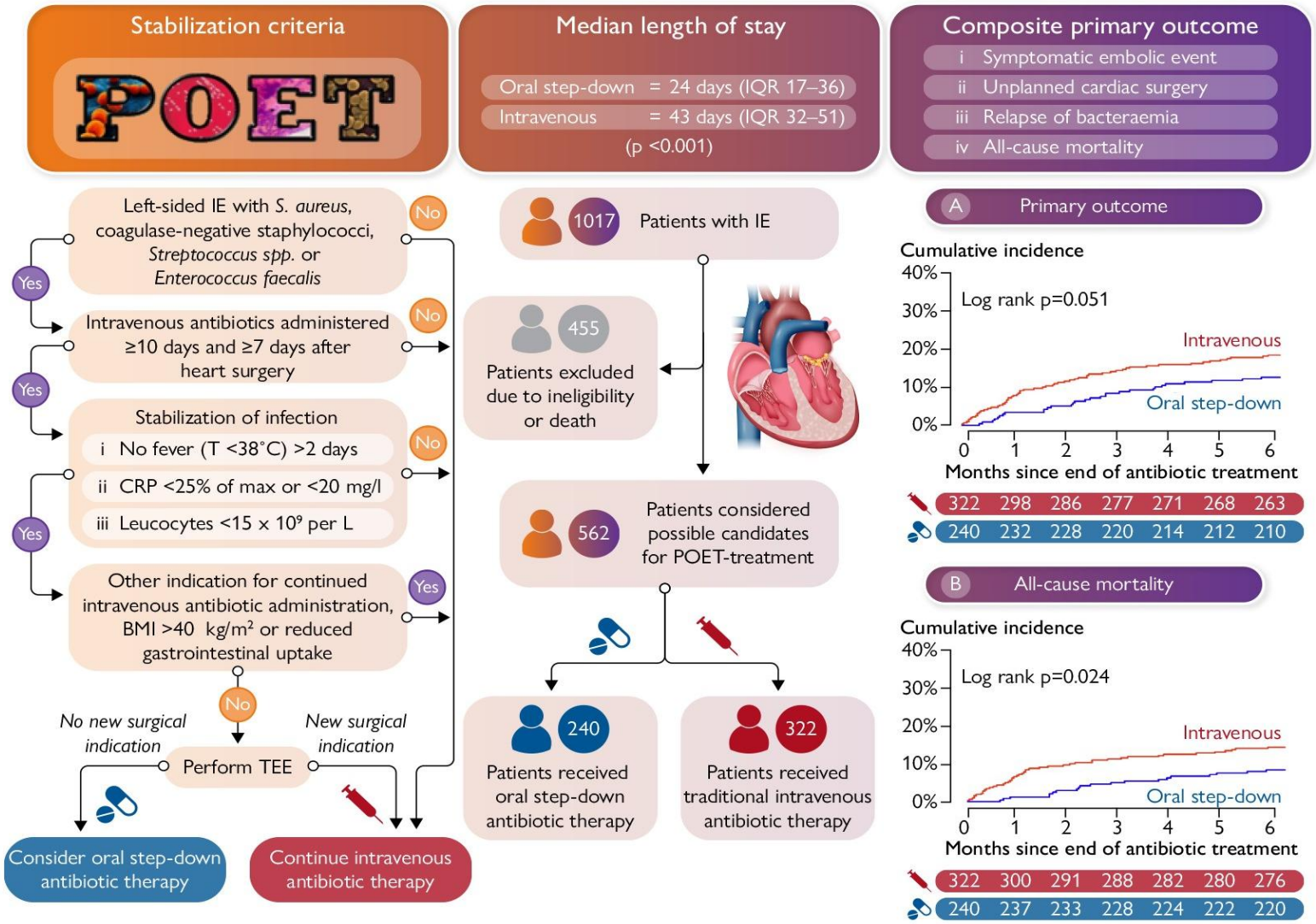


- Choix du traitement à la discrétion du clinicien
  - Très grande variabilité des schémas mais bithérapie systématique
  - Analyses PKPD pour 236 patients:
    - PTA of 88-100% for amoxicillin and linezolid
    - PTA of 71-100% for moxifloxacin and rifampicin
    - PTA of 9-17% for dicloxacillin !!

Pries-Heje MM et al, NEJM 2022 – Bock M et al, CID 2023

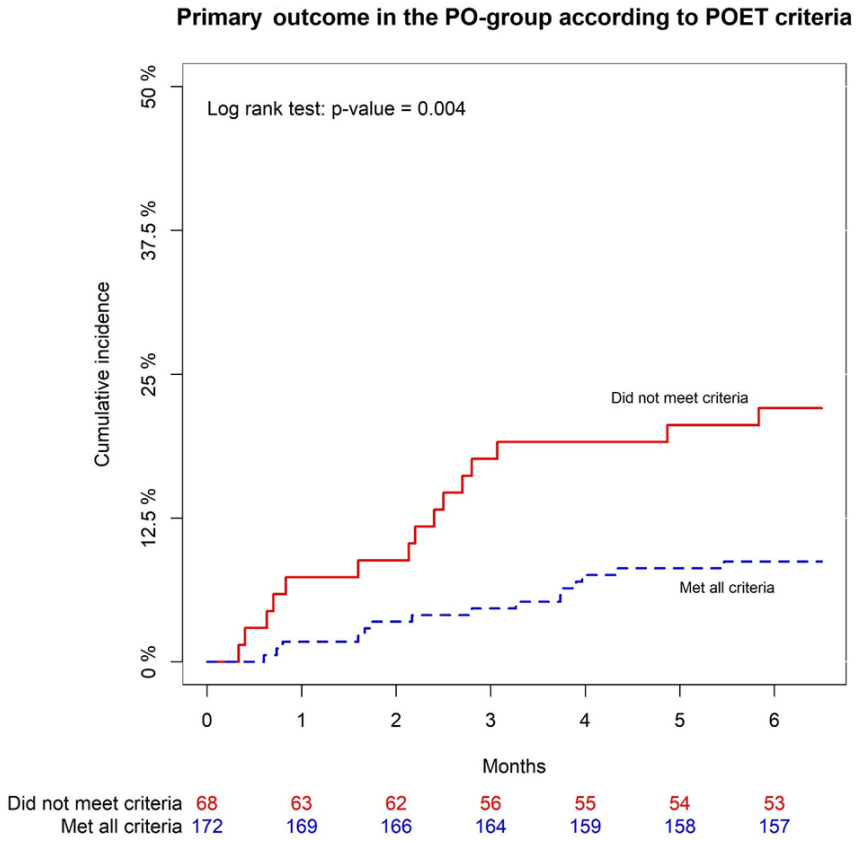
Relais par voie orale en vie réelle

43 % des patients ont un relais par voie orale
18 % d'EI à *E.faecalis*

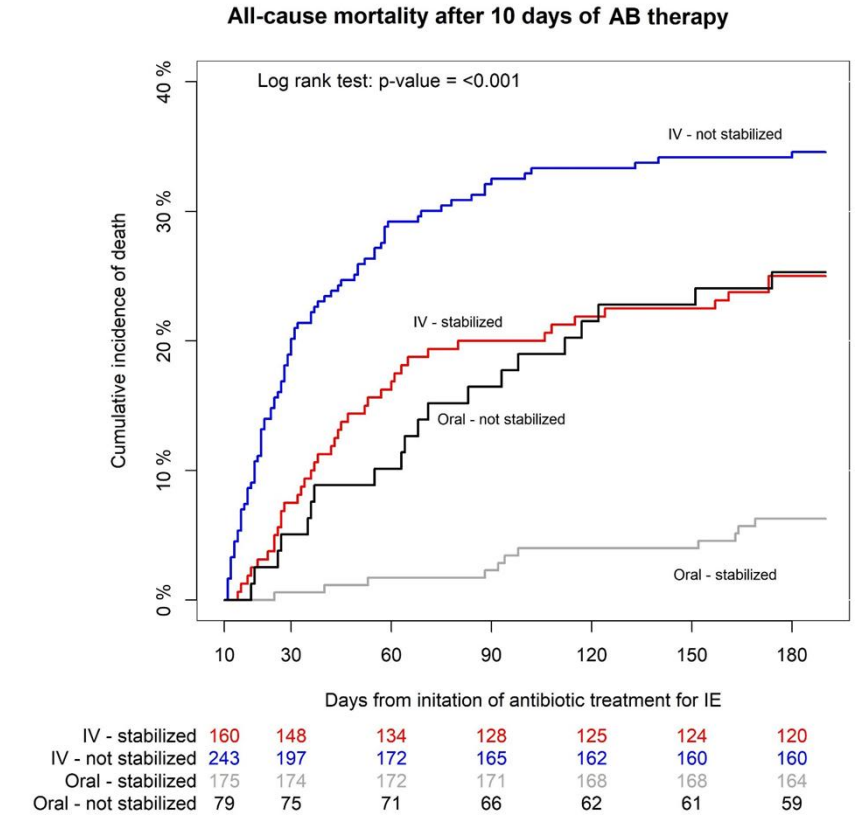


Mia Marie Pries-Heje et al. Eur Heart J. 2023

ETO avant le relais par voie orale



68 patients du groupe per os ne satisfaisaient pas le critère maladie stabilisée, parmi eux 62 % n'avaient pas eu d'ETO avant relais



Cependant, mortalité inférieure par voie orale que les critères de stabilité soient réunis ou non

Mia Marie Pries-Heje et al. Eur Heart J. 2023

RODEO:

RODEO I (staphylococci)

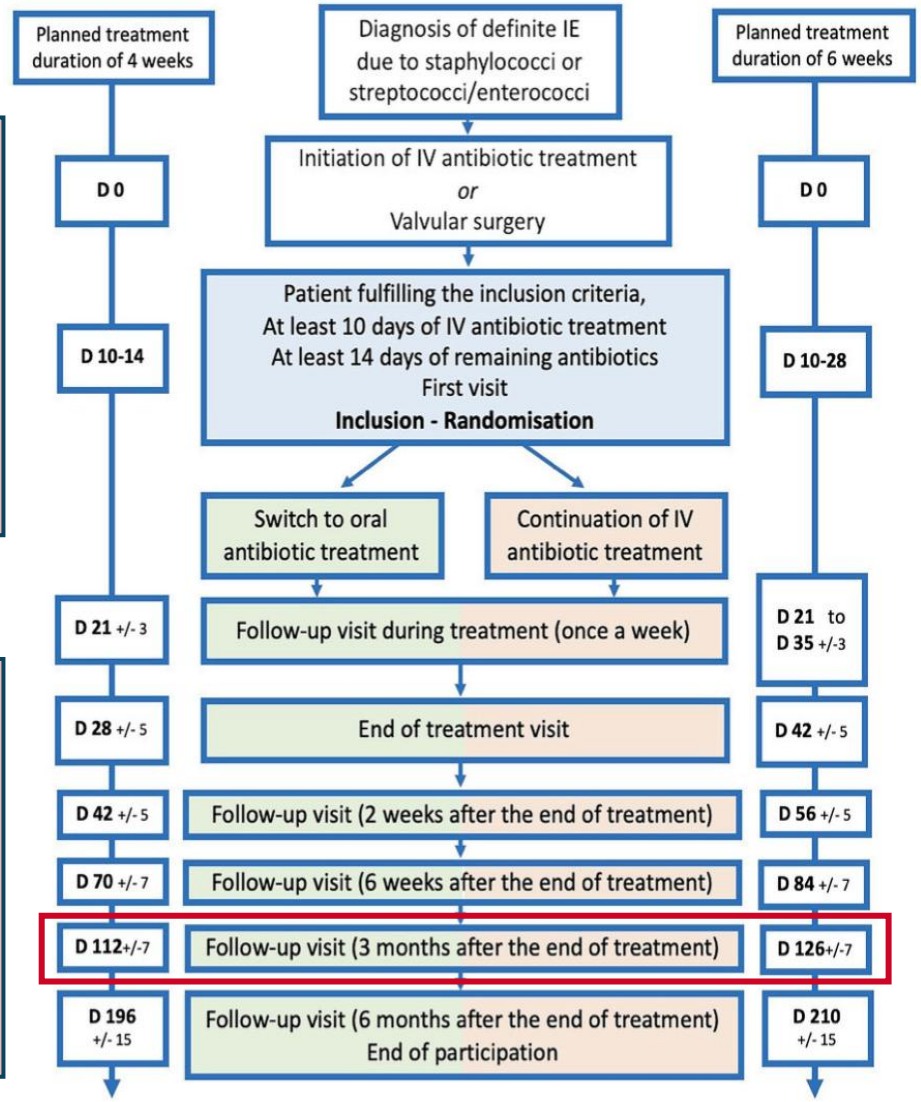
Experimental oral group:
< 70 kg : Levofloxacin 500 mg/d + Rifampicin 600 mg/d
> 70 kg : Levofloxacin 750 mg/d + Rifampicin 900 mg/d

Control IV group:
Conventional IV treatment of staphylococci IE as recommended in ESC guidelines

RODEO II (strepto/enterococci)

Experimental oral group:
< 70 kg : Amoxicillin 1500 mg x 3/d
> 70 kg : Amoxicillin 2000 mg x 3/d

Control IV group:
Conventional IV treatment of staphylococci IE as recommended in ESC guidelines



Primary Endpoint

Treatment failure D90 post-ttt
- Death from any cause
- Symptomatic emboli
- Unplanned valvular surgery
- Microbiological relapse

Independent blinded adjudication committee

Secondary Endpoints

- Components of composite primary endpoint
- Outcome M6
- Echographic outcome
- Catheter-related AEs
- Quality of life
- Antibiotic modification
- Compliance to oral ttt
- Medico-economics

Lemaignen A et al, BMJ Open 2020

Diapositive Adrien Lemaignen

Antibiothérapie des EI : relai per os

- **Relai oral chez patient stable :**
  - Après au moins 10j d'antibiothérapie par voie IV
  - Après au moins 7j après une chirurgie valvulaire
- **EI à streptocoques :**
  - Apyrexie depuis au moins 2 jours
  - CRP < 25% de la valeur maximale ou < 20 mg/l
  - Leucocytes < 15000/mm3
  - ETO récente sans critère d'indication de chirurgie (notamment abcès)
  - Aucun facteur de risque de sous dosage (IMC <40kg/m2 et pas de malabsorption digestive)

Guidelines

Oral antibiotic therapy may be used for patients with streptococcal IE meeting stability criteria as defined in the POET trial (apyrexia for at least 2 days, C-reactive protein < 25 % of its maximum value or < 20 mg/L, and leukocytes < 15 x10^9/L). In addition, recent transoesophageal echocardiography (TEE) must show no remaining criteria for surgical management (especially no abscess), and the patient should have no risk factor for oral antibiotic underdosing (BMI $\leq$ 40 kg/m^2 and no digestive malabsorption) and no psychosocial criteria entailing risk of poor adherence.

Caution is advised concerning enterococcal and staphylococcal IE. Awaiting the results of the RODEO trial seems reasonable.

Oral treatment may be feasible for patients with Gram-Negative Bacilli (GNB) IE (HACEK, *Enterobacterales* or *Pseudomonas aeruginosa*).

Antibiothérapie des EI : relai per os

Avis d'expert en cas d'allergie avec contre indication aux pénicillines

	Relai oral de 1ère ligne	Relai oral en alternative
Streptococcus spp.	Amoxicilline + rifampicine ou Amoxicilline + moxifloxacine	*Attente des résultats de l'essai RODEO* Amoxicilline
Enterococcus faecalis	Amoxicilline + moxifloxacine	*Attente des résultats de l'essai RODEO* Amoxicilline
Staphylococcus spp.	Rifampicine + lévofloxacine	*Attente des résultats de l'essai RODEO* Cotrimoxazole
BGN	Ciprofloxacine	

Take-home messages

Probabiliste:

- Viser le SAMS+++ et couverture strepto entérocoque
- Amoxicilline Céfazoline
- Cut off de 1 an PVE
- CEF DPC PVE < 1 an

Bétalactamines:

- Privilégier ASP et Céfazoline+++
- Y compris:
  - En probabiliste
  - en cas de bithérapie avec aminoside
- Switch en cas d'échec

Rifampicine:

- Uniquement PVE
- Recommandée en l'absence de contre-indication en attendant l'essai RIFREE
- Attendre la stérilisation de la bactériémie avant de l'introduire

Résistance à la méticilline:

- Daptomycine recommandée en première intention
- Forte posologie (10 mg/kg)
- Surveillance CPK/éosino
- Bithérapie ceftaroline ou fosfomycine pendant 7 jours

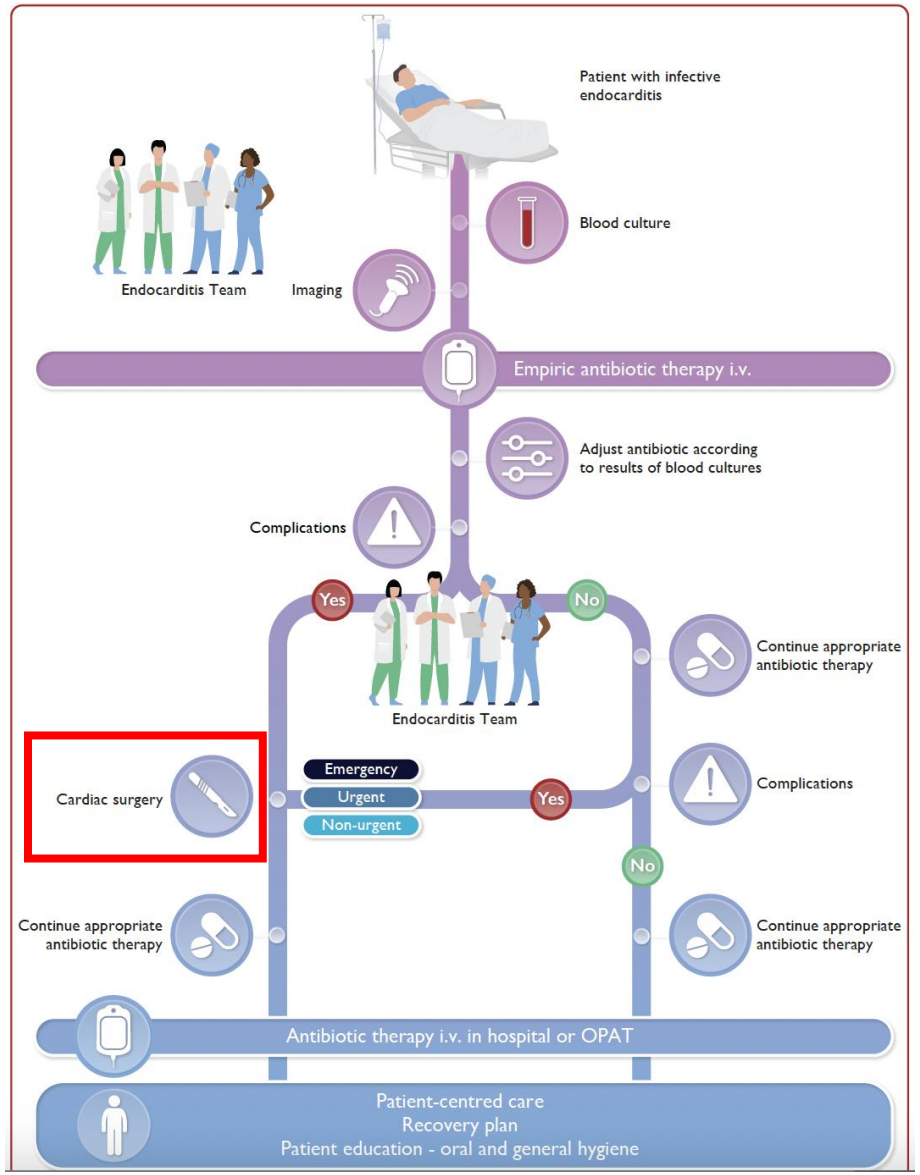
Entérocoque/strepto:

- Amoxicilline + Ceftriaxone
- Peu de certitudes:
  - Ceftriaxone 2g ou 4g?
  - Pas de comparaison face à face des 2 traitements historiques.
- Strepto : importance CMI amox

Relai per os:

- Au moins non inférieur
- Bithérapie quelque soit le germe
- Pas de nécessité d'ETO avant le relai contrairement à POET.

Recommandations ESC 2023



Ne pas passer à côté d'une indication chirurgicale+++

Merci de votre attention

raphael.lecomte@chu-nantes.fr