Principe de l'antibiothérapie des IPOAs

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Infections ostéo-articulaires

- **Famille nombreuse**
  - Arthrite
  - Ostéomyélite
  - Spondylodiscite
  - **Prothèses**
    - **Articulations variées**
    - **Matériel divers**
- **Diffusion médiocre des ATB**
  - Biofilm
  - Traitements prolongés
- **MULTI-DISCIPLINAIRE +++**

Diagnostic ?

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

	Minor criteria	Score	Decision
Preoperative Diagnosis – Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
Preoperative Diagnosis – Serum	Elevated ESR	1	2-5 Possibly Infected*
Preoperative Diagnosis – Synovial	Elevated Synovial WBC *or* LE	3	0-1 Not Infected
Preoperative Diagnosis – Synovial	Positive Alpha-defensin	3	
Preoperative Diagnosis – Synovial	Elevated Synovial PMN (%)	2	
Preoperative Diagnosis – Synovial	Elevated Synovial CRP	1	

	*Inconclusive pre-op score *or* dry tap	Score	Decision
Intraoperative Diagnosis	Preoperative Score	-	≥6 Infected
Intraoperative Diagnosis	Positive Histology	3	4-5 Inconclusive**
Intraoperative Diagnosis	Positive Purulence	3	≤3 Not Infected
Intraoperative Diagnosis	Single Positive Culture	2	

IDSA/ICM 2018

Major criteria (at least one of the following)	Decision
Two positive growth of the same organism using standard culture methods	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Minor Criteria	Threshold		Score	Decision
	Acute[€]	Chronic		
Serum CRP (mg/L) *or* D-Dimer (ug/L)	100 / Unknown	10 / 860	2	Combined preoperative and postoperative score: ≥6 Infected; 3-5 Inconclusive*; <3 Not Infected
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/µL) *or* Leukocyte Esterase *or* Positive Alpha-defensin (signal/cutoff)	10,000 / ++ / 1.0	3,000 / ++ / 1.0	3	
Elevated Synovial PMN (%)	90	70	2	
Single Positive Culture			2	
Positive Histology			3	
Positive Intraoperative Purulence[$]			3	

	Infection Unlikely (all findings negative)	Infection Likely (two positive findings)[a]	Infection Confirmed (any positive finding)
Clinical and blood workup			
Clinical features	Clear alternative reason for implant dysfunction (e.g. fracture, implant breakage, malposition, tumour)	1) Radiological signs of loosening within the first five years after implantation 2) Previous wound healing problems 3) History of recent fever or bacteraemia 4) Purulence around the prosthesis[b]	Sinus tract with evidence of communication to the joint or visualization of the prosthesis
C-reactive protein		> 10 mg/l (1 mg/dl)[c]	
Synovial fluid cytological analysis[d]			
Leukocyte count[c] (cells/µl)	≤ 1,500	> 1,500	>3,000
PMN (%)[c]	≤ 65%	> 65%	> 80%
Synovial fluid biomarkers			
Alpha-defensin[e]			Positive immunoassay or lateral-flow assay[e]
Microbiology[f]			
Aspiration fluid		Positive culture	
Intraoperative (fluid and tissue)	All cultures negative	Single positive culture[g]	≥ two positive samples with the same microorganism
Sonication[h] (CFU/ml)	No growth	> 1 CFU/ml of any organism[g]	> 50 CFU/ml of any organism
Histology[c,i]			
High-power field (400x magnification)	Negative	Presence of ≥ five neutrophils in a single HPF	Presence of ≥ five neutrophils in ≥ five HPF
			Presence of visible microorganisms
Others			
Nuclear imaging	Negative three-phase isotope bone scan[c]	Positive WBC scintigraphy[l]	

EBJIS 2021

EBJIS 2021

Table 3. Final diagnosis classification according to different definitions. Values are count (%)

EBJIS	*Infection unlikely*	*Infection likely*	*Infection confirmed*
	255 (54)	22 (5)	195 (41)
ICM 2018	*Not infected*	*Inconclusive*	*Infected*
	258 (55)	42 (9)	172 (36)
IDSA	*Not infected*	–	*Infected*
	284 (60)	–	188 (40)
MSIS 2013	*Not infected*	–	*Infected*
	327 (69)	–	145 (31)

Sousa R et al. The European Bone and Joint Infection Society definition of periprosthetic joint infection Acta Orthop. 2023

Ponction articulaire

- Rentabilité modérée
  - Se 59%

    Barker et al. JBJI 2021.
- Interprétation (parfois) difficile
  - Micro-organismes commensaux

- Geste simple, peu invasif
  - PTG
- Répétable
- Marqueurs synoviaux
  - Leucocyte estérase
  - Alpha-défensine
  - Calprotectine

Marqueurs synoviaux

Table 3
Synovasure performance.

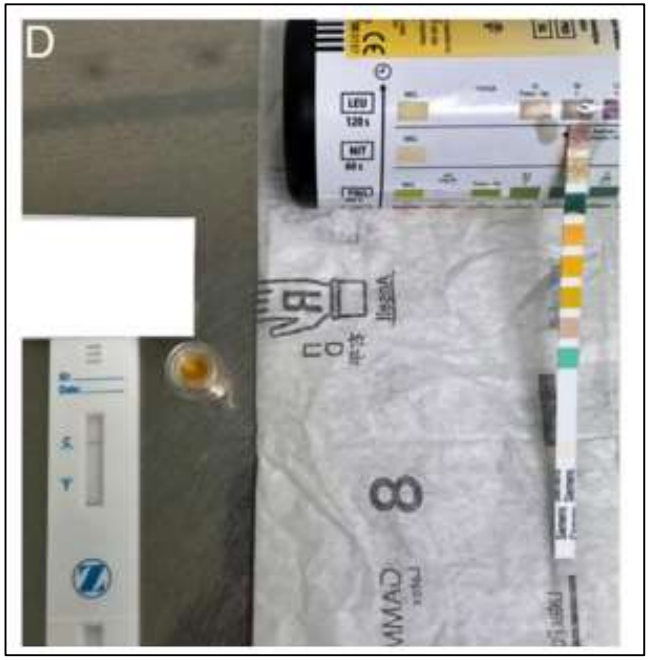
Performance of Synovasure™ test	MSIS indicating infection	MSIS ruling out infection
Synovasure Positive	21 Sensitivity: 95.5%	8* PPV: 72.4%
Synovasure Negative	1 NPV: 98.8%	81 Specificity: 91%

PPV: positive predictive value; NPV: negative predictive value.
* One case of positive Synovasure™ test with metallosis identified on macroscopic joint fluid aspect, excluded from analysis.

- **Leucocyte estérase**
  - Pas de sang OU centrifugé
    - Se : 85% MSIS ; 81% EBJIS
    - Spe : 95% MSIS ; 91% EBJIS
- **Alpha défensine**
  - Se : 86% MSIS ; 74% EBJIS
  - Spe : 93% MSIS ; 93% EBJIS
- **Calprotectine**
  - Se : 94% MSIS ; 93% EBJIS
  - Spe : 94% MSIS ; 100% EBJIS
- **CRP** *Vale et al. Journal of Arthroplasty. 2023*
  - Se : 83%
  - Spe : 92%

Chirurgie > 3 mois

Volume suffisant
(5 à 10mL)



Diagnostic : en résumé

Signes cliniques :
-Retard de cicatrisation
-Ecoulement
-Fistule

-Douleur
-Fièvre

Signes biologiques :
-Syndrome inflammatoire (CRP)
-Liquide articulaire inflammatoire
-Marqueurs synoviaux *(leucocyte estérase, alpha-defensine, calprotectine…)*

-Microbiologie

Signes morphologiques :

-Descellement (dans les 5 ans +++)
-Collections
-Imageries nucléaires (TEP, Scintigraphies aux leucocytes marqués)

Principes de prise en charge

Lavage (DAIR)	Remplacement en 1 temps	Remplacement en 2 temps
• < 30 jours de la pose • < 3 semaines de symptômes	• > 30 jours de la pose • > 3 semaines de symptômes	• > 30 jours de la pose • > 3 semaines de symptômes
• Pas de descellement • Pas de fistule	• Descellement • Fistule • Intégrités tissus mous, fermeture cutanée possible	• Descellement • Fistule • Nécrose, abcès • Endocardite
		• Micro-organismes « difficiles »
• Risque chirurgical/Terrain	• Risque chirurgical/Terrain	• Risque chirurgical/Terrain

Quand ?
Fenêtre antibiotique

- Maximiser les chances de prélèvements informatifs
  - Risque X4 de prélèvements négatifs

Malekzadeh et al. Clin Orthop Relat Res. 2010

  - Sensibilité avec fenêtre : 60% (49%-71%)
  - Sensibilité sans fenêtre : 45%

Trampuz et al. NEJM. 2007

- **Durée : 2 semaines** *IDSA, EFORT, EBJIS*
  - 3-4 semaines si : cyclines, clindamycine, fluoroquinolones, rifampicine

Wito et al. Acta Orthop Scand. 1999

JAMAIS au détriment du pronostic vital et/ou d'une possibilité de DAIR

Antibiothérapie d'attente

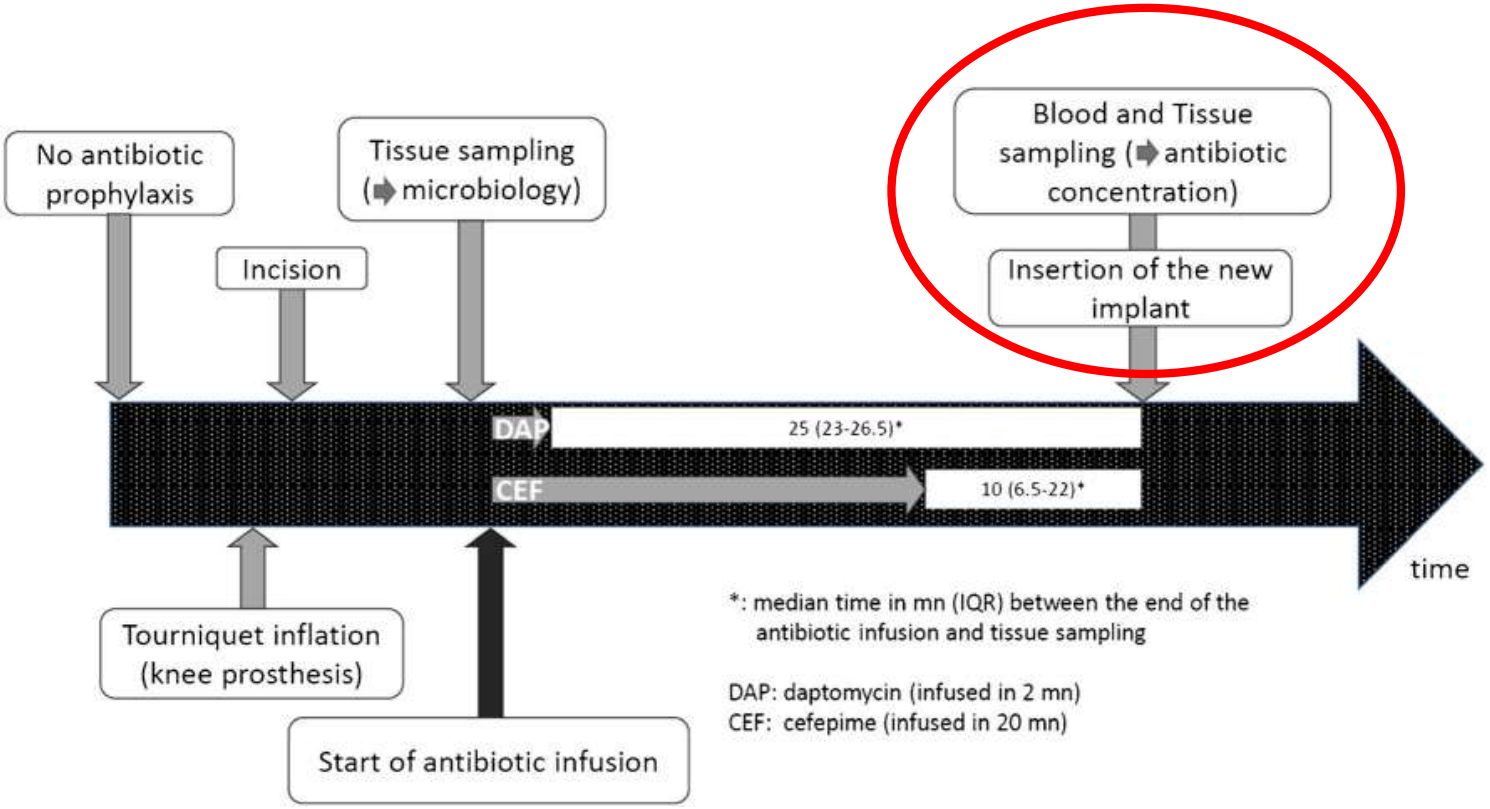
- **Large spectre**
- **IV**
- ~~**Débuter dès les prélèvements réalisés**~~
- **Temporalité de l'antibioprophylaxie per-opératoire standard**

TABLE 3 Culture yield of patients with a confirmed PJI prior to surgery[a]

			Patients with acute and chronic infections			Patients with chronic infections only		
Study authors	Reference test	Prophylaxis	No. of patients with culture yield/total no. (%)	95% CI	*P* value	No. of patients with culture yield/total no. (%)	95% CI	*P* value
Bedenčič et al. (22)[b]	Intraoperative samples before prophylaxis	Yes No	19/24 (79)	58–93		19/24 (79)	58–93	
Tetreault et al. (21)	Control group without prophylaxis	Yes No	29/34 (85) 29/31 (94)	73–98 84–100	0.43	13/16 (81) 14/16 (88)	60–100 70–100	1.00
Burnett et al. (19)	Preoperative synovial fluid	Yes No	26/26 (100)	NA		19/19 (100)	NA	
Ghanem et al. (23)	Control group without prophylaxis	Yes No	63/72 (88) 91/99 (92)	80–95 86–98	0.44	27/30 (90) 38/41 (93)	79–100 84–100	1.00
Al-Mayahi et al. (3)	Control group without prophylaxis	Yes No	8/9 (89) 224/232 (97)	63–100 95–99	0.29	ND ND		
Pooled (all studies)		Yes No	145/165 (88) 344/362 (95)	83–93 93–97	0.004	78/89 (88) 52/57 (91)	80–99 83–99	0.59

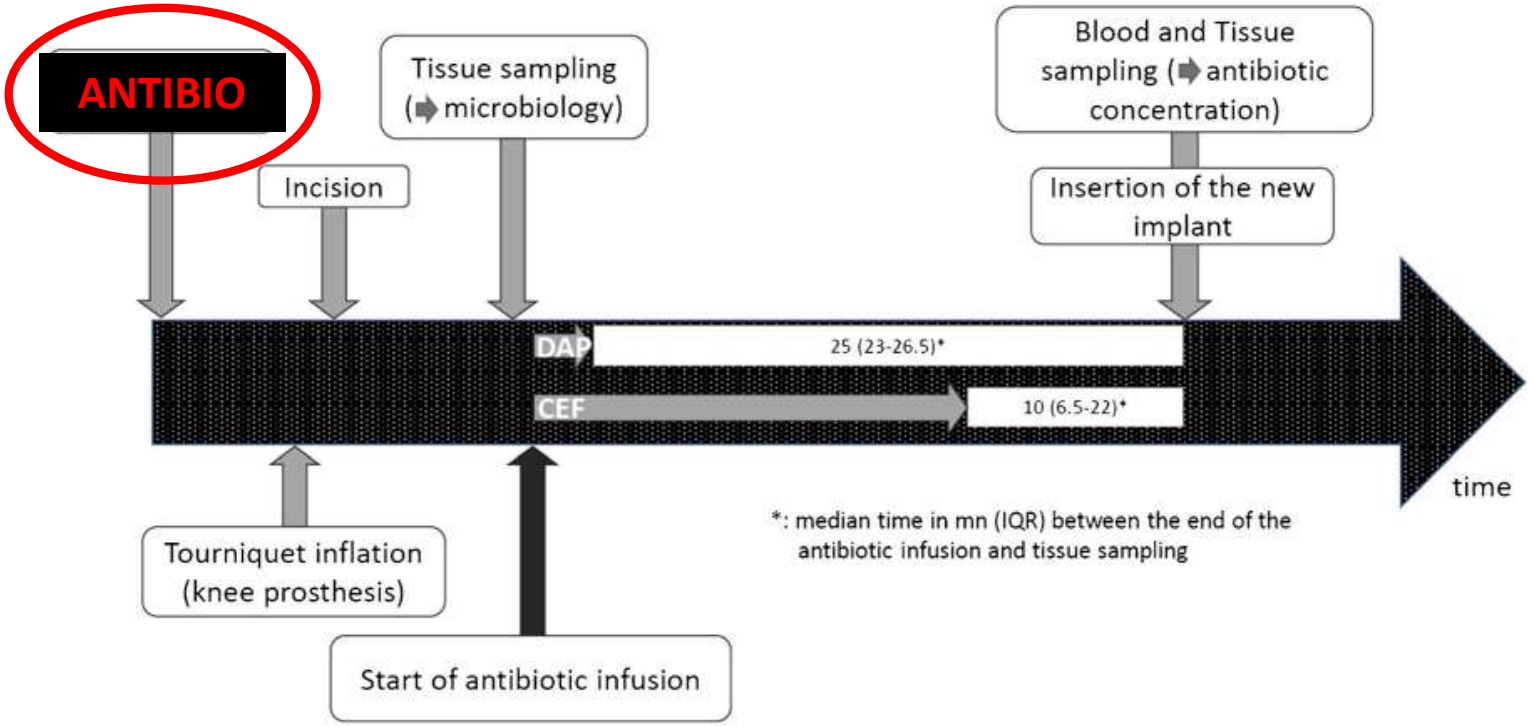
Wouthuyzen-Bakker M et al J Clin Microbiol. 2017.

DOSOS



Robineau et al. Eur J of Clin Microbiol and Infect Diseases. 2021

DOSOS 2 (projet)



Quel spectre ?

Table 2 Microbiological results from cultured tissue specimens

Microbe	Number of patients (%) N=113
Staphylococcus aureus[a]	42 (37.2)
Coagulase-negative staphylococci	23 (20.4)
Streptococcus species	17 (15.0)
Enterococcus species	3 (2.7)
Gram-negative rods	11 (9.7)
Polymicrobial infection	17 (15.0)

Puhto et al. Int Orthopaedics. 2015

Table 1. Microorganisms Identified in Hip and Knee Periprosthetic Joint Infection (PJI).*

Microorganism	Frequency (%)
Aerobic gram-positive bacteria	82
Coagulase-negative staphylococcus species (other than *S. lugdunensis*)	37
S. aureus	24
S. lugdunensis	4
Streptococcus species	14
Enterococcus species	8
Corynebacterium species	5
Aerobic gram-negative bacteria	11
Enterobacterales	7
Pseudomonas species	3
Anaerobic bacteria	13
Cutibacterium species	8
Other species	5
Fungi	3
Mycobacteria	0.5

Patel et al. NEJM. 2023

	Late Acute (n = 267)	Early (n = 160)	Chronic (n = 142)	Late (Not Classifiable) (n = 84)
Staphylococcus aureus	135 (51%)	65 (41%)	39 (27%)	29 (35%)
MRSA	8 (3%)	5 (3%)	7 (5%)	3 (4%)
CoNS	29 (11%)	47 (29%)	45 (32%)	24 (29%)
Beta-hemolytic Strep	45 (17%)	14 (9%)	3 (2.0%)	8 (10%)
Enterococci	6 (2%)	26 (16%)	7 (5%)	4 (5%)
Enterobacteriaceae	10 (4%)	19 (12%)	9 (6%)	6 (7%)

Joshua S Davis et al. CID. 2022

Antibiothérapie d'attente (3)

Table 4. Microorganisms and groups of organisms involved in non-hematogenous prosthetic joint infections according to time of infection after surgery (≤1 month, 2–3 months, 4–12 months, >12 months).

Microorganism or Microorganism Group	PJI within 1 Month after Surgery $n = 844$	PJI 2-3 Months after Surgery $n = 243$	PJI 4-12 Months after Surgery $n = 277$	PJI > 12 Months after Surgery $n = 619$	*p*-Value
	Total no. (%)*				
Staphylococcus species					
• Coagulase-negative staphylococci	236 (28.2) **	107 (44) ** †	167 (60.3) †	348 (56.2)	<0.001
○ *Staphylococcus epidermidis*	132 (15.6) **	68 (28) ** †	106 (38.3) †	203 (32.8)	<0.001
○ *Staphylococcus lugdunensis*	2 (0.2) **	3 (1.3) **	10 (3.6)	22 (3.6)	<0.001
• *Staphylococcus aureus*	301 (35.7)	60 (24.7)	60 (21.7)	108 (17.4)	<0.001
Streptococcus species	36 (4.3) **	25 (10.3) **	14 (5.1)	49 (7.9)	<0.001
○ *Streptococcus agalactiae*	8 (0.9) **	11 (4.5) **	6 (2.2)	10 (1.6)	0.003
○ Viridans group streptococci not identified to species level	6 (0.7) **	7 (2.9) **	2 (0.7) †	18 (2.9) †	0.003
Enterococcus species	106 (12.6)	23 (9.5)	15 (5.4)	32 (5.4)	<0.001
Aerobic Gram-negative bacilli	396 (46.9) **	50 (20.6) ** †	37 (13.4) †	37 (13.4)	<0.001
• *Enterobacteriaceae*	303 (35.9) **	37 (15.2) ** †	25 (9) †	48 (7.8)	<0.001
○ *Escherichia coli*	129 (15.3)	12 (4.9)	10 (3.6)	21 (3.4)	<0.001
○ *Proteus* spp.	75 (8.9)	7 (2.9)	7 (2.5)	14 (2.3)	<0.001
○ *Enterobacter* spp.	73 (8.6) **	11 (4.5) ** †	2 (0.7) †	6 (1)	<0.001
○ *Klebsiella* spp.	48 (5.7)	2 (0.8)	4 (1.4)	3 (0.5	<0.001
• Non-fermenting Gram-negative bacilli	138 (16.4) **	16 (6.6) **	11 (4)	41 (6.6)	<0.001
○ *Pseudomonas* spp.	128 (15.2) **	17 (7) **	11 (4)	35 (5.7)	<0.001
Aerobic Gram-positive bacilli	16 (1.9)	3 (1.2)	7 (2.5)	23 (3.7)	0.083
Anaerobic Gram-positive bacilli	19 (2.3) **	14 (5.7) **	16 (5.8)	61 (9.7)	<0.001
• *Cutibacterium* spp.	17 (2) **	12 (4.9) **	16 (5.8)	51 (8.2)	<0.001
Anaerobic Gram-positive cocci	8 (0.9)	4 (1.6)	5 (1.8)	13 (2.1)	0.330
Anaerobic Gram-negative bacilli	12 (1.4)	2 (0.8)	1 (0.4)	5 (0.8)	0.409
Mycobacterium species	2 (0.2)	1 (0.9)	4 (1.4)	2 (0.3)	0.068
Fungi	8 (0.9)	3 (1.2)	3 (1.1)	12 (1.9)	0.418
Multidrug-resistant organisms	202 (23.9)	20 (8.2)	20 (7.2)	43 (6.9)	<0.001
• Methicillin-resistant *S. aureus*	93 (11)	14 (5.8)	14 (5.1)	30 (4.8)	<0.001
• Multidrug-resistant Gram-negative bacilli	112 (13.3)	7 (2.5)	5 (1.8)	14 (2.3)	<0.001
• Extended-spectrum beta-lactamases producing *Enterobacteriaceae*	36 (4.3)	1 (0.4)	2 (0.7)	1 (0.3)	<0.001
Ciprofloxacin-resistant Gram-negative bacilli	84 (10)	5 (2.1)	4 (1.4)	11 (1.8)	<0.001
Polymicrobial infections	230 (27.2)	36 (14.7)	32 (11.1)	77 (11.1)	<0.001

Natividad et al. J. Clin. Med. 2019

Facteur pronostic

Table 2. Characteristics of Surgical Procedures and Antibiotic Therapy in 98 Patients With Total Hip or Knee Prosthesis Infection Due to *Staphylococcus aureus* According to Outcome

Characteristic	Remission (n = 77)	Treatment failure (n = 21)	P
Delay from onset of infection to revision, mean days ± SD	119.4 ± 238.2	79 ± 111.7	.80
Removal of all infected implants	45 (58.4)	12 (57.1)	.99
Gentamicin-loaded cement spacer[a]	27 (35.1)	7 (33.3)	.84
Adequate empirical postsurgical antibiotic therapy[b]	73 (94.8)	17 (80.9)	.04
Rifampin-fluoroquinolone combination therapy	37 (48.1)	2 (9.5)	.001
Rifampin combination therapy	58 (75.3)	10 (47.6)	.002
Total duration of antibiotic therapy, mean days ± SD	165.7 ± 108.8	145.1 ± 101.6	.44

Senneville et al. CID. 2011

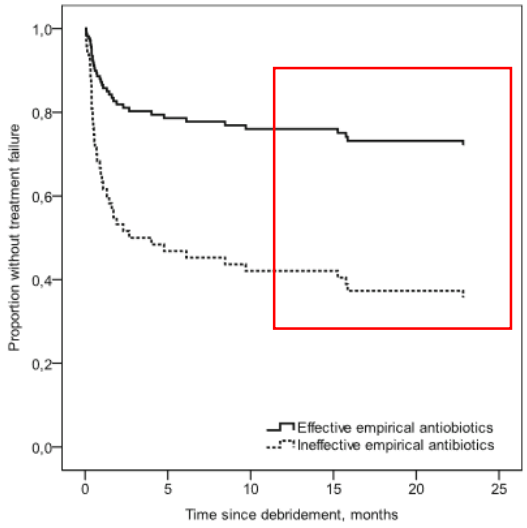


Fig. 2 Survival curves for effective and ineffective empirical antibiotics

Puhto et al. Int Orthopaedics. 2015

Et donc : Antibiothérapie d'attente (3)

- **Bêta-lactamine**
  - Pipéracilline-tazobactam < 80kg 4g/8h >80kg 4g/6h
  - Céfépime 60mg/kg/j
    - Encéphalopathie

+

CEFTOBIPROLE
500mg-1g/8h

- **Anti cocci Gram +**
  - Daptomycine 10-12 mg/kg/j
    - CPK, éosinophilie, pneumopathie interstitielle
  - Linezolide 600mg 2x/j
  - ~~Vancomycine / Teicoplanine~~

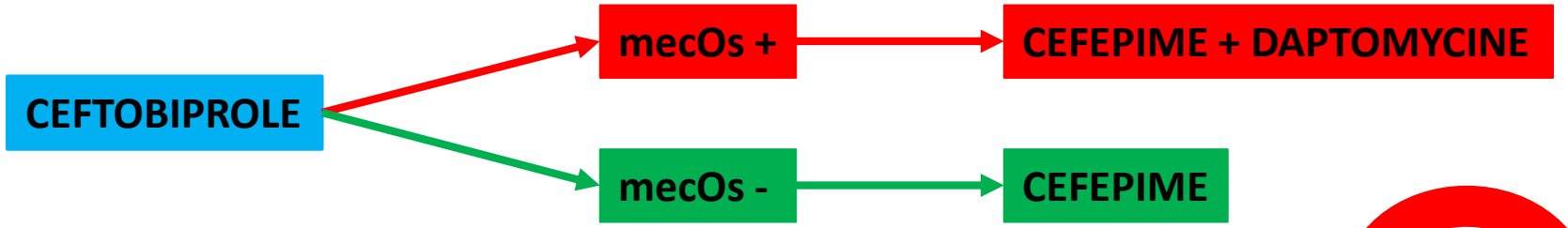
Protocole mecOS

Table 3
Performances of Xpert® assay compared to standard culture, before and after interpretation of discordant results.

	Raw data		Data after interpretation of discordant results	
	All samples ($N = 104$)	All patients ($N = 30$)	All samples ($N = 104$)	All patients ($N = 30$)
Sensitivity (%)	84.6	90.9	87.1	92.3
Specificity (%)	93.2	90.9	100	100
PPV (%)	81.5	90.9	100	100
NPV (%)	94.5	94.4	94.5	94.4

PCR mecA (GeneXpert®)

Titécat et al. Diagnostic Microbiology and Infectious Disease. 2012



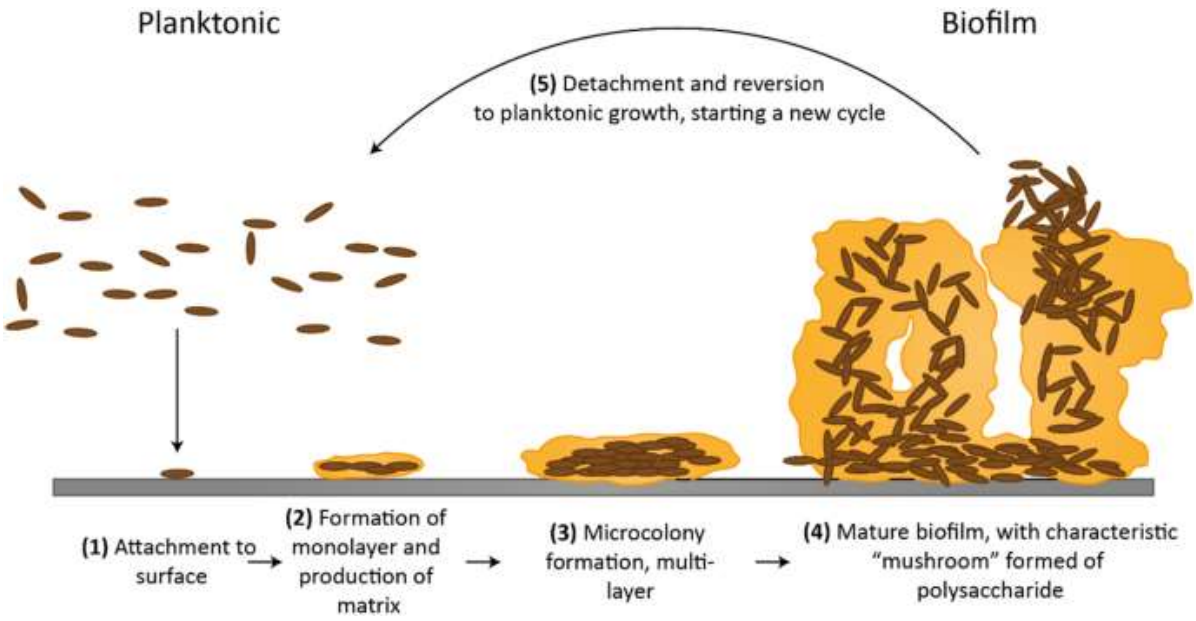
Antibiothérapie documentée

Staphylococcus spp.

 2012	 2008/2014	 2017
Rifampicine + Ciprofoxacine Levofloxacine	Rifampicine + Ofloxacine + Levofloxacine	Rifampicine + Levofloxacine
Rifampicine + Clindamycine Minocycline Doxycycline Ac fusidique Cortimoxazole Céfalexine	Rifampicine + Linézolide Clindamycine Minocycline Doxycycline Ac fusidique Cortimoxazole	Rifampicine + Linézolide Clindamycine Minocycline Ac fusidique Cortimoxazole
	Ofloxacine + Ac Fusidique	Levofloxacine + Linézolide Clindamycine Minocycline Ac fusidique Cortimoxazole
	Clindamycine + Ac Fusidique	Clindamycine + Ac Fusidique Linezolide + Ac Fusidique + Cotrimoxazole

Biofilm

Composition variée
- -Polysaccharides
- -Glycoprotéines
- -Lipides
- -DNA



Planctoniques	Biofilm

• Circulantes
• Virulentes
• Sensibles aux ATB
	• Adhérentes
	• Métabolisme ralenti
	• Echappement aux ATB
	  • 3h CMI Vanco x 100
	  • 3h échappement PNN

Staats A. et al. Ann Joints. 2021

Gilbertie JM et al. PLoS One. 2019
Niranjan G et al. Infect Immun. 2019

Table 2 Results of susceptibility studies: MIC_{50}, MIC_{90} ($mg\,l^{-1}$), nonsusceptibility rate and percentage of bactericidal activity

	S. aureus					*S. epidermidis*				
			% Nonsusceptible strains					% Nonsusceptible strains		
Test agent	MIC_{50}	MIC_{90}	*CLSI*	*EUCAST*	*% Bactericidal activity*	MIC_{50}	MIC_{90}	*CLSI*	*EUCAST*	*% Bactericidal activity*
Rifampin	0.015	4	11.11	16.67	0	0.015	0.015	5.26	5.26	27.78
Vancomycin	1	2	5.56	5.56	55.56	2	4	0	0	94.74
Tigecycline	0.25	0.5	—	0	0	0.12	0.25	—	0	5.26
Ciprofloxacin	>8	>8	66.67	66.67	66.67	1	>8	47.37	47.37	73.33
Cotrimoxazole	1	2	5.56	5.56	27.78	2	>32	42.10	42.10	6.25
Cloxacillin	>32	>32	66.67	66.67	50	0.5	>32	68.42	68.42	50
Clindamycin	0.12	>8	11.11	11.11	0	0.25	>8	31.58	36.84	7.69
Daptomycin	0.5	1	0	0	77.78	0.5	1	0	0	78.95
Fosfomycin	1	16	—	5.56	0	1	4	—	0	5.26

Molina-Manso D. et al. Journal of Antibiotics. 2012

Table 1
Susceptibility results for *Staphylococcus aureus* strains.

Antibiotic	MBEC		
	$MBEC_{50}$	$MBEC_{90}$	Range
Rifampicin	64	>64	≥64
Vancomycin	>1024	>1024	>1024
Tigecycline	512	512	128–512
Clindamycin	>1024	>1024	≥1024
SXT	>1024	>1024	>1024
Ciprofloxacin	>1024	>1024	≥1024
Cloxacillin	>1024	>1024	>1024
Daptomycin	>1024	>1024	≥1024
Fosfomycin	>1024	>1024	>1024

Table 2
Susceptibility results for *Staphylococcus epidermidis* strains.

Antibiotic	MBEC		
	$MBEC_{50}$	$MBEC_{90}$	Range
Rifampicin	32	64	≤0.5 to >64
Vancomycin	>1024	>1024	≤8 to >1024
Tigecycline	256	512	≤8–512
Clindamycin	>1024	>1024	≤8 to >1024
SXT	>1024	>1024	16 to >1024
Ciprofloxacin	512	>1024	≤8 to >1024
Cloxacillin	>1024	>1024	≤8 to >1024
Daptomycin	>1024	>1024	≤8 to >1024
Fosfomycin	>1024	>1024	≤8 to >1024

Molina-Manso D. et al. IJAA. 2013

RIFAMPICINE

- Découverte 1957, introduite en 1968
- Bactéricide concentration dépendant
- Action sur l'ARN polymérase
  - Inhibition transcription ADN bactérien
- Diffusion tissulaire +++
  - Lipophile
- Tolérance digestive… aléatoire
- Colorations oranges
- Surveillance bilan hépatique

RIFAMPICINE (2)

- Spectre Gram +
  - *Staphylococcus, Streptococcus, Enterococcus*
  - *Listeria*

- INDUCTEUR ENZYMATIQUE — Interactions médicamenteuses
  - CYP3A4

- Résistance facile → JAMAIS en monothérapie / JAMAIS en probabiliste / JAMAIS en infection non contrôlée
  - 1 seule mutation

- **Prise à jeun**
  - 10mg/kg/j

Table 2 Outcome for patients treated with Rifampicin for the full length of treatment (n = 321/411)

	Total	Low-dose	Intermediate-dose	High-dose
Recovery, n (%)	237 (73.8)	10 (55.5)	189 (76.2)	38 (69)
Treatment failure, n (%)	52 (16.2)	5 (27.8)	35 (14.1)	12 (21.8)
Lost to follow-up, n (%)	32 (10)	3 (16.7)	24 (9.7)	5 (9.1)

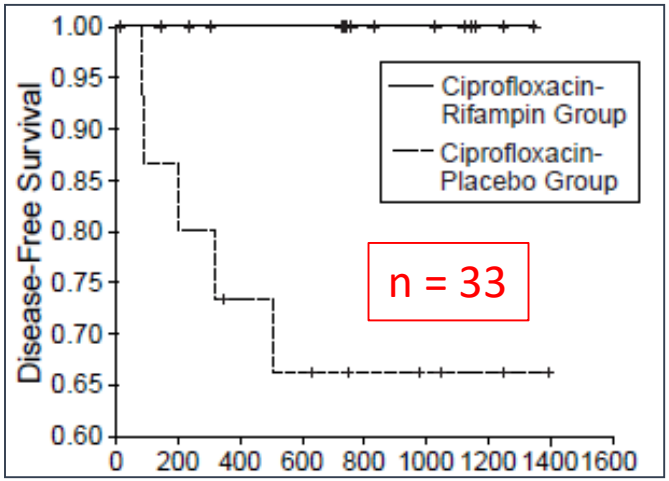
Tonnelier et al. BMC Infectious Diseases. 2021

RIFAMPICINE : modèle cage

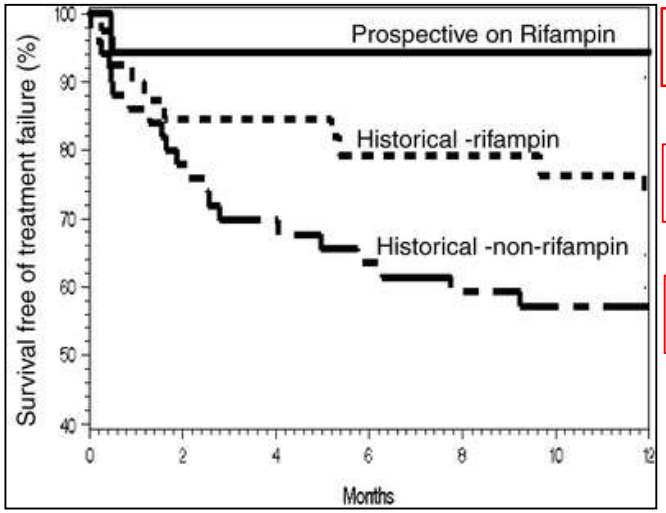
Microorganism	Antibiotic regime	Cure rate	*P* [a]	Reference
S. epidermidis B3972 (clinical strain)	Ciprofloxacin	0/12 (0 %)	<0.01	Widmer et al. 1990 (15)
	Ciprofloxacin + Rifampin	12/12 (100 %)		
S. aureus ATCC 29213 (MSSA)	Vancomycin	0/12 (0 %)	<0.01	Zimmerli et al. 1994 (16)
	Vancomycin + Rifampin	9/12 (75 %)		
	Ciprofloxacin	2/12 (17 %)	<0.001	
	Ciprofloxacin + Rifampin	11/12 (92 %)		
S. aureus ATCC 29213 (MSSA)	Levofloxacin	0/12 (0 %)	<0.05 for comparisons Levofloxacin alone versus combination therapy	Trampuz et al. 2007 (17)
	Levofloxacin + Rifampin	21/24 (88 %)		
	Levofloxacin + ABI-0043[b]	22/24 (92 %)		
S. aureus ATCC 43300 (MRSA)	Linezolid	0/12 (0 %)	<0.001 for comparisons Linezolid alone versus combination therapy	Baldoni et al. 2009 (36)
	Linezolid + Rifampin	12/20 (60 %)		
	Levofloxacin + Rifampin	20/22 (91 %)		
S. aureus ATCC 43300 (MRSA)	Daptomycin	0/12 (0 %)	<0.001	John et al. 2009 (7)
	Daptomycin + Rifampin	8/12 (67 %)		
S. aureus ATCC 43300 (MRSA)	Dalbavancin	0/12 (0 %)	<0.001	Baldoni et al. 2013 (37)
	Dalbavancin + Rifampin	5/14 (36 %)		
S. aureus ATCC 43300 (MRSA)	Fosfomycin	0/12 (0 %)	<0.001	Mihailescu et al. 2014 (42)
	Fosfomycin + Rifampin	10/12 (83 %)		

Zimmerli et al. AAC. 2019

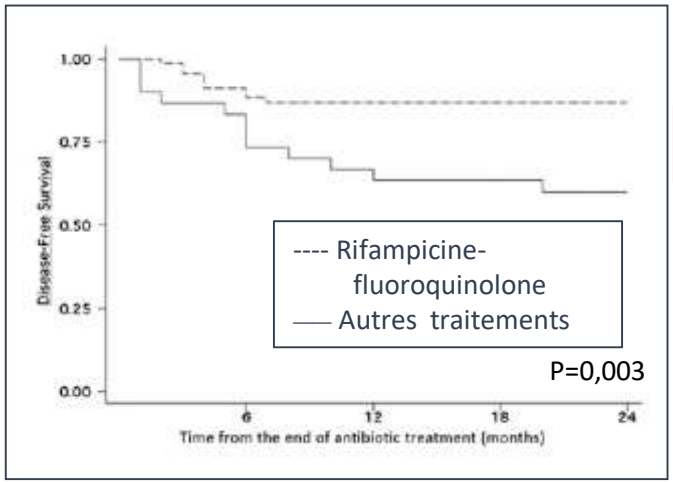
Association reine : RIFAMPICINE + FLQ



Zimmerli W et al. JAMA. 1998.

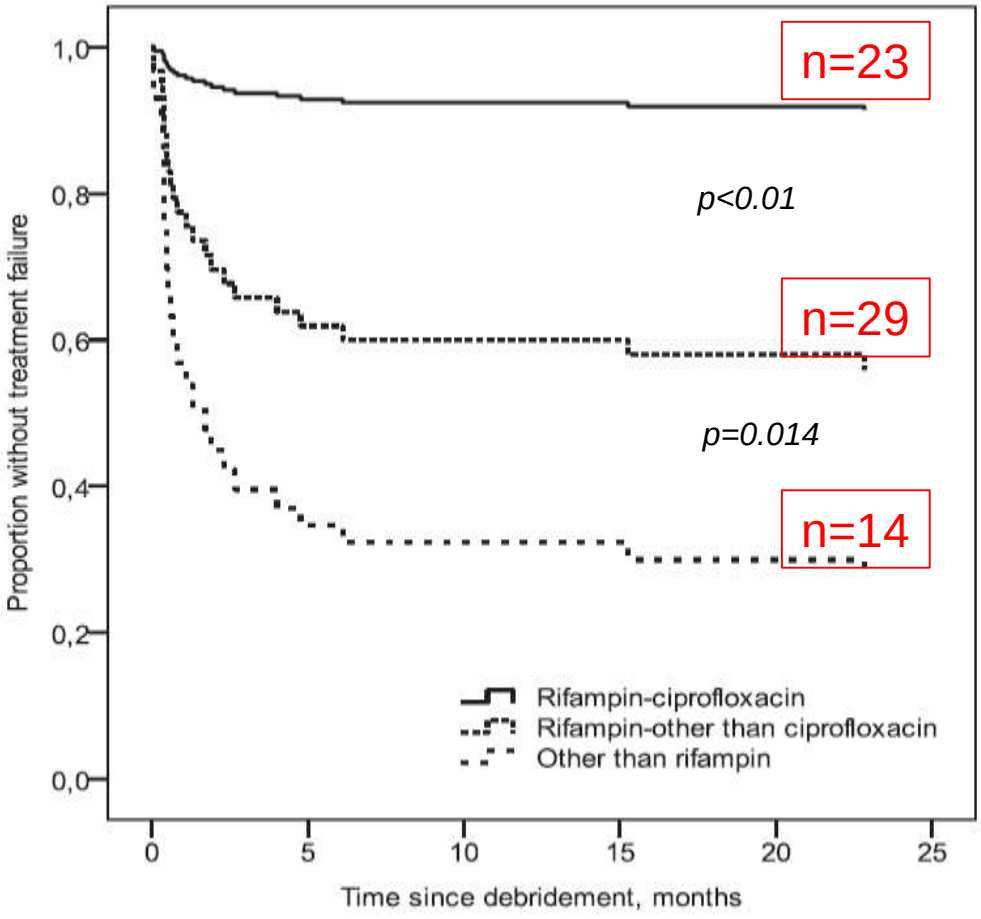


El Helou OC. Eur J Clin Microbiol Infect Dis. 2010



Senneville et al. CID. 2011

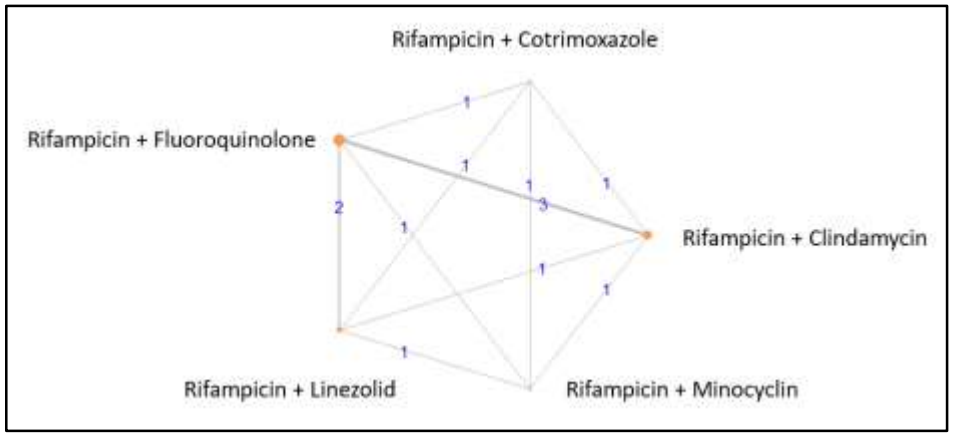
RIFAMPICINE + compagnon



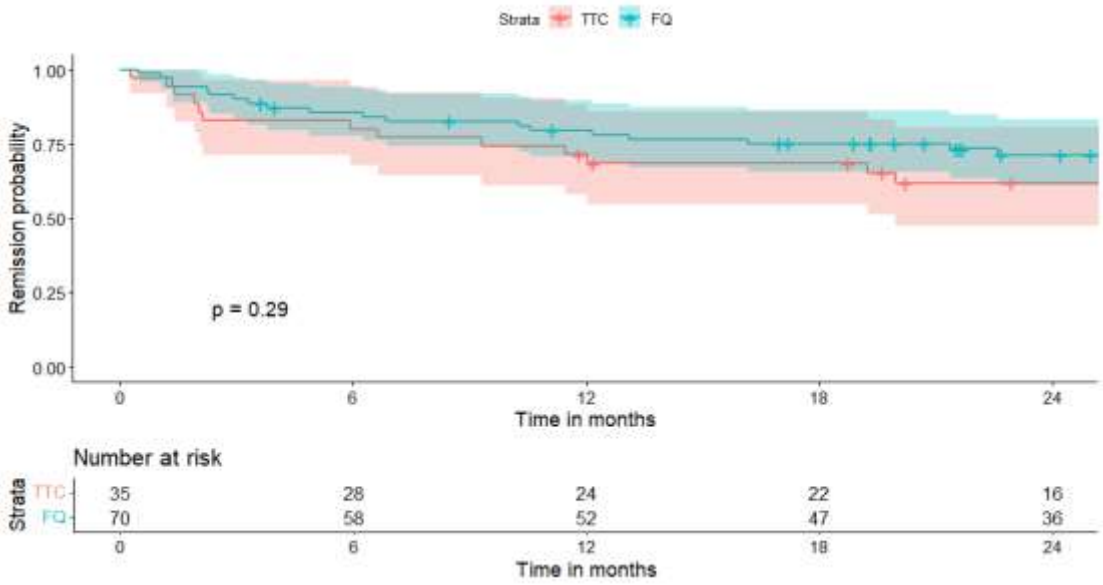
Puhto AP et al. Int Orthop 2015

Alternatives aux FLQ ?

2012	2008/2014	2017
Rifampicine + Ciprofoxacine Levofloxacine	Rifampicine + Ofloxacine + Levofloxacine	Rifampicine + Levofloxacine
Rifampicine + Clindamycine Minocycline Doxycycline Ac fusidique Cortimoxazole Céfalexine	Rifampicine + Linézolide Clindamycine Minocycline Doxycycline Ac fusidique Cortimoxazole	Rifampicine + Linézolide Clindamycine Minocycline Ac fusidique Cortimoxazole
	Ofloxacine + Ac Fusidique	Levofloxacine + Linézolide Clindamycine Minocycline Ac fusidique Cortimoxazole
	Clindamycine + Ac Fusidique	Clindamycine + Ac Fusidique Linezolide + Ac Fusidique + Cotrimoxazole



Gachet B, J Antimicrob Chemo. 2024



Gachet B, Lafon-Desmurs B. En cours de publication

Antibiothérapie documentée

Streptococcus spp.

- AMOXICILLINE + FLQ
- CLINDAMYCINE + FLQ

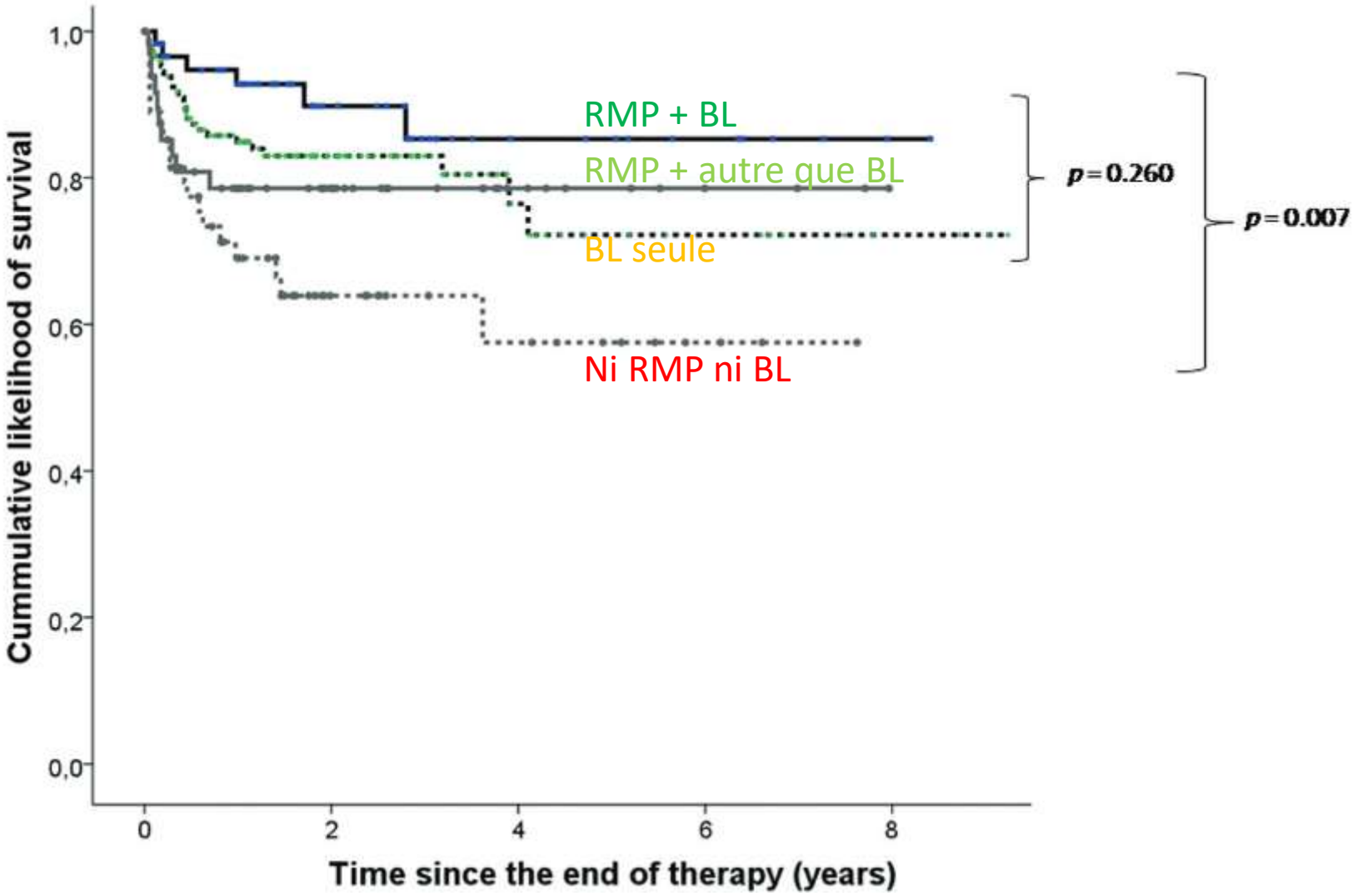
- RIFAMPICINE ?
  - Intérêt dans les DAIR

Table 3 Outcome of 95 episodes of streptococcal prosthetic joint infections; univariate analysis

Variables	Remission ($n = 67$)	Failure ($n = 28$)	p
Age > 70 years	35 (36.8 %)	11 (39.3 %)	.25
≥1 comorbidity	46 (68.7 %)	24 (85.7 %)	.09
Total hip arthroplasty	40 (42.1 %)	10 (35.7 %)	.03
Type of infection (early/delayed/late)	20 (29.8 %)/18 (26.9 %)/29 (43.3 %)	11 (39.3 %)/7 (25 %)/10 (35.7 %)	.19
Fever	35 (36.8 %)	17 (60.7 %)	.45
CRP in mg/L, mean value ± SD	154.6 ± 121.9	207.2 ± 148.3	.09
S. agalactiae (group B streptococci)	27 (28.4 %)	10 (35.7 %)	.68
Antibiotic treatment prior to admission	18 (18.9 %)	8 (28.6 %)	.86
Sinus tract	15 (15.8 %)	3 (10.7 %)	.18
Concomitant bacteremia at the time of diagnosis	11 (16.4 %)	8 (28.6 %)	.18
DAIR	32 (33.7 %)	23 (82.1 %)	.002
Primary arthroplasty	53 (79.1 %)	20 (71.4 %)	.42
Hematogenous origin	10 (14.9 %)	8 (28.6 %)	.12
Rifampicin based combinations	44 (46.3 %)	8 (28.6 %)	.001
Rifampicin + levofloxacin	24 (25.2 %)	4 (14.3 %)	.04

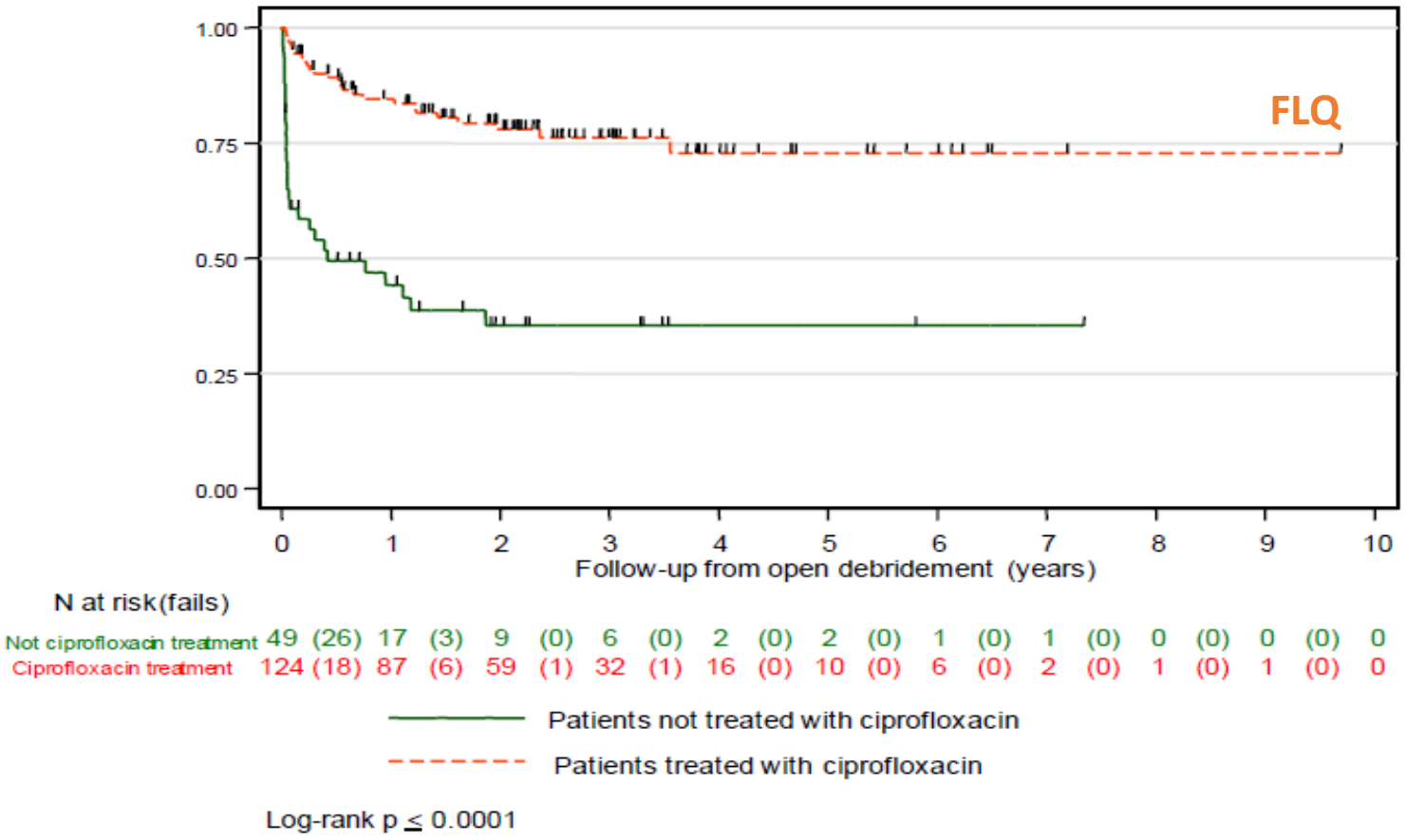
Fiaux et al. BMC Infectious Diseases. 2016

Streptococcus spp.



Lora-Tamayo et al. CID. 2017

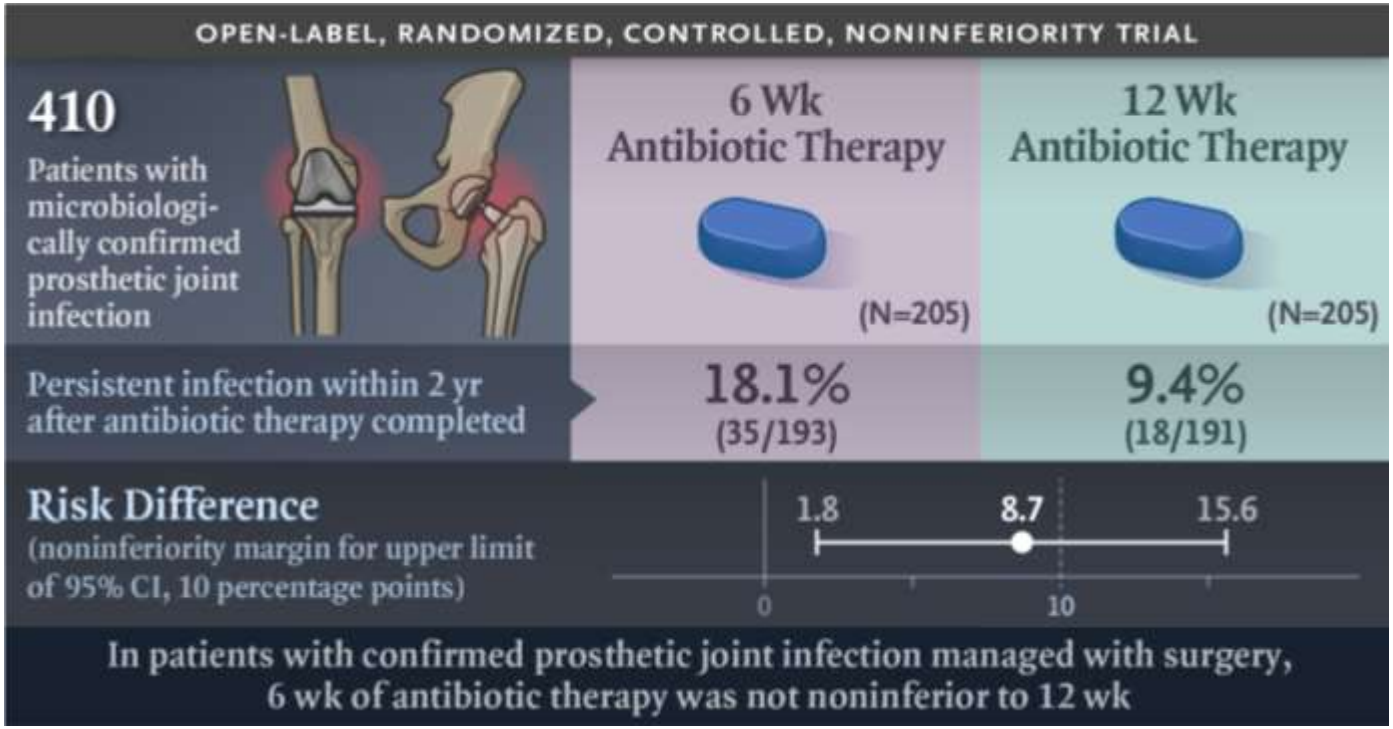
Infection de prothèse articulaire à BGN



D. Rodríguez-Pardo et al. Clin Microb Infect 2014

Quelle durée ?

- **VARIABLES +++**
  - 3 à 6 mois
  - 6 à 12 semaines



Etude DATIPO
Bernard L. et al. NEJM 2021

Thérapeutique en résumé

Antibiothérapie D'ATTENTE/PROBABILISTE

=

LARGE SPECTRE ; IV

- **BÊTA-LACTAMINE**
  - **CEFEPIME**
  - **Ou PIPERACILLINE-TAZOBACTAM**
  - **Ou CEFTOBIPROLE**

+

- **Anti cocci + méti-R**
  - **DAPTOMYCINE**
  - Ou LINEZOLIDE

+ Prise en compte documentation antérieure

Antibiothérapie DOCUMENTEE

=

CIBLEE ; ORALE

- RIFAMPICINE
- + compagnon
  - FLQ, cyclines orales, oxazolidinones; acide fusidique

Staphylococcus (+/- Streptococcus)

- FLUOROQUINOLONES
  - + Bêta-lactamines 7-10 premiers jours

BGN

Antibiothérapie suppressive (SAT)

- **Antibiothérapie chronique, au long cours, de durée indéterminée…**
  - **> 6 mois**

- Sans possibilité curative
  - Maintien des implants en place
  - Contexte pathologique, terrain…

- Après un traitement d'attaque

- **<u>Choix multiples :</u>**
  - Cyclines orales
  - Cotrimoxazole
  - Cephalexin
  - Dalbavancine

Escudero-Sanchez et al. CMI 2017
Pradier et al. Infections 2017
Osmon et al. CID 2012

Reference	Number of Patients	Type of Infection	Aetiology (%)	Follow-Up (Months)	Criteria for Success	Success Rate	Toxicity
Siqueira, 2015 [16]	92	61% chronic 39% acute	*S. aureus* (48%), CoNS (35%)	69.1	Absence of the following: Subsequent surgical intervention for infection after the index procedure, persistent sinus tract, drainage, or joint pain at the last follow-up visit, or death related to the PJI	69%	No data
Prendki, 2017 [10]	136	No data	*S. aureus* (62%), CoNS (21%)	24	Absence of the following: Local or systemic progression of the infection, death, or discontinuation because an adverse drug reaction	61%	18.4% discontinued antibiotics, but in half of cases, the antibiotic could be replaced by another.
Pradier, 2017 [8] 	39	61% delayed or late 39% acute	*S. aureus* (79%), CoNS (10%)	24	Absence of the following: Signs of infection assessed ≥24 months after the end of the curative treatment and then at the last contact with the patient, or death related to the PJI	74%	15% (photo-toxicity and gastrointesti-nal intolerance)
Wouthuyzen-Bakker, 2017 [17]	21	62% late or delayed 38% early	*S. aureus* (33%), CoNS (38%)	21	Absence of the following: Pain during follow-up, surgical intervention is needed to control the infection, or death related to PJI	67%	43% reported side effects and needed change or adjustment of the dosage.
Pradier, 2018 [18] 	78	60% delayed or late 40% early	*S. aureus* (40%), CoNS (32%)	34	Absence of the following: Signs of infection assessed ≥24 months after the end of the curative treatment and then at the last contact with the patient, or death related to the PJI	72%	18% phototoxicity and gastroin-testinal disturbance
Escudero-Sánchez, 2019 [19]	302	73% chronic 11% haematoge-nous 16% early postopera-tive	*S. aureus* (31%), CoNS (33%)	36.5	Absence of the following: Appearance or persistence of a sinus tract, need for debridement or replacement of the prosthesis due to persistence of the infection, or the presence of uncontrolled symptoms, death related to PJI	59%	17% gastroin-testinal 5% cutaneous

SAT : quelle efficacité ?

- Molécules utilisées :
  - Amoxicilline
  - Amoxicilline-Acide clavulanique
  - Cefalexine
  - Imipenem
  - Ciprofloxacine, moxifloxacine
  - Clindamycine
  - **Doxycycline, minocycline**
  - Trimethoprime-sulfamethoxazole
  - Linezolide
  - Pristinamycine
  - **Dalbavancine ? Oritavancine ?**

Cobo J, Escudero-Sanchez R. Suppressive Antibiotic Treatment in Prosthetic Joint Infections: A Perspective. Antibiotics. 2021

Conclusion

- **DOCUMENTATION**
  - Hémocultures
  - Ponction
  - Prélèvements chirurgicaux

Fenêtre ATB

- **ATB d'attente LARGE SPECTRE**
  - Documentation antérieure (BLSE, méti-R, fongique…)

- **ATB documentée**
  - **Variable selon le micro-organisme**
  - Prolongée (12 semaines)
  - Surveillance tolérance

MULTIDISCIPLINAIRE

CHU LILLE

Centre Hospitalier de Tourcoing

Merci de votre attention

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