Principes de l'antibiothérapie au cours des IOA

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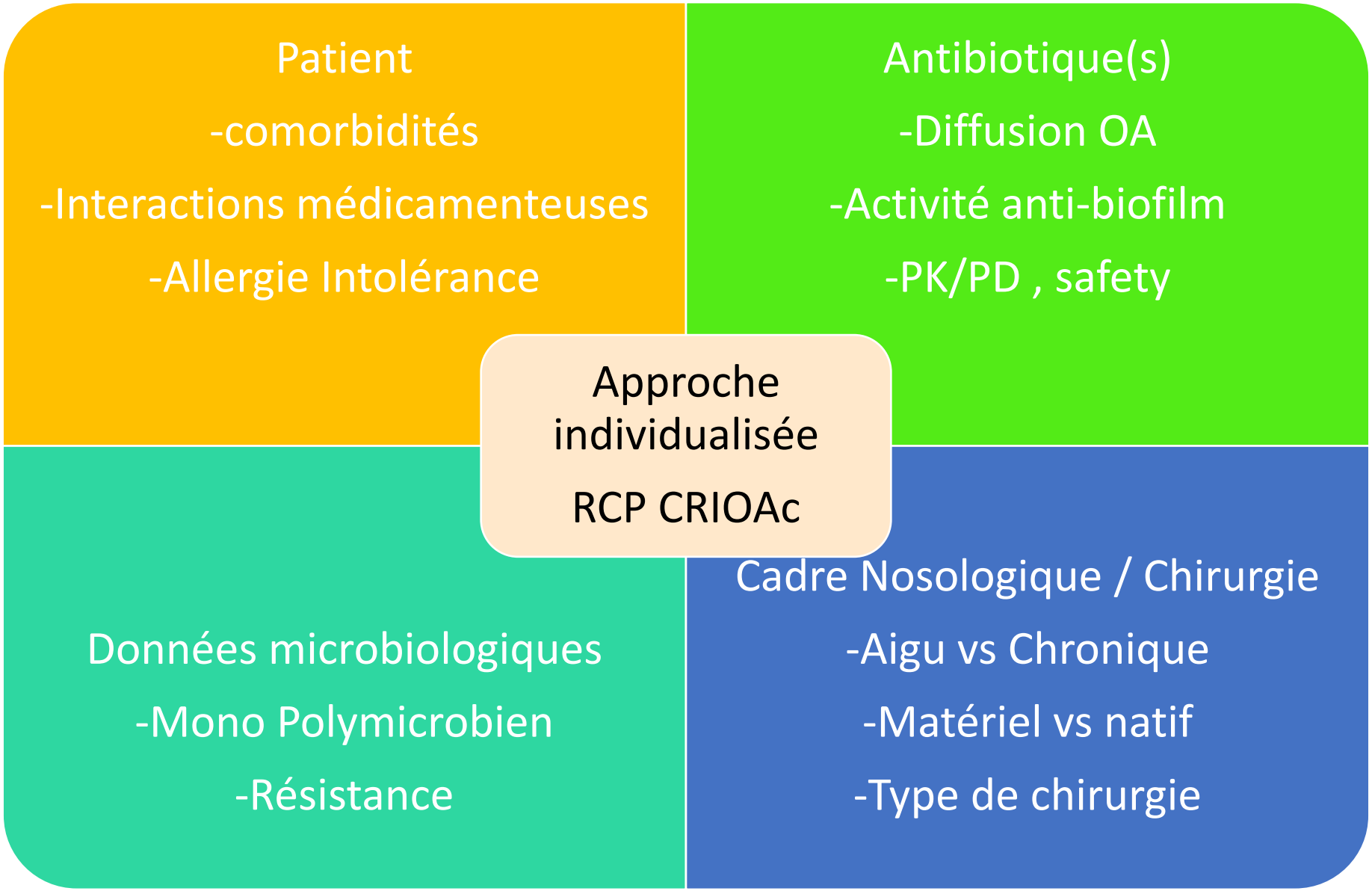
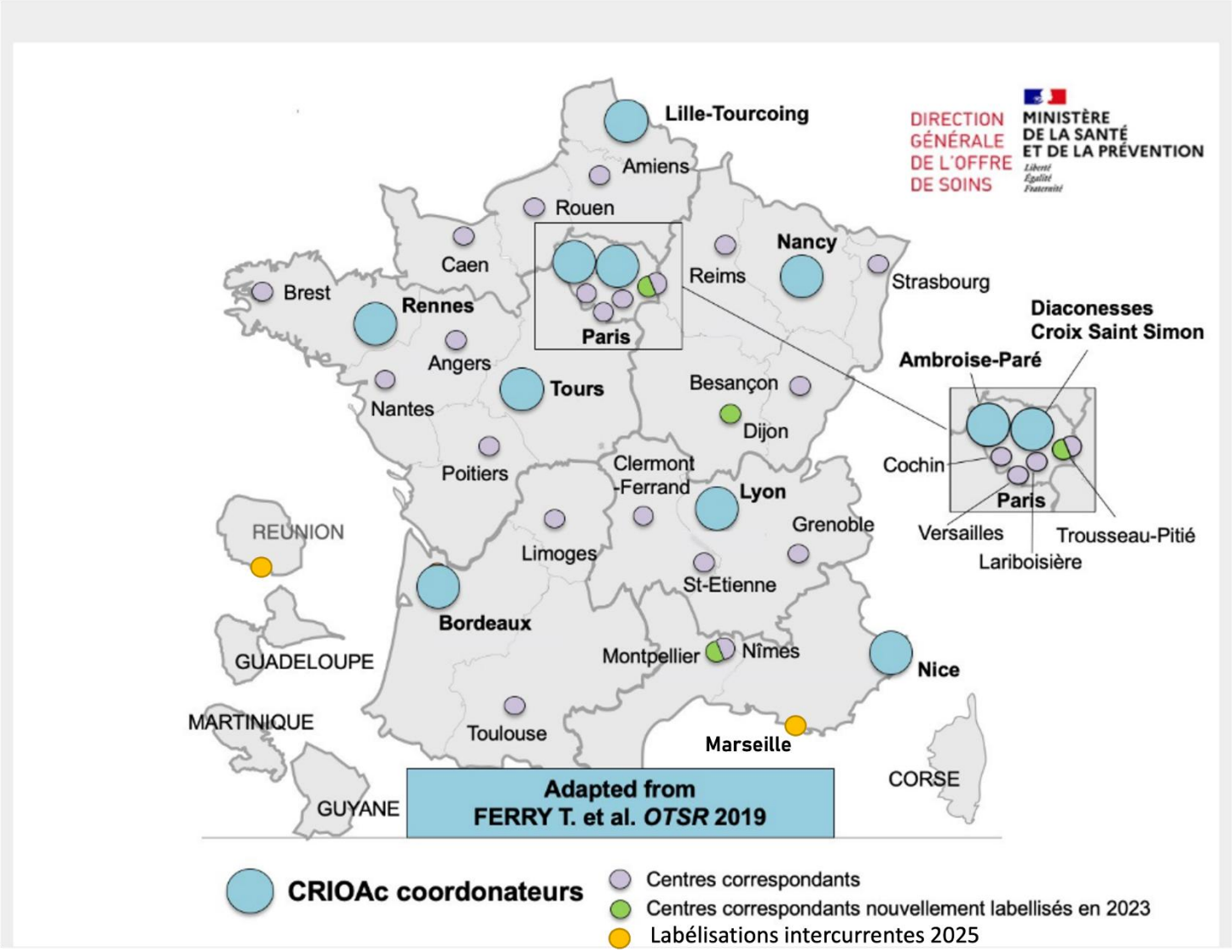

Patient
-comorbidités
-Interactions médicamenteuses
-Allergie Intolérance
Antibiotique(s)
-Diffusion OA
-Activité anti-biofilm
-PK/PD , safety
Approche individualisée
RCP CRIOAc
Données microbiologiques
-Mono Polymicrobien
-Résistance
Cadre Nosologique / Chirurgie
-Aigu vs Chronique
-Matériel vs natif
-Type de chirurgie

Réseau des CRIOAc



33 Centres:
-9 Centres Coordonnateurs
-24 Centres Correspondants

Mandat 5 ans = 2023-2028

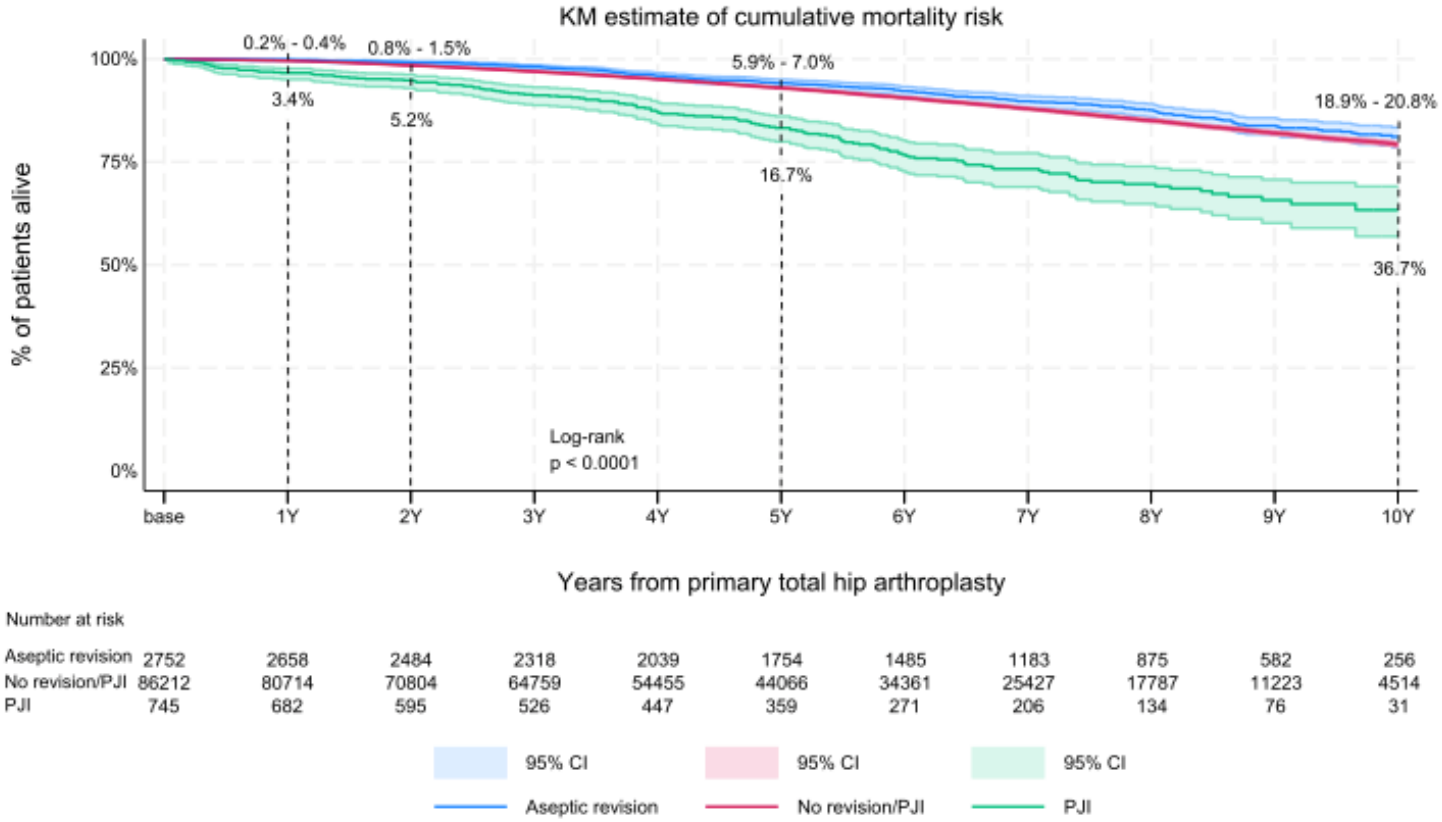
Missions

Soins
RCP
Enseignement
Recherche

Increased long-term mortality of patients with prosthetic joint infection after primary total hip arthroplasty – A large observational cohort study

Andreas Widmer [a,1], Nadine Imhasly [b,1], Christian Brand [c], Vilijam Zdravkovi [d], Adrian Spoerri [c], Kurt Schmidlin [c], Melanie Wicki [e], Martin Beck [f], Rami Sommerstein [b,g,*], for SIRIS and SWISSNOSO

2026



2012-2022
10 ans de suivi
90 000 patients
745 PJI
Gompertz regression, controlling for sex, age, BMI, and ASA.

PJI was associated with increased mortality (**aHR 2.15**; 95% CI, 1.79–2.57; p < 0.001) compared to no PJI/revision

Highest aHR (3.17) for GNB

Complications - Infection

The Journal of Arthroplasty 34 (2019) S337–S342

Mortality During Total Hip Periprosthetic Joint Infection

Kyle M. Natsuhara, MD *, Trevor J. Shelton, MD, John P. Meehan, MD,

- 23 études
- 19 169 patients
- Taux de mortalité à 1 an 4.22%
- Taux de mortalité à 5 ans 21.12%
- Odds ratio de décès par rapport à la population générale USA : 3.58

Au-delà de la mortalité, par rapport aux patients avec arthroplastie non compliquée d'infection baisse de la qualité de vie et du niveau d'autonomie

Wildeman P et al. 2021 Clin Orthop Relat Res

The changing epidemiology of bacteraemic osteoarticular infections in the early 21st century

CMI 2015

O. Murillo[1], I. Grau[1], J. Lora-Tamayo[1], J. Gomez-Junyent[1], A. Ribera[1], F. Tubau[2], J. Ariza[1] and R. Pallares[1]

1) *Infectious Disease Service and* 2) *Microbiology Department, Hospital Universitari de Bellvitge, Barcelona, Spain*

	Total (n=601)	1985-1991 (n=70)	2007-2011 (n=183)
Age médian (IQR)	63 (50-74)	49 (24-64)	65 (53-77)
≥ 1 comorbidité	307 (51%)	16 (23%)	107 (59%)
Diabète	153 (26%)	11 (16%)	50 (27%)
Cardiovasculaire	88 (15%)	1 (1%)	42 (23%)
Insuffisance rénale	44 (7%)	0	20 (11%)
Ttt immunosupp.	88 (15%)	6 (9%)	30 (16%)

RESEARCH ARTICLE Open Access

Polypharmacy and adverse outcomes after hip fracture surgery

Maria Härstedt[1], Cecilia Rogmark[2], Richard Sutton[3], Olle Melander[1,4] and Artur Fedorowski[1,5*]

Härstedt *et al. Journal of Orthopaedic Surgery and Research* (2016) 11:151

272 fractures de hanche
à 6 mois

- 36 (13,2%) décès
- 86 (31,6%) réadmission
  - -nombre de ttt = fdr réadmission
  - -AVK diurétique tramadol = fdr chute

Diffusion ostéo-articulaire des antibiotiques

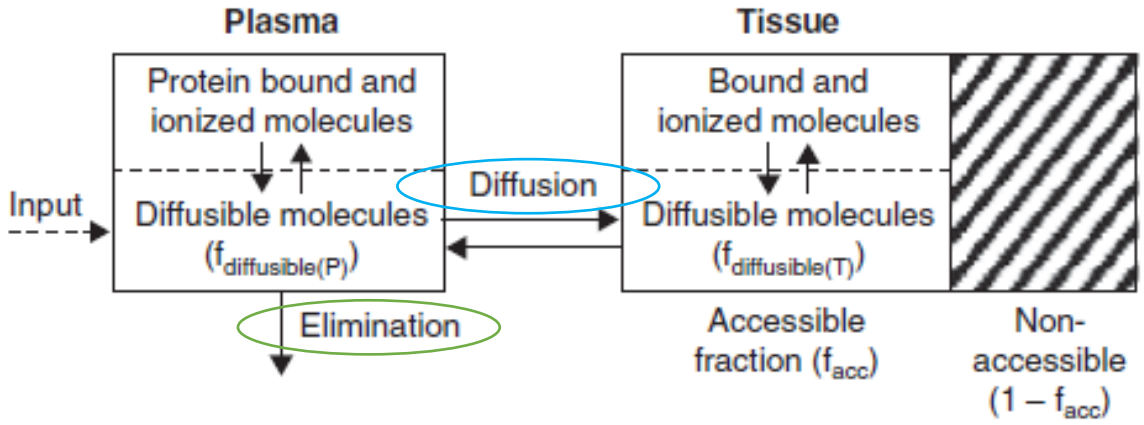
- Hétérogénéité des données
- Données chez l'humain vs modèles animaux
- Os cortical vs Os spongieux (cort. < spon.)
- Avec ou sans inflammation
- Dosages après dose unique vs doses répétées
- Souvent prélèvement unique
- Technique de dosages des antibiotiques
- Estimation de la densité osseuse (mg/kg vers mg/L) pour calcul des ratios C_{os}/C_{plasma} variable (1,3 à 1,9)

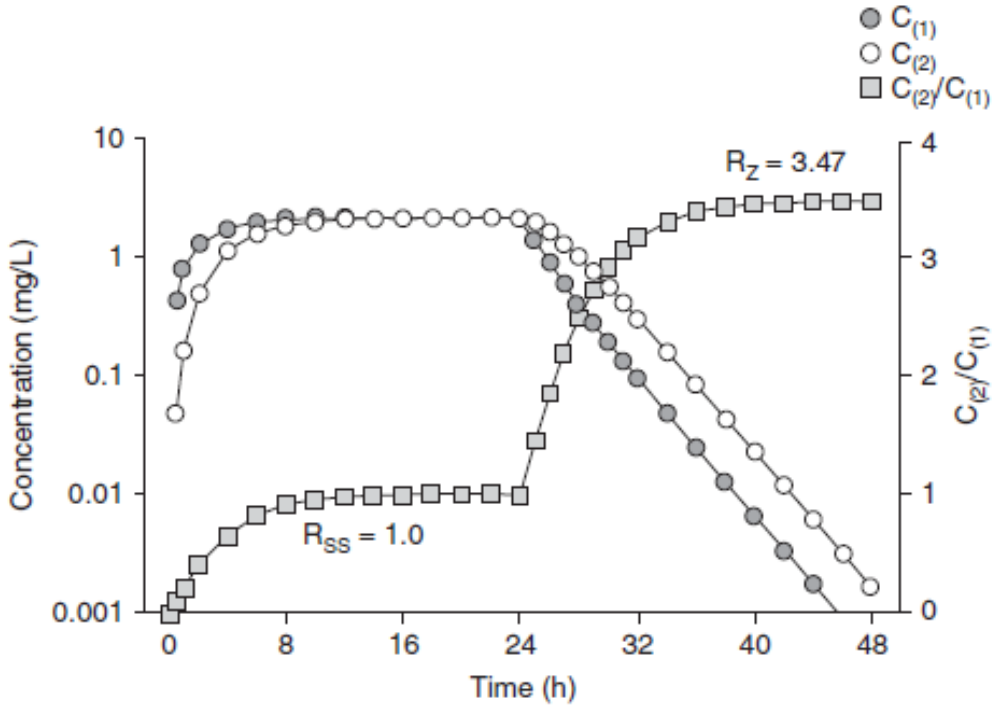
Clin Pharmacokinet 2009

Penetration of Antibacterials into Bone

Pharmacokinetic, Pharmacodynamic and Bioanalytical Considerations

Cornelia B. Landersdorfer,[1] *Jürgen B. Bulitta,*[1] *Martina Kinzig,*[1] *Ulrike Holzgrabe*[2] and *Fritz Sörgel*[1,3]





Simulated plasma and bone tissue concentrations and bone : plasma concentration ratio for a two-compartment model after a 24-hour constant-rate infusion

Extended-Duration Dosing and Distribution of Dalbavancin into Bone and Articular Tissue

April 2015 Volume 59 Number 4 Antimicrobial Agents and Chemotherapy

Michael W. Dunne,[a] Sailaja Puttagunta,[a] Craig R. Sprenger,[c]* Chris Rubino,[b] Scott Van Wart,[b] James Baldassarre[a]

Durata Therapeutics, Inc., Branford, Connecticut, USA[a]; Institute for Clinical Pharmacodynamics, Latham, New York, USA[b]; PRACS Institute, Ltd., Fargo, North Dakota, USA[c]

TABLE 4 Dalbavancin tissue concentrations (safety population)

	Dalbavancin concn (mean [SD]; no. of samples) at hours (days) postdose that samples were collected:					
Tissue	12 (0.5)	24 (1)	72 (3)	168 (7)	240 (10)	336 (14)
Plasma (μg/ml)[a]	85.3 (18.9); 31	ND[b]	ND	ND	ND	15.3 (4.1); 31
Synovium (μg/g)[c]	25.0 (0); 3	17.9 (7.8); 3	19.5 (4.9); 3	19.2 (8.9); 4	25.0 (0); 2	15.9 (7.9); 3
Synovial fluid (μg/ml)[c]	22.9; 1	27.4 (10.8); 4	19.2 (4.9); 3	11.6 (3.3); 2	13.9 (1.0); 3	6.2 (1.7); 2
Bone (μg/g)	6.3 (3.1); 5	5.0 (3.5); 5	4.6 (3.8); 5	3.8 (2.7); 5	3.7 (2.2); 5	4.1 (1.6); 5
Skin (μg/g)[c]	19.4 (7.9); 2	12.5 (6.5); 3	13.8 (1.4); 2	15.7 (1.0); 2	21.6; 1	13.8 (2.1); 2

[a] Mean (SD) plasma concentrations in 31 subjects at 772 and 1,080 h were 6.2 (2.4) and 3.4 (1.7), respectively.
[b] ND, not detected.
[c] Concentrations above the upper limit of quantification are reported as 25 μg/unit.

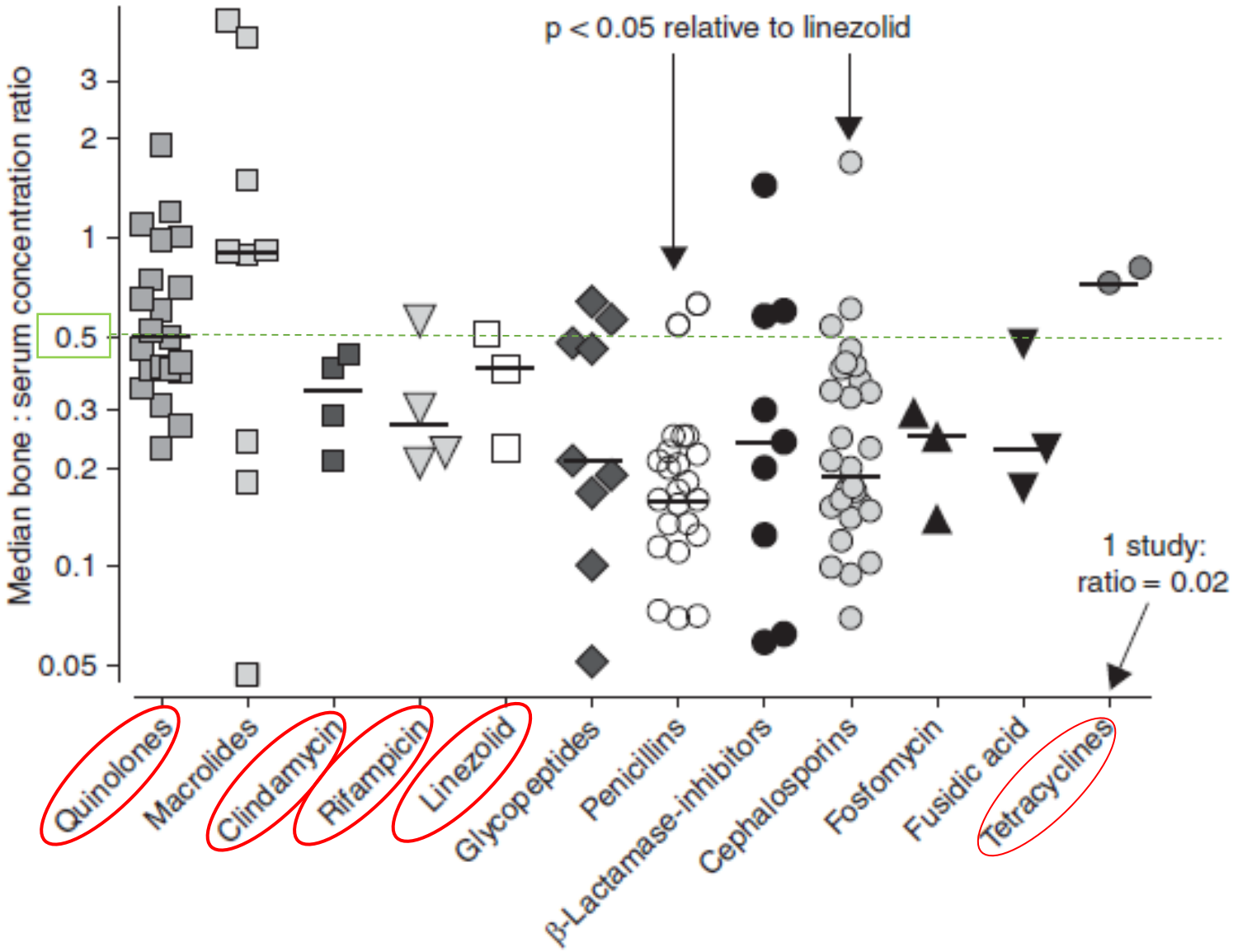
7.4%

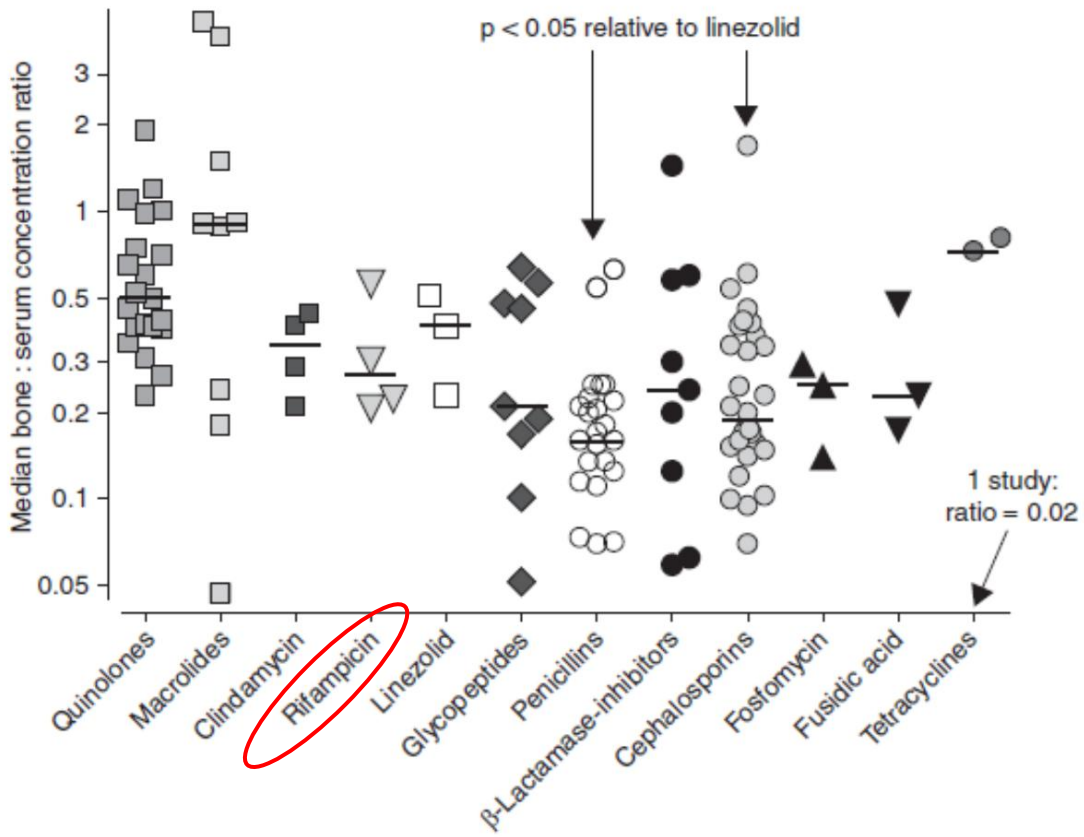
27%

Ratio AUC/CMI os/plasma : 13%

CMI_{90} MSSA : 0,06 mg/l

Human bone : serum or bone : plasma concentration ratios





Rifampicine

Pic plasmatique possible 6 à 10 mg/L

Breakpoint EUCAST: 0,06 mg/L

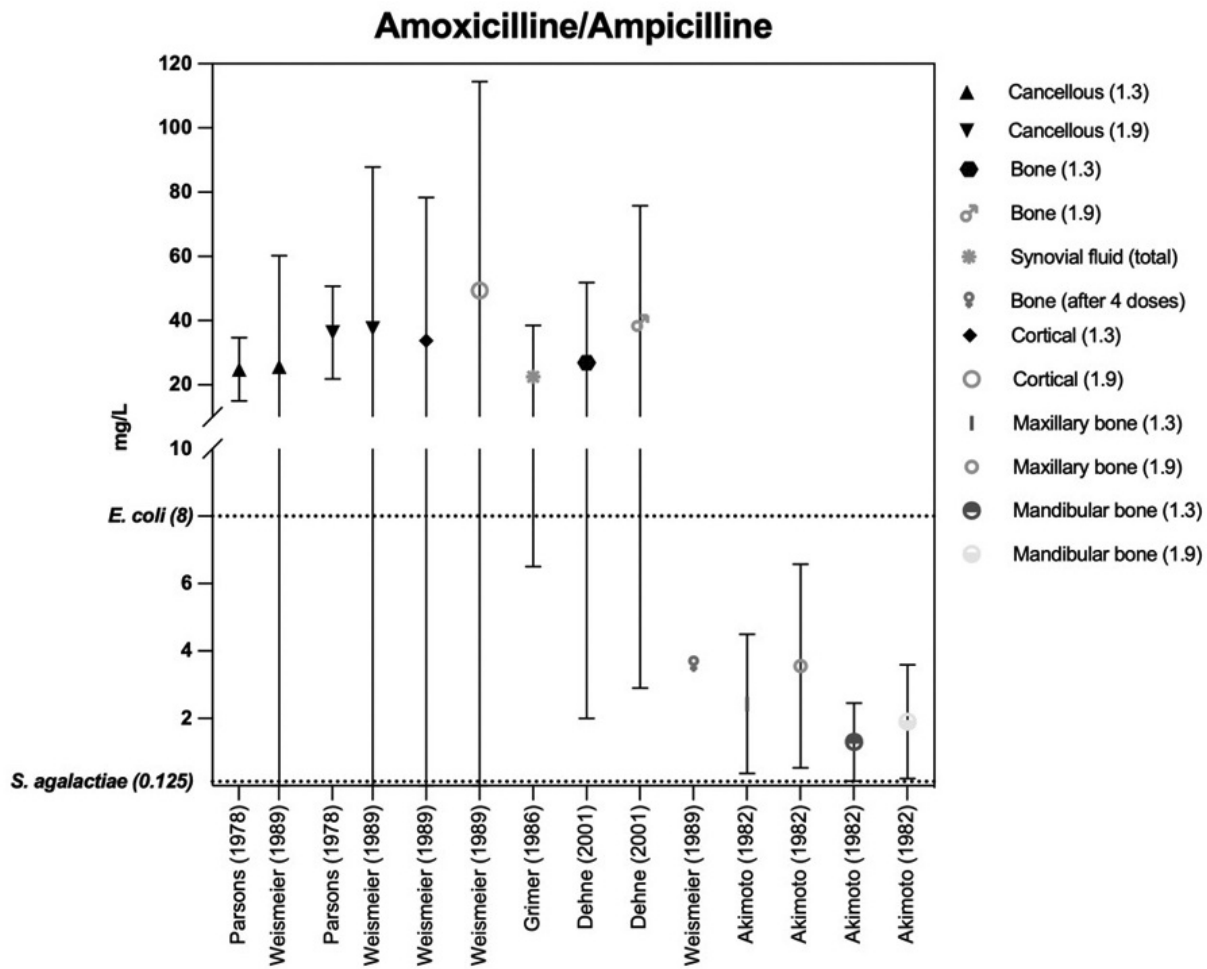
REVIEW

OPEN ACCESS Check for updates

EXPERT OPINION ON DRUG METABOLISM & TOXICOLOGY
2022, VOL. 18, NO. 9, 587–600
https://doi.org/10.1080/17425255.2022.2117607

The mysteries of target site concentrations of antibiotics in bone and joint infections: what is known? A narrative review

Birgit C.P. Koch[a,b,c], Qiaolin Zhao[a,c], Maartje Oosterhoff[a], Jakob van Oldenrijk[d], Alan Abdulla [a,b,c], Brenda C.M. de Winter[a,b,c], Koen Bos[d] and Anouk E. Muller[b,e,f]



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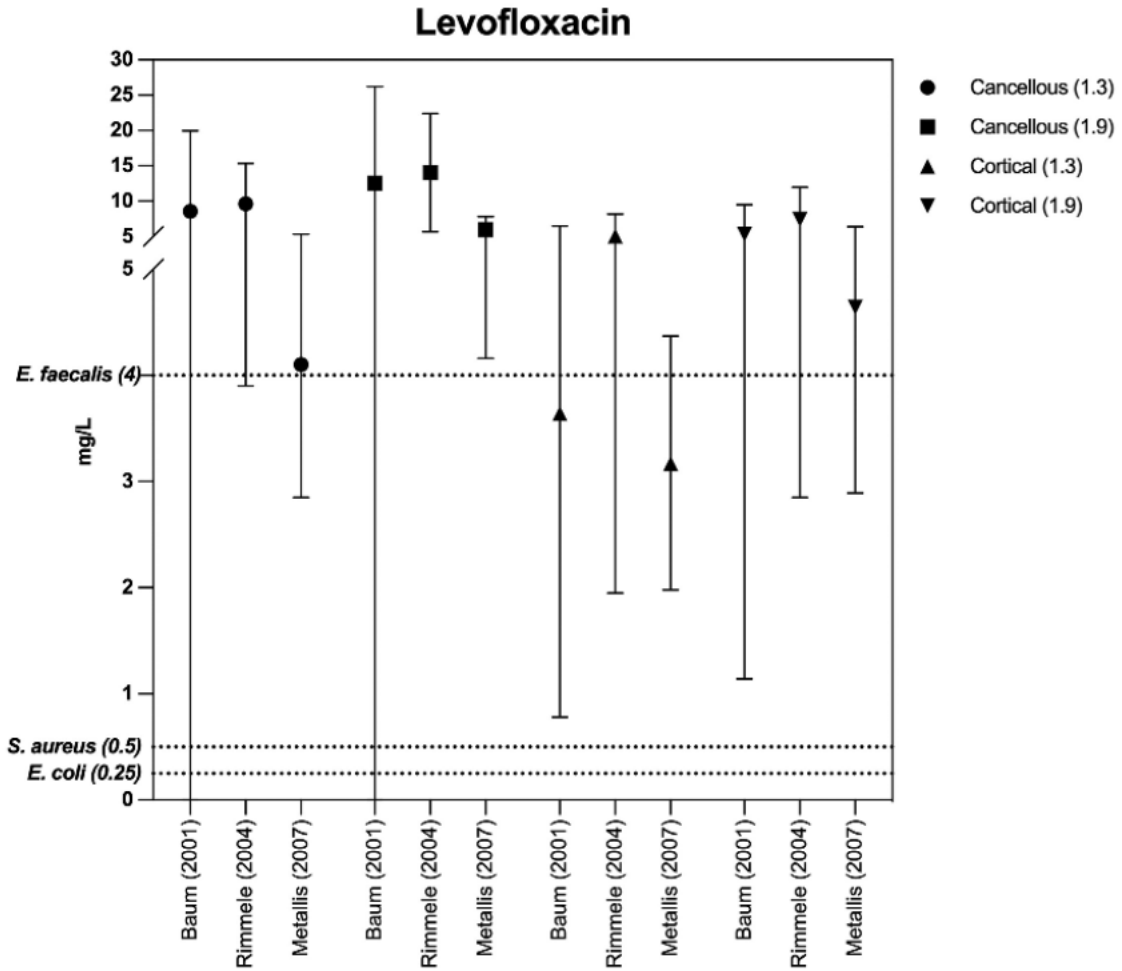


Outcome of Debridement, Antibiotics, and Implant Retention for Staphylococcal Hip and Knee Prosthetic Joint Infections, Focused on Rifampicin Use: A Systematic Review and Meta-Analysis

OFID 2021

H. Scheper,[1] L. M. Gerritsen,[1] B. G. Pijls,[2] S. A. Van Asten,[3] L. G. Visser,[1] and M. G. J. De Boer[1]

[1]Department of Infectious Diseases, Leiden University Medical Centre, Leiden, The Netherlands, [2]Department of Orthopaedic Surgery, Leiden University Medical Centre, Leiden, The Netherlands, [3]Department of Microbiology, Leiden University Medical Centre, Leiden, The Netherlands

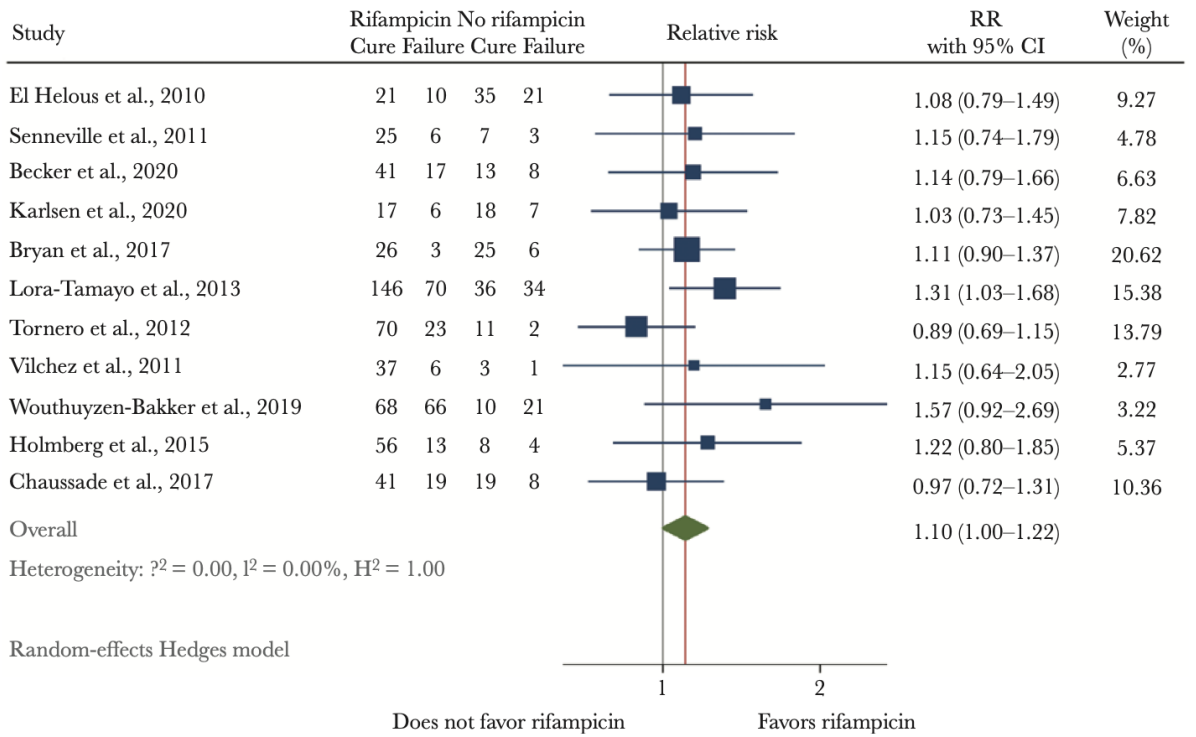


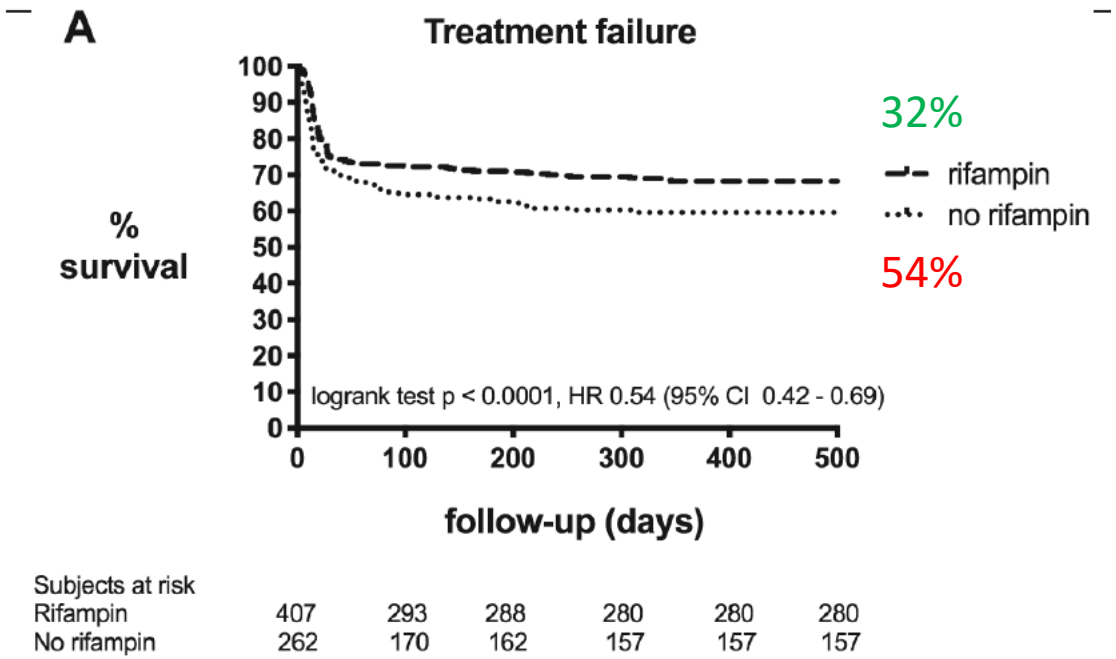
Figure 5. Meta-analysis of 11 studies in which outcome for staphylococcal prosthetic joint infection (PJI) after debridement, antibiotics, and retention of the implant (DAIR) could be compared between patients treated and not treated with rifampicin. The point estimate (relative risk) for each study is represented by a square. The 95% confidence interval (CI) for each study is represented by a horizontal line intersecting the square. The size of the square represents the relative precision of the study estimates: the bigger the square, the more precise the study.

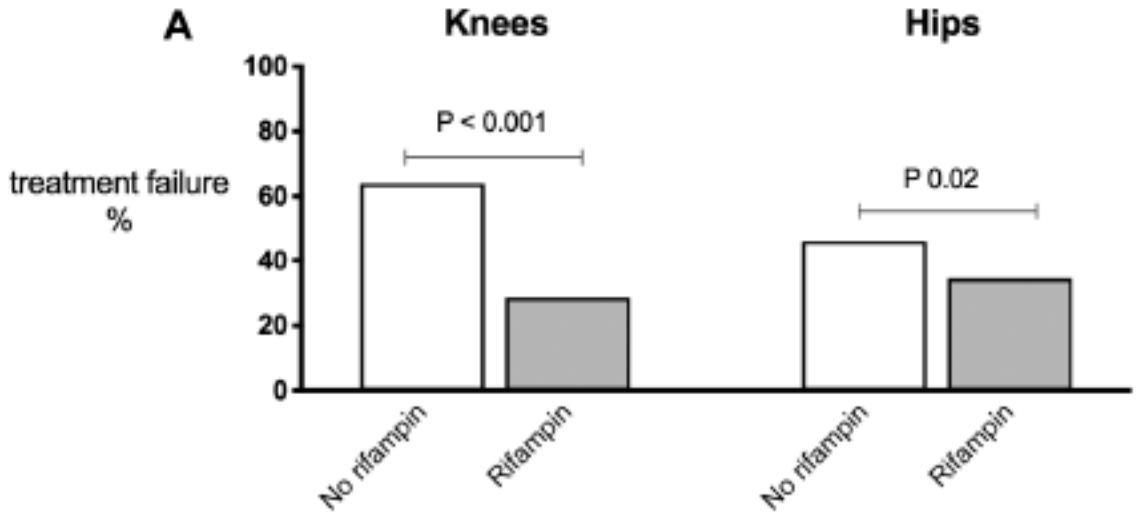
CID 2021:73 (1 November) • Beldman et al

If, When, and How to Use Rifampin in Acute Staphylococcal Periprosthetic Joint Infections, a Multicentre Observational Study

Mark Beldman,[1] Claudia Löwik,[1] Alex Soriano,[2] Laila Albiach,[2] Wierd P. Zijlstra,[3] Bas A. S. Knobben,[4] Paul Jutte,[1] Ricardo Sousa,[5] André Carvalho,[5] Karan Goswami,[6] Javad Parvizi,[6] Katherine A. Belden,[7] and Marjan Wouthuyzen-Bakker[8]

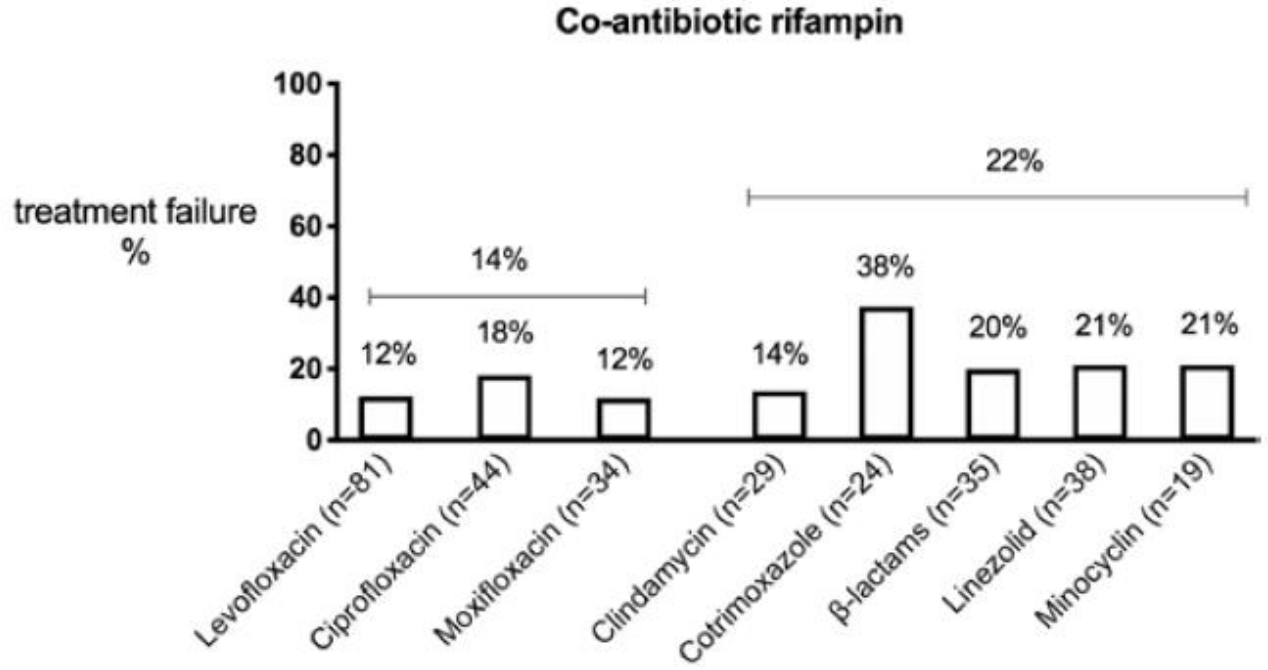
669 patients, 617 infections aiguës, 52 secondaires aiguës
Rifampicine chez 407 (61%) patients





Importance des FQ dans le traitement des IOA associées à du matériel étranger

staphylocoques



Beldman *et al.* 2021 CID

P. aeruginosa

TABLE 2 | Multivariate Cox analysis that includes significant determinants for failure identified in the univariate analysis.

	HR	95% CI	*p*
Optimal surgical treatment*	0.32	0.11–0.98	0.045
IV effective treatment of at least 3 weeks*	0.15	0.004–0.054	0.003
Ciprofloxacin for at least 3 months*	0.23	0.07–0.75	0.015

HR, Hazard ratio; 95% CI, 95% confidence interval.
**After exclusion of the five patients who finally received suppressive antimicrobial therapy.*

Cerrioli *et al.* 2020 Front Med

Safety and Tolerability of Fluoroquinolones in Patients with Staphylococcal Periprosthetic Joint Infections

Nicholas J. Vollmer,[1] Christina G. Rivera,[1] Ryan W. Stevens,[1] Caitlin P. Oravec,[2] Kristin C. Mara,[3] Gina A. Suh,[2] Douglas R. Osmon,[2] Elena N. Beam,[2] Matthew P. Abdel,[4] and Abinash Virk[2]

Clinical Infectious Diseases

MAJOR ARTICLE

2022

156 patients, RFP in both groups

Overall, unplanned drug discontinuation occurred in 35.6% of patients in the FQ group and 3% of patients in the non-FQ group.

Severe adverse effects were reported in 7.8% of patients in the FQ arm and 1.5% in the non-FQ arm, respectively (*P* = .14)

Rifampicine (RFP) et Fluoroquinolones (FQ) : (in)tolérance

Etudes / localisation	Taux d'effets secondaires RFP/FQ	Taux d'effets secondaire autres molécules
« Essai randomisé de Zimmerli »	RFP+FQ 28%	
« Série 98 IOAM à *S. aureus* de Senneville »	RFP+FQ 33%	
CHU de Nice, 238 IOA *Staphylococcus* spp	RFP+FQ 14%	CD+RFP 9%, CD+FQ 5.5%
HCL, 200 IOA SAMS	RFP ou FQ 9.5%	

CD: Clindamycine

Zimmerli W et al. *JAMA* 1998
Senneville E et al. *Clin Infect Dis* 2011
Danré A et al. *Joint Bone Spine* 2015
Valour F et al. *Antimicrobs Agent Chemoter* 2014

Mesures associées

Original article Infectious Diseases Now 53 (2023) 104671

Assessment of the impact of pharmacist-led intervention with antibiotics in patients with bone and joint infection

Philippine Marque [a], Gwenael Le Moal [b], Chloé Labarre [c], Jérémy Delrieu [a], Pierre Pries [c,d], Antoine Dupuis [a,d], Guillaume Binson [a,d], Pauline Lazaro [a,*]

Période contrôle 105 patients
Période intervention 59 patients

- Ré hospitalisation pour un motif en lien avec l'IOA : 23 (22%) contrôle, 3 (5%) intervention
- Moins de modifications de traitement dans la période intervention

Original article Infectious diseases now 54 (2024) 104958

Impact of pharmacist-led interventions in a multidisciplinary consultation meeting for bone and joint infection

Anne Elisabeth Royere [a], Xavier Pourrat [a], Louis-Romée Le Nail [b], Marie-Frederique Lartigue [c,d], Adrien Lemaignen [e,f], Vianney Tuloup [a,g,*], Marion Lacasse [f], upon members of the Tours CRIOAC

Alexa DEBARD
Olivier Villanova, Blandine Garric, Guillaume Martin-Blondel, Pierre Delobel
Service des Maladies Infectieuses et Tropicales - CHU Toulouse

ANTIBIO-HOME

Organisation innovante de télésurveillance des patients sous antibiothérapie par :

- un infirmier référent en antibiothérapie supervisé par un infectiologue
- une plateforme de télésurveillance et application mobile sécurisée : MHLink

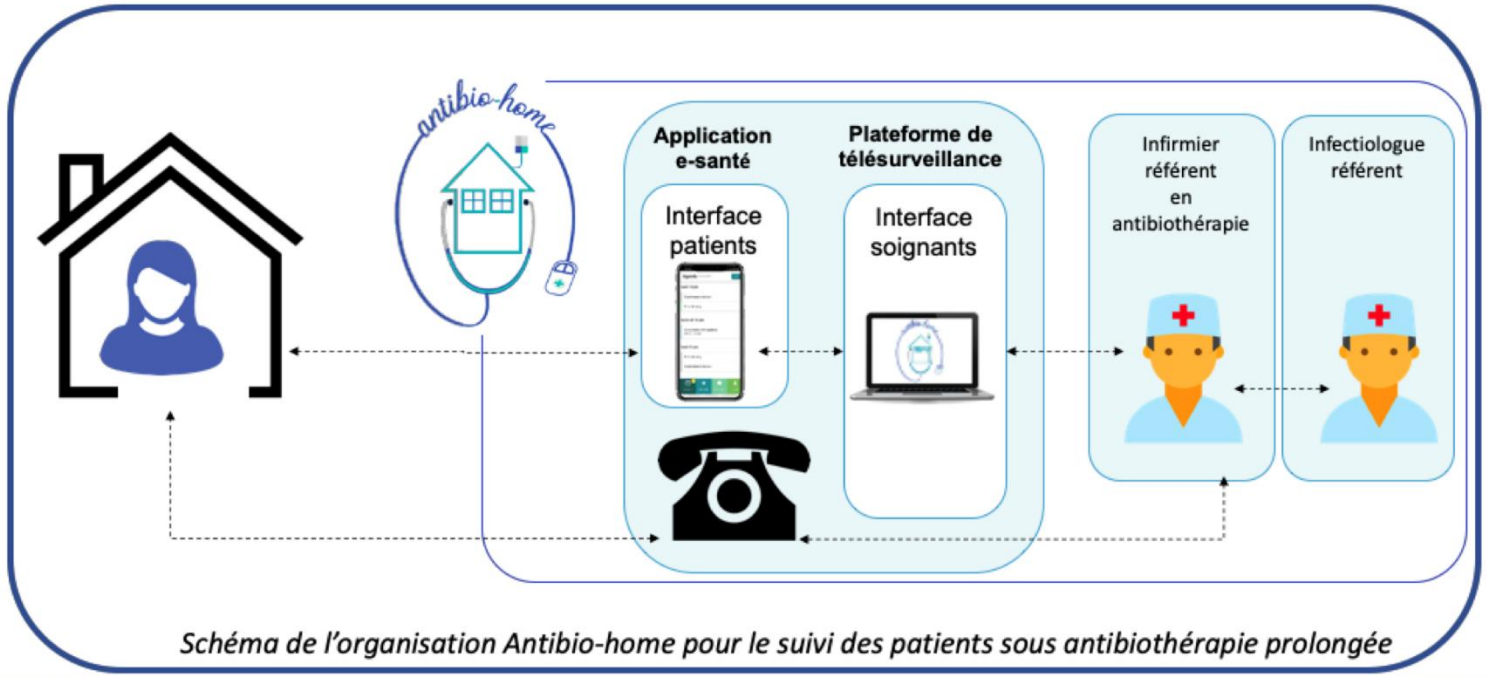


Schéma de l'organisation Antibio-home pour le suivi des patients sous antibiothérapie prolongée

PJI

Antibiothérapie probabiliste

Utilité ?

Contexte	Type d'IPA	Chir	Evolution	ATB probabiliste inadaptée	Facteurs d'échec	Ref
Espagne monocentrique rétro. 2009-2018, 80 patients	Précoce <3 mois 84%	DAIR	34 échecs 46 succès	14 (41%) 1 (2.2%)	**ATB proba inadaptée** ASA > 2	Barbero-Allende 2021 J Span Soc of Chem
Finlande monocentrique rétro. 2001-2009, 113 patients	Précoce <4 sem 69% Hématogène 31%	DAIR	43 échecs 70 succès	10 (23.3%) 3 (4.3%)	**ATB proba inadaptée** øRFP	Puhto 2015 International Orthop
Australie multicentrique rétro. 2006-2008, 147 patients	Précoce <3 mois	DAIR (76%)	43 échecs 104 succès	30 (70%) 20 (19%)	**ATB proba inadaptée** ATCD d'IPA Durée ATB<90j	Peel 2012 J Hosp Infection

Quelles molécules ?

Molécule anti-Gram -	Nombre de réponses
Carbapénème	1
Céfépime	5
Ceftazidime	1
Pipéracilline-Tazobactam	19
Molécule anti-Gram +	
Daptomycine	10
Linézolide	3
Vancomycine	9

Autres	
Ceftobiprole	2
Gentamicine	1

Le Maréchal M et al. 2021 BMC Inf Dis

A adapter selon l'épidémiologie locale

- Entérobactéries groupe 3 ? Pyo ?
- Choix de la βL, C3G suffisante ?

Anti G -

- Impact écologique céfépime mieux que P/T ?
- Effets secondaires Vanco + P/T ≫ Vanco + Céfépime
- Neurotoxicité du céfépime

Triffault-Fillit, JAC, 2020

Anti G +

SCN Méthi-R

- Gestion de la daptomycine + facile que vancomycine
- Linézolide : Per Os, bien toléré sur des durée courtes, danger des interactions

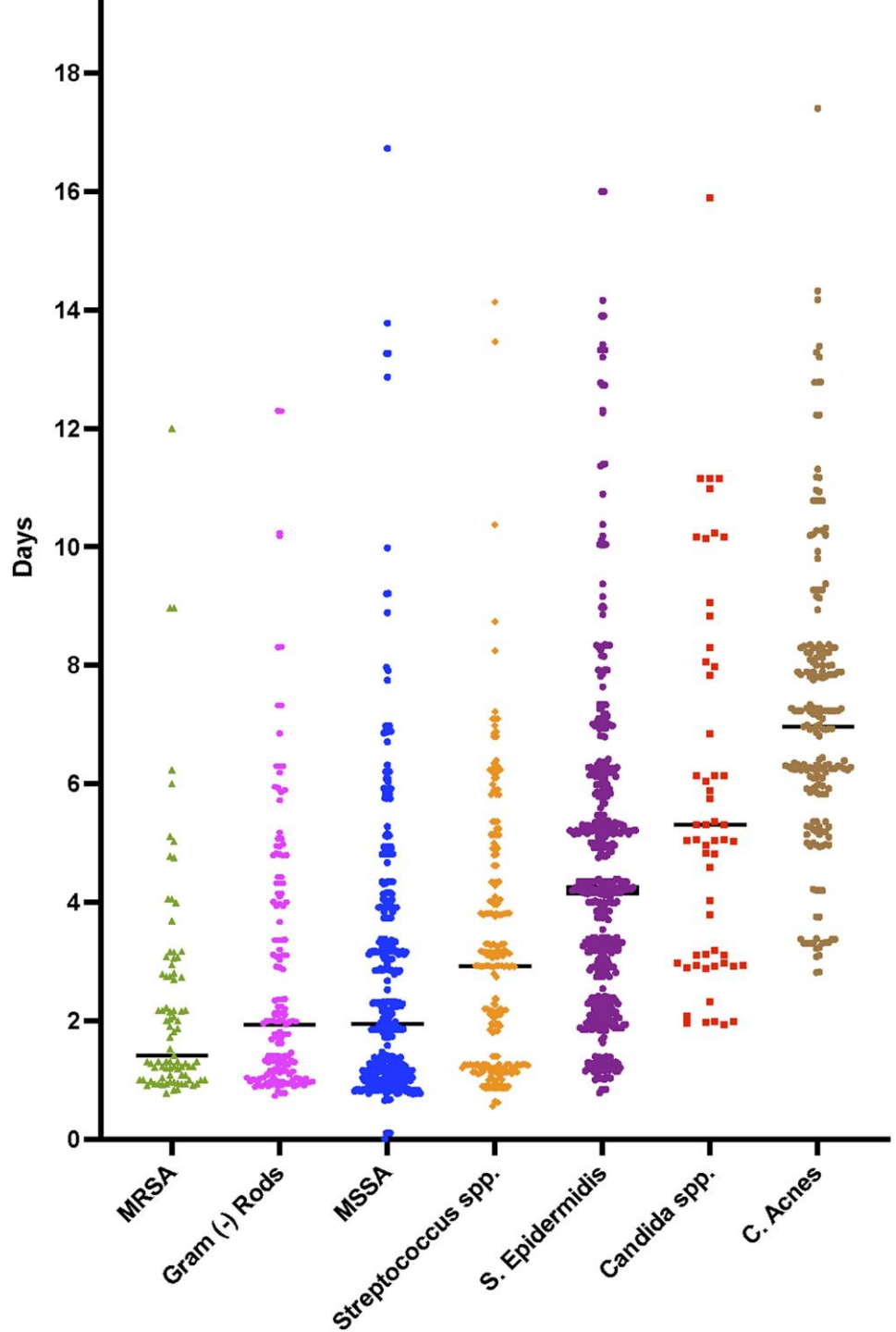
Time to Positivity of Cultures Obtained for Periprosthetic Joint Infection

Saad Tarabichi, MD, Graham S. Goh, MD, Luigi Zanna, MD, Qudratullah S. Qadiri, BS, Colin M. Baker, BS, Thorsten Gehrke, MD, Mustafa Citak, MD, PhD, and Javad Parvizi, MD, FRCS

Investigation performed at the Rothman Orthopaedic Institute, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

J Bone Joint Surg Am. 2023;105:107-12 • http://dx.doi.org/10.2106/JBJS.22.00766

536 IOAP chroniques
Temps médian de positivité: 3.3j (IQR 1.9 5.4)



Relais Per Os, quand ?

Hors bactériémie / endocardite

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

Li et al. 2019

J Antimicrob Chemother 2021; **76**: 3033–3036
doi:10.1093/jac/dkab271 Advance Access publication 18 August 2021

Journal of Antimicrobial Chemotherapy

Fully oral targeted antibiotic therapy for Gram-positive cocci-related periprosthetic joint infections: a real-life before and after study

Alexandre Coehlo[1], Olivier Robineau [1,2,3,4], Marie Titecat[4], Nicolas Blondiaux[4], Hervé Dezeque[4], Pierre Patoz[1], Caroline Loiez[4], Sophie Putman[4], Eric Beltrand[4], Henri Migaud[2,3,4] and Eric Senneville[1,2,3,4]*

Passage de 13 à 9 jours IV en post-op

J Antimicrob Chemother 2024; **79**: 327–333
https://doi.org/10.1093/jac/dkad382 Advance Access publication 19 December 2023

Journal of Antimicrobial Chemotherapy

Prosthetic joint infections: 6 weeks of oral antibiotics results in a low failure rate

Pierre-Marie Roger [1,2]*, Frédéric Assi[1] and Eric Denes[3]

3 jours ou moins IV, 90.8% de succès

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

2021

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. Ansart, J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. Bentayeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Begué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille

Subgroup	6-Wk Therapy	12-Wk Therapy	Risk Difference (95% CI)
	no. of patients with event/total no. (%)		*percentage points*
All patients	32/190 (16.8)	15/188 (8.0)	8.9 (2.2 to 15.6)
Surgical procedure			
Débridement	23/75 (30.7)	11/76 (14.5)	16.2 (2.9 to 29.5)
Two-stage revision	6/40 (15.0)	2/41 (4.9)	10.1 (–3.1 to 23.3)
One-stage revision	3/75 (4.0)	2/71 (2.8)	1.2 (–4.8 to 7.1)
Affected joint			
Hip	19/122 (15.6)	9/117 (7.7)	7.9 (–0.2 to 16.0)
Knee	13/68 (19.1)	6/71 (8.5)	10.7 (–0.9 to 22.2)
Episode of prosthetic joint infection			
First	27/162 (16.7)	13/160 (8.1)	8.5 (1.4 to 15.7)
At least the second	5/28 (17.9)	2/28 (7.1)	10.7 (–7.0 to 28.4)

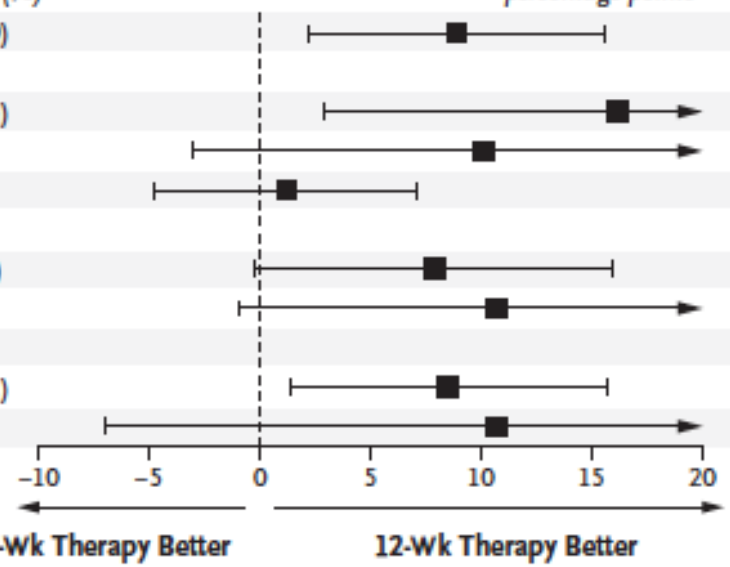


Figure 2. Exploratory Subgroup Analyses of Persistent Infection within 2 Years after the Completion of Antibiotic Therapy (Primary Outcome).

IDV (PVO)

Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial

*Louis Bernard, Aurélien Dinh, Idir Ghout, David Simo, Valerie Zeller, Bertrand Issartel, Vincent Le Moing, Nadia Belmatoug, Philippe Lesprit, Jean-Pierre Bru, Audrey Therby, Damien Bouhour, Eric Dénes, Alexa Debard, Catherine Chirouze, Karine Fèvre, Michel Dupon, Philippe Aegerter, Denis Mulleman, on behalf of the Duration of Treatment for Spondylodiscitis (DTS) study group**

Antibiothérapie (hors endocardite infectieuse associée) 6 semaines

- S. aureus

➢Traitement d'une bactériémie identifiée: IV 7 jours

➢PO : LEVO + RFP ou Clindamycine monothérapie

- Streptocoques

➢Amoxicilline 2-3g / 8h ou Clindamycine ou Levofloxaxine

- Entérocoque

➢Amoxicilline 2-3g / 8h

- Enterobacterales

➢Levofloxacine

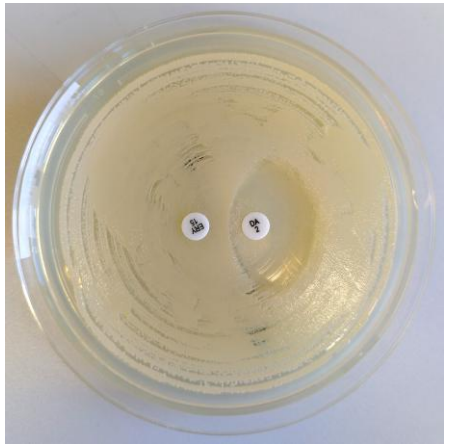
Arthrite septique sur articulation native

Traitement probabiliste: choix des molécules

- Céfazoline ou pénicilline M (cloxacilline, oxacilline)

  +/- élargissement du spectre si l'anamnèse suggère une bactérie particulière
- En cas d'allergie grave aux bêta-lactamines : daptomycine ou à défaut un glycopeptide (vancomycine ou teicoplanine)
- Si sepsis ou choc septique : ajout amikacine pendant 24-48h dans tous les cas
- Non discuté dans la mise au point SPILF: les situations liées aux soins qui incluent des SCoN résistants à la méticilline dans plus de 50% des cas

S. aureus



Remerciements : M. Arnaud Riat

- Monothérapie clindamycine (absence de souche MLSb inductible)
- Levofloxacine/rifampicine ou levofloxacine/clindamycine possibles
- Si souche MLSb inductible: doxycycline, oxazolidinone, cotrimoxazole
- levofloxacine et rifampicine en association

Streptococcus spp

- Amoxicilline
- si allergie clindamycine en l'absence de phénotype MLSb
- En deuxième intention: oxazolidinone positionnée devant levofloxacine

Entérocoques sensibles à l'amoxicilline

- Amoxicilline
- Si allergie : oxazolidinone

Enterobacterales

- Levofloxacine si les données de sensibilité l’autorisent

Durée des traitements antibiotiques selon les situations cliniques ou microbiologiques

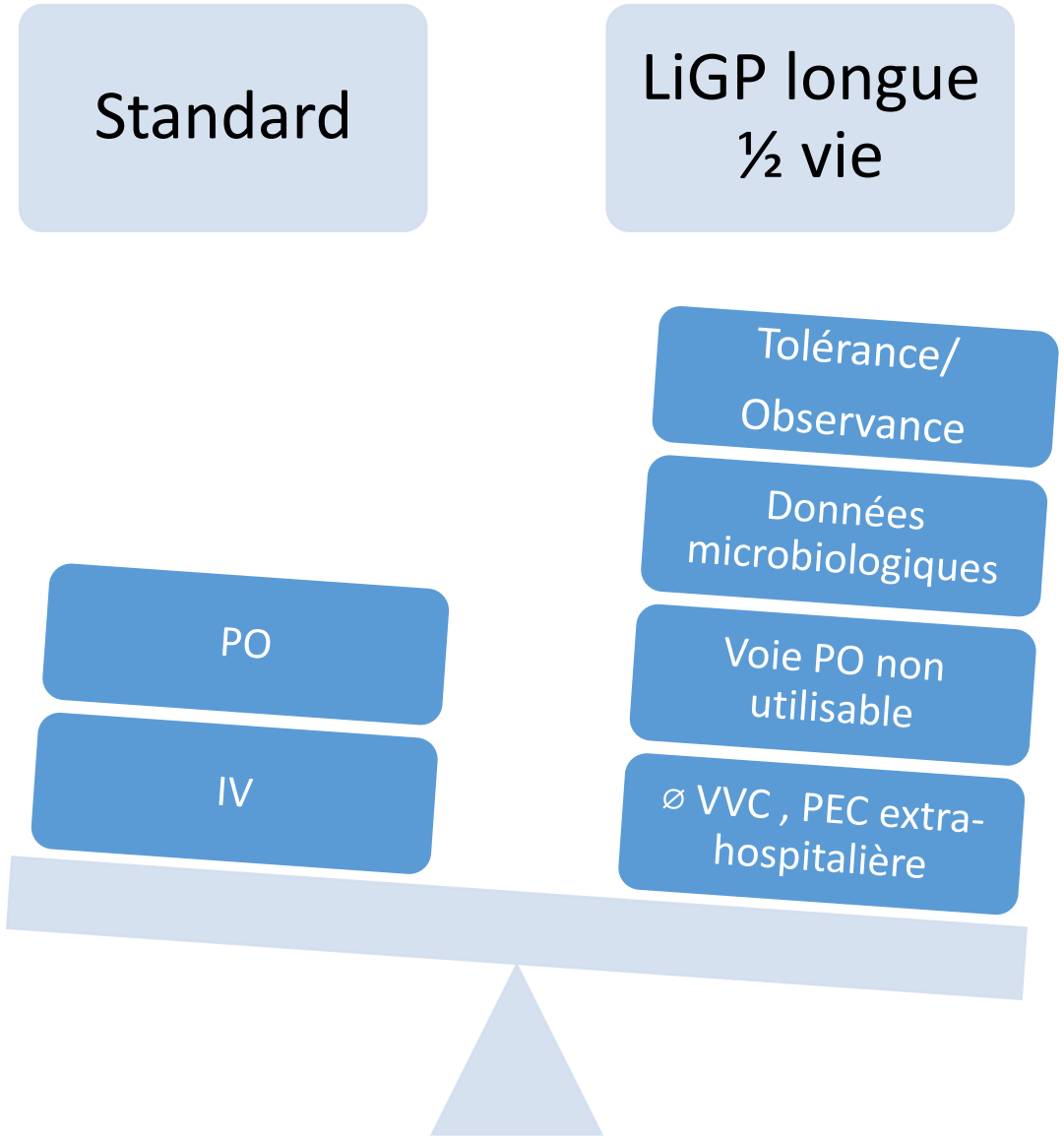
- *S. aureus* et enterobacterales: 6 semaines
- Streptococcus spp et autres bactéries
- *Neisseria gonorrhoeae*: 7 jours
- Arthrites de la main et du poignet, mécanise d'inoculation et lavage chirurgical mis en œuvre: 2 semaines

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Short 3-week antibiotic treatment versus 6 weeks in adults with septic arthritis of native joint: a randomized, open label, non-inferiority trial

SHASAR

Pourquoi utiliser un LiGP à longue demi-vie?




Professor Josh Davis
Professor
School of Medicine and Public Health

RandOmised Arthroplasty infection worlDwide Multidomain Adaptive Platform trial – Synopsis

1.1 Overview of initial trial design (given only as an example, at initial trial launch)

SILOS	DOMAINS			
	Surgical Rx	*Antibiotic duration*	*Antibiotic choice*	*Future domain*
Early* PJI	No randomisation options[1]	For one stage: Total 6 weeks versus 12 weeks post the one-stage For two-stage – 7 days versus 12 weeks post 2nd stage	Backbone regimen with or without adjunctive oral rifampicin	A vs B *(e.g. choice of irrigation fluids; adjunctive vitamin C; antidepressants)*
Late acute* PJI	DAIR versus revision[2]			
Chronic* PJI	One stage versus two stage revision			

	Adaptations: renal function, weight, means of infusion	**Total daily dosage reference for normal renal function (clearance from 60 to 90 ml/min) and normal BMI (from 18 to 30 kg/m^2)**	**Recommended pharmacological follow-up treatment**
Amoxicillin		***Streptococcus spp, anaerobes:*** **IV**: 100 mg/kg/d in continuous administration (stability up to 12h) after loading dose of 2g for 1h) or discontinuous in 6 administrations (infusions from 30 to 60 min every 4 h) **PO**: 100 mg/kg/d in 3 to 4 doses of 2 to 3g ***Enterococcus spp:*** **IV**: 200 mg/kg/d in continuous administration (stability up to 12h) after loading dose of 2g for 1h) or discontinuous in 6 administrations (infusions from 30 to 60 min every 4 h) **PO**: 200 mg/kg/d in 3 to 4 doses of 2 to 3g	**IV**: systematic if $\geq$ 12g/d **PO**: systematic if $\geq$ 9g/d
Amoxicillin-clavulanate		**IV**: Discontinuous administration: 100 mg/kg/d amoxicillin in 4 to 6 administrations, not exceeding 1200 mg of clavulanate/d **PO**: 100 mg/kg/day amoxicillin in 3 to 4 doses of 2 to 3g	
Cloxacillin/ oxacillin		**IV**: 150 mg/kg/d in continuous administration (stability up to 12h) after loading dose of 2g for 1h or discontinuous in 6 administrations (infusions from 30 to 60 min every 4 h)	Systematic if $\geq$ 12g/d
Cefazolin		**IV**: 100 mg/kg/d in continuous administration (stability up to 12h) after loading dose of 2g for 1h or discontinuous in 3 administrations (infusions of 60 min every 8 h)	Systematic if $\geq$ 6g/d
Ceftriaxone		**IV**: 35 mg/kg/d in 1 to 2 infusions of 2g maximum	
Cefotaxime		**IV:** 100mg/kg/d in continuous administration (stability up to 12h) after loading dose of 2g for 30 min or discontinuous in 3 to 4 infusions of 2g prolonged for 4h	

Ceftazidime		**IV**: 100mg/kg/d in continuous administration (stability up to 8h) after loading dose of 2g for 30 min or discontinuous in 3 to 4 infusions of 2g prolonged for 4h	Systematic if *P. aeruginosa*
Cefepime		**IV**: 80 mg/kg/d in continuous administration (stability up to 8h) after loading dose of 2g for 30 min or discontinuous in 3 to 4 infusions of 2g prolonged for 4h without exceeding 8g/d	Systematic
Aztreonam		**IV**: 6g/d in continuous administration (stability up to 24h) or discontinuous in prolonged infusions (4h) of 2g every 8h	Systematic if *P.aeruginosa*
Piperacillin-tazobactam		**IV**: Discontinuous administration in prolonged infusions: [4g piperacillin + 0.5g tazobactam] every 6h in infusions for 3h OR continuous infusion with dosage $\geq$ 12g/d	
Imipenem-cilastatin		**IV:** 1g every 6 h in infusions for 30 min	
Meropenem		**IV**: 2g every 8 h in infusions from 3 to 8h	
Levofloxacin		***Staphylococcus spp:*** **IV** or **PO:** 750 mg/d in a single administration ***Enterobacterales*:** **IV** or **PO**: 500 mg/d in a single administration	
Ciprofloxacin		***Pseudomonas spp*:** **IV**: 400 mg/ 8h **PO**: 750 mg/ 12h	

Linezolid	**IV** or **PO**: 600 mg/12h	Useful to evaluate hematological toxicity.
Tedizolid	**IV** or **PO**: 200 mg/24h	
Dalbavancin	**IV**: 1500 mg on D1 followed by 1500 mg at D7, schema covering 6 weeks of treatment)	
Clindamycin	**IV or PO**: -weight <70 kg: 600mg/ 8h - weight > 70kg: 900 mg/ 8h	
Rifampicin	**IV or PO**: 10 mg/kg/d (900 mg/d if weight > 70 Kg)	
Metronidazole	**IV or PO**: 500 mg/ 8h	
Cotrimoxazole	**IV or PO**: [320 mg trimethoprim + 1600 mg sulfamethoxazole]/ 12h	
Doxycycline	**PO**: 200 mg by day in 1 or 2 doses	

Merci