QUAND LE STAPHYLOCOQUE RÉSISTE À TOUT

8ème réunion d'échange sur les Infections sur Prothèse

Jeudi 16 mai 2019

Dr Olivier GROSSI / Dr Anne-Gaëlle LEROY

Quand le staphylocoque résiste à tout ?

Quand le staphylocoque résiste à tout ?

- Impossibilité de prescrire une combinaison antibiotique usuelle par voie orale ?

Quand le staphylocoque résiste à tout ?

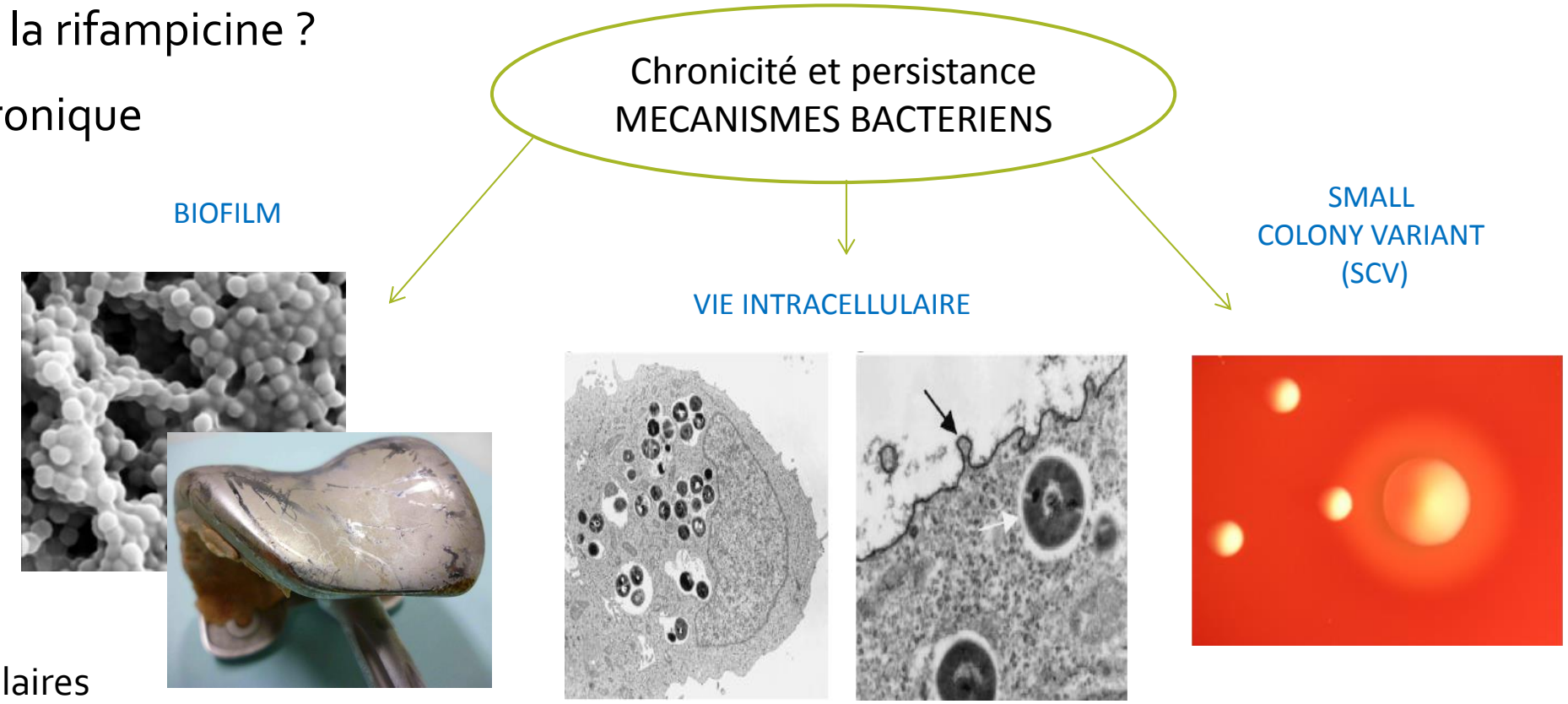
- Impossibilité de prescrire une combinaison antibiotique usuelle par voie orale ?
- Résistance à la rifampicine ?

Quand le staphylocoque résiste à tout ?

- Impossibilité de prescrire une combinaison antibiotique usuelle par voie orale ?
- Résistance à la rifampicine ?
- Infection chronique ?

Quand le staphylocoque résiste à tout ?

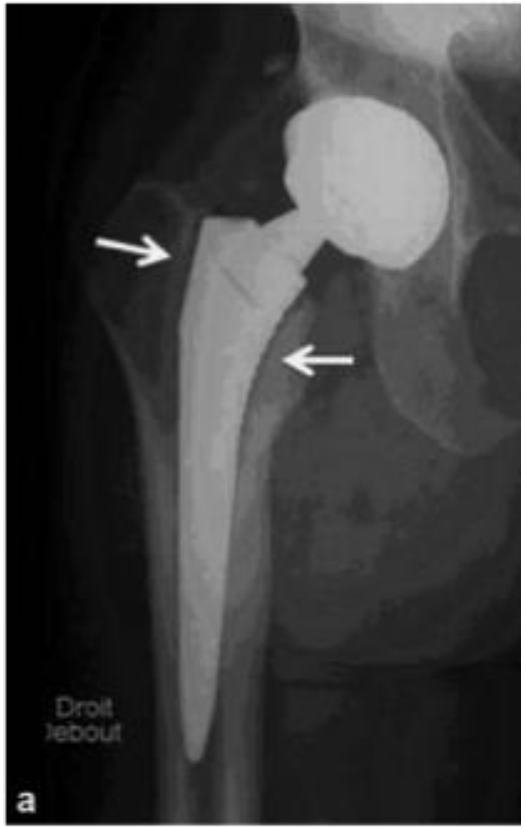
- Impossibilité de prescrire une combinaison antibiotique usuelle par voie orale ?
- Résistance à la rifampicine ?
- Infection chronique



Dr F Valour,
DIU infections ostéoarticulaires

Cas clinique hypothétique: Mme P. Th.

- 80 ans.
- PTH droite de 2 ans d'âge
- Impotence fonctionnelle douloureuse croissante
- CRP 25 mg/L
- Rx: descellement
- => changement de prothèse en 1 temps + prélèvements pour analyses microbiologiques
- Mise en place d'une antibiothérapie probabiliste par pipéracilline/tazobactam + linézolide



Résultats cultures prélèvements per-opératoires

- 8/10 + à *Staphylococcus epidermidis*

Résultats cultures prélèvements per-opératoires

- 8/10 + à *Staphylococcus epidermidis*

10 prélèvements ???

Reprise chirurgicale sur matériel de prothèse : combien de prélèvements?

- 2 prélèvements
- 4 prélèvements
- 6 prélèvements
- 8 prélèvements
- 10 prélèvements

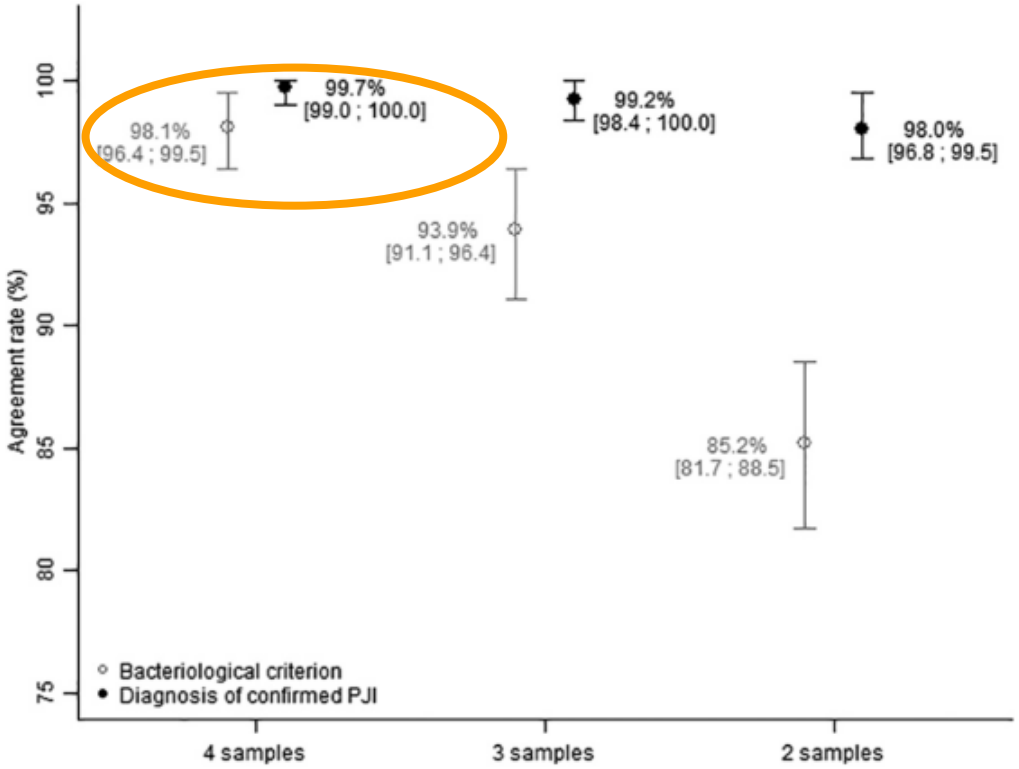
Cultures prélèvements per-opératoires

Combien de prélèvements ?

Journal of Clinical Microbiology

How Many Samples and How Many Culture Media To Diagnose a Prosthetic Joint Infection: a Clinical and Microbiological Prospective Multicenter Study

Pascale Bémer,[a] Julie Léger,[b] Didier Tandé,[c] Chloé Plouzeau,[d] Anne Sophie Valentin,[e] Anne Jolivet-Gougeon,[f] Carole Lemarié,[g] Marie Kempf,[g] Geneviève Héry-Arnaud,[c] Laurent Bret,[h] Marie Emmanuelle Juvin,[a] Bruno Giraudeau,[b] Stéphane Corvec,[a] Christophe Burucoa,[d] the Centre de Référence des Infections Ostéo-articulaires du Grand Ouest (CRIOGO) Study Team



=> 4 prélèvements font aussi bien que 5

Cultures prélèvements per-opératoires

Nouvelles pratiques

Journal of Clinical Microbiology

How Many Samples and How Many Culture Media To Diagnose a Prosthetic Joint Infection: a Clinical and Microbiological Prospective Multicenter Study

Pascale Bémer,[a] Julie Léger,[b] Didier Tandé,[c] Chloé Plouzeau,[d] Anne Sophie Valentin,[e] Anne Jolivet-Gougeon,[f] Carole Lemarié,[g] Marie Kempf,[g] Geneviève Héry-Arnaud,[c] Laurent Bret,[h] Marie Emmanuelle Juvin,[a] Bruno Giraudeau,[b] Stéphane Corvec,[a] Christophe Burucoa,[d] the Centre de Référence des Infections Ostéo-articulaires du Grand Ouest (CRIOGO) Study Team

Bloc opératoire

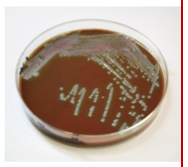
- Tissus
  - 3 prélèvements de taille moyenne

  - Avec changement instruments
- Liquide articulaire
  - Ensemencement en flacon d'hémoculture anaérobie
  - Directement au bloc op
  - Envoyer AUSSI LA dans flacon à vis spécifique ortho

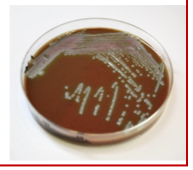
Ensemencement

- Flacon d'hémoculture

- Gélose anaérobie



- Gélose chocolat enrichie



Reprise chirurgicale sur prothèse

Diapo empruntée à P. Bémer

Mme P. Th.

Bactérie N°: 1

Staphylococcus epidermidis

	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	>8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	<=0.5
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	SENSIBLE	0.5
Lincomycine	SENSIBLE	<=1.
Pristinamycine	SENSIBLE	<=0.5
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	4.
Ac. fusidique	SENSIBLE	<=0.5
Cotrimoxazole	RESISTANT	>160.
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	2.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	SENSIBLE	<=0.03

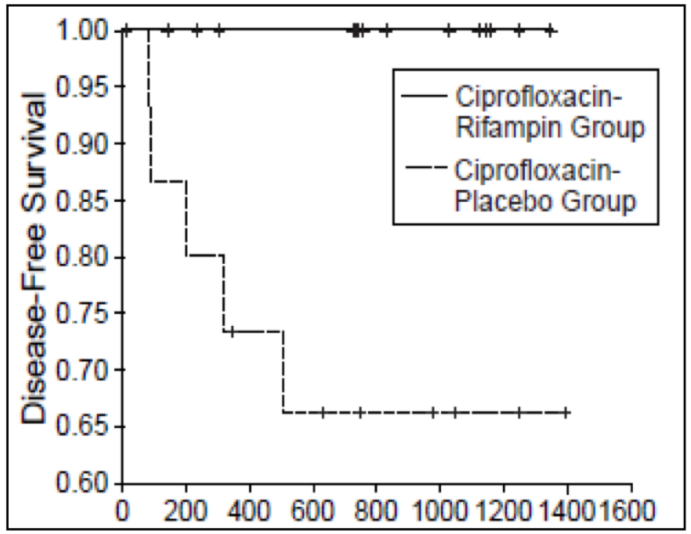
Mme P. Th.

Bactérie N°: 1

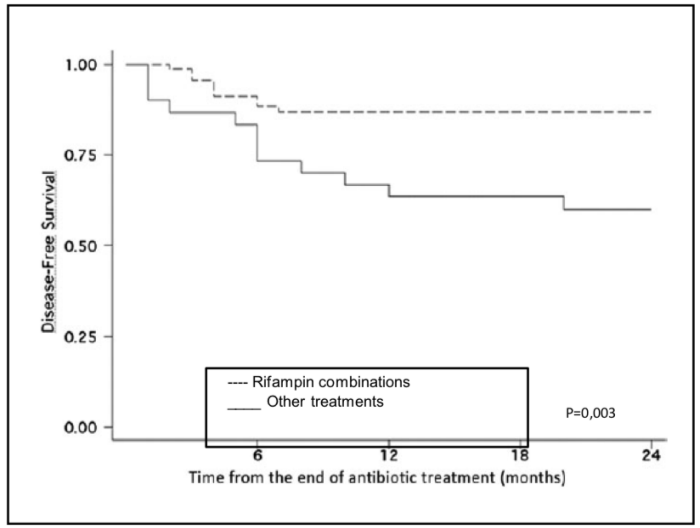
Staphylococcus epidermidis

	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	>8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	<=0.5
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	SENSIBLE	0.5
Lincomycine	SENSIBLE	<=1.
Pristinamycine	SENSIBLE	<=0.5
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	4.
Ac. fusidique	SENSIBLE	<=0.5
Cotrimoxazole	RESISTANT	>160
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	2.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	SENSIBLE	<=0.03

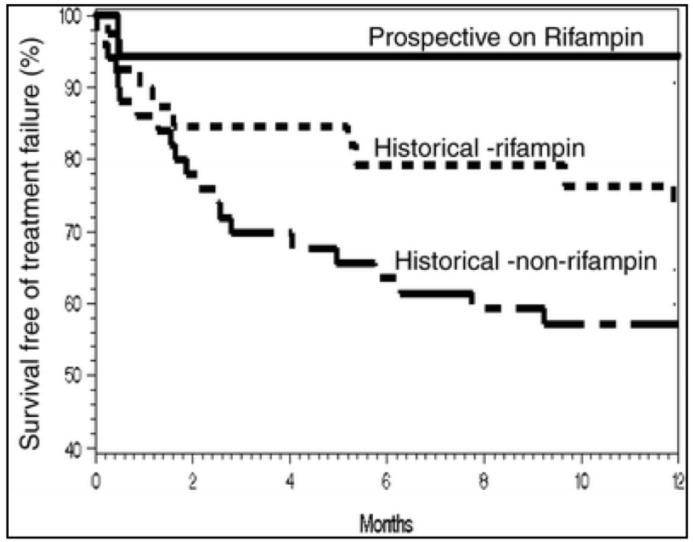
Antibiothérapie ?



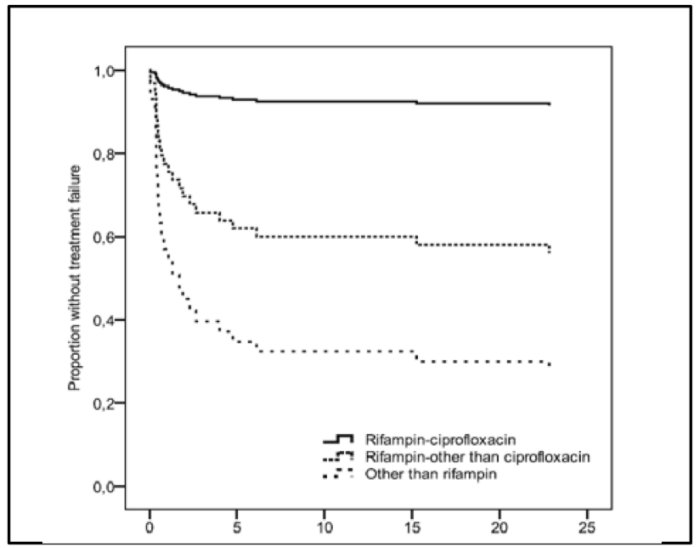
Zimmerli W *et al.* JAMA 1998



Senneville E *et al*. Clin Infect Dis 2011



El Helou OC *et al*. Eur J Clin Microbiol Infect Dis. 2010



Puhto AP *et al.* Int Orthop 2015

Mme P. Th.

- Clindamycine 600 mgx3/j + rifampicine 900 mg/j, durée 3 mois
- Évolution initialement favorable
- 2 mois après arrêt des antibiotiques: douleur, aspect inflammatoire de la cicatrice, fistulisation

ELSEVIER

BIAM
British Infection Association

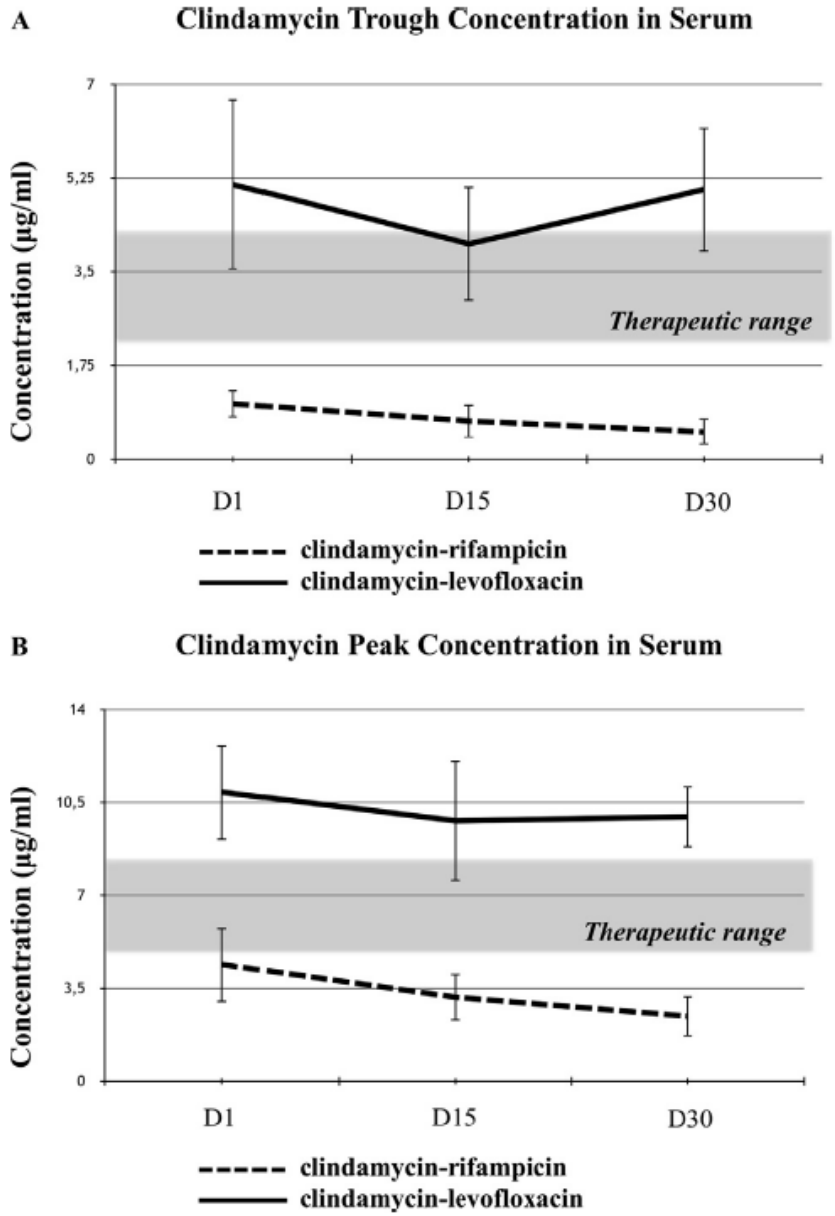
www.elsevierhealth.com/journals/jinf

Dramatic reduction of clindamycin serum concentration in staphylococcal osteoarticular infection patients treated with the oral clindamycin-rifampicin combination

CrossMark

Bernard A. *et al*. Journal of Infection (2015) 71, 200e206

Infections ostéoarticulaires
16 patients clinda/rifam
18 patients Levo/rifam
Clinda 600mgx3 po
Dosages pic/vallée J1, J15, J30



Mme P. Th.

- Clindamycine 600 mgx3/j + rifampicine 900mg/j, durée 3 mois
- Évolution initialement favorable
- 2 mois après arrêt des antibiotiques: douleur, aspect inflammatoire de la cicatrice, fistulisation
- **Réalisation ponction liquide articulaire au bloc opératoire + biopsie True-Cut**

Mme P. Th.

Bactérie N°: 1 2/2

Staphylococcus epidermidis

	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	>2.
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	2.
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	RESISTANT	>4.
Lincomycine	RESISTANT	>8.
Pristinamycine	RESISTANT	>4.
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	>8.
Ac. fusidique	RESISTANT	16.
Cotrimoxazole	RESISTANT	>160.
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	1.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	RESISTANT	>2.

Mme P. Th.

Bactérie N°: 1 2/2

Staphylococcus epidermidis

	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	>2.
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	2.
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	RESISTANT	>4.
Lincomycine	RESISTANT	>8.
Pristinamycine	RESISTANT	>4.
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	>8.
Ac. fusidique	RESISTANT	16.
Cotrimoxazole	RESISTANT	>160.
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	1.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	RESISTANT	>2.

Attitude thérapeutique?

Traitement chirurgical ?

Changement PTH en 1 temps ?

Changement PTH en 2 temps ?

Traitement chirurgical ?

Changement PTH en 1 temps ?

- Germe identifié et sensible
- Pas de destruction osseuse majeure
- Pas de problème sur les parties molles
- Pas de localisations septiques multiples
- Contamination hématogène si porte d'entrée traitée
- Absence de fistule ?

Changement PTH en 2 temps ?

Traitement chirurgical ?

Changement PTH en 1 temps ?

- Germe identifié et sensible
- Pas de destruction osseuse majeure
- Pas de problème sur les parties molles
- Pas de localisations septiques multiples
- Contamination hématogène si porte d'entrée traitée
- Absence de fistule ?

Changement PTH en 2 temps ?

- Germe non identifié ou multirésistant
- Sepsis chronique multiopéré
- Destruction osseuse majeure
- Problème de couverture/parties molles
- Localisations septiques multiples
- Contamination hématogène si porte d'entrée non traitée
- Fistule ?

Traitement chirurgical ?

Changement PTH en 1 temps ?

- Germe identifié et sensible
- Pas de destruction osseuse majeure
- Pas de problème sur les parties molles
- Pas de localisations septiques multiples
- Contamination hématogène si porte d'entrée traitée
- Absence de fistule ?

Changement PTH en 2 temps ?

- Germe non identifié ou multirésistant
- Sepsis chronique multiopéré
- Destruction osseuse majeure
- Problème de couverture/parties molles
- Localisations septiques multiples
- Contamination hématogène si porte d'entrée non traitée
- Fistule ?

Mme P. Th.

Bactérie N°: 1

Staphylococcus epidermidis

	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	>2.
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	2.
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	RESISTANT	>4.
Lincomycine	RESISTANT	>8.
Pristinamycine	RESISTANT	>4.
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	>8.
Ac. fusidique	RESISTANT	16.
Cotrimoxazole	RESISTANT	>160.
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	1.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	RESISTANT	>2.

Antibiothérapie ?

Mme P. Th.

Bactérie N°: 1

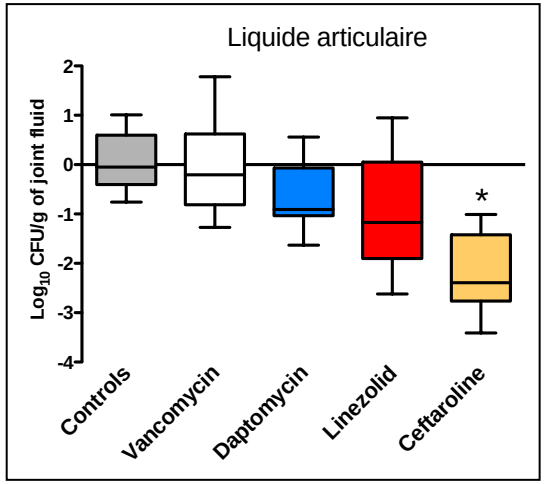
Staphylococcus epidermidis

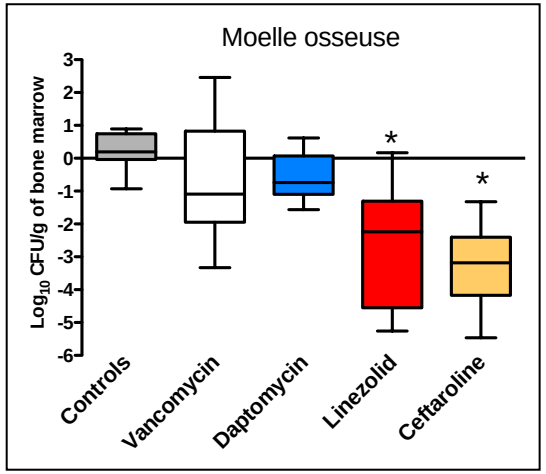
	SIR	CMI (mg/L)
Technique antibiogramme :	automate Vitek 2	
BETA-LACTAMINES		
Méticillino-résistance	POSITIF	
Oxacilline	RESISTANT	>2.
AMINOSIDES		
Kanamycine	RESISTANT	>32.
Tobramycine	RESISTANT	8.
Gentamicine	RESISTANT	>8.
QUINOLONES		
Ofloxacine	RESISTANT	>4.
GLYCO./LIPOPEPTIDES		
Vancomycine	SENSIBLE	2.
MACROL. LINCOS. SYNERGISTINES		
Erythromycine	RESISTANT	>4.
Lincomycine	RESISTANT	>8.
Pristinamycine	RESISTANT	>4.
AUTRES ANTIBIOTIQUES		
Tétracycline	RESISTANT	>8.
Ac. fusidique	RESISTANT	16.
Cotrimoxazole	RESISTANT	>160.
Fosfomycine	SENSIBLE	<=8.
Linézolide	SENSIBLE	1.
Nitrofuranes	SENSIBLE	<=16.
Rifampicine	RESISTANT	>2.

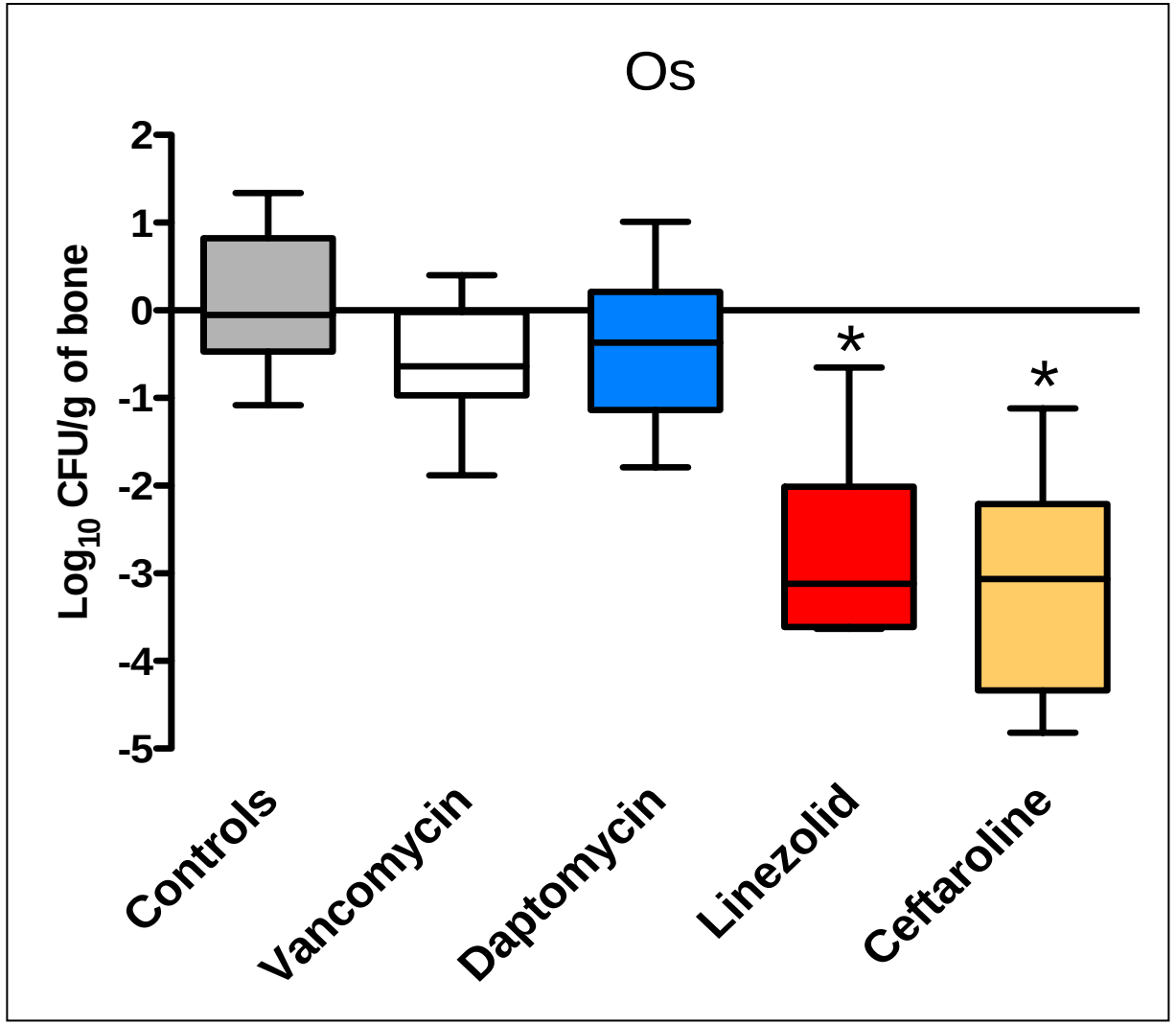
Antibiothérapie ?

CMI Ceftaroline	0.250	mg/L	SENSIBLE
Technique:	*Diffusion en milieu gélosé (Etest)*		
CMI Ceftobiprole	1.000	mg/L	
Technique:	*Diffusion en milieu gélosé (Etest)*		
CMI Dalbavancine	0.032	mg/L	
Technique:	*Diffusion en milieu gélosé (Etest)*		
CMI Daptomycine	0.380	mg/L	
Technique:	*Diffusion en milieu gélosé (Etest)*		

Evaluation de molécules antistaphylococciques

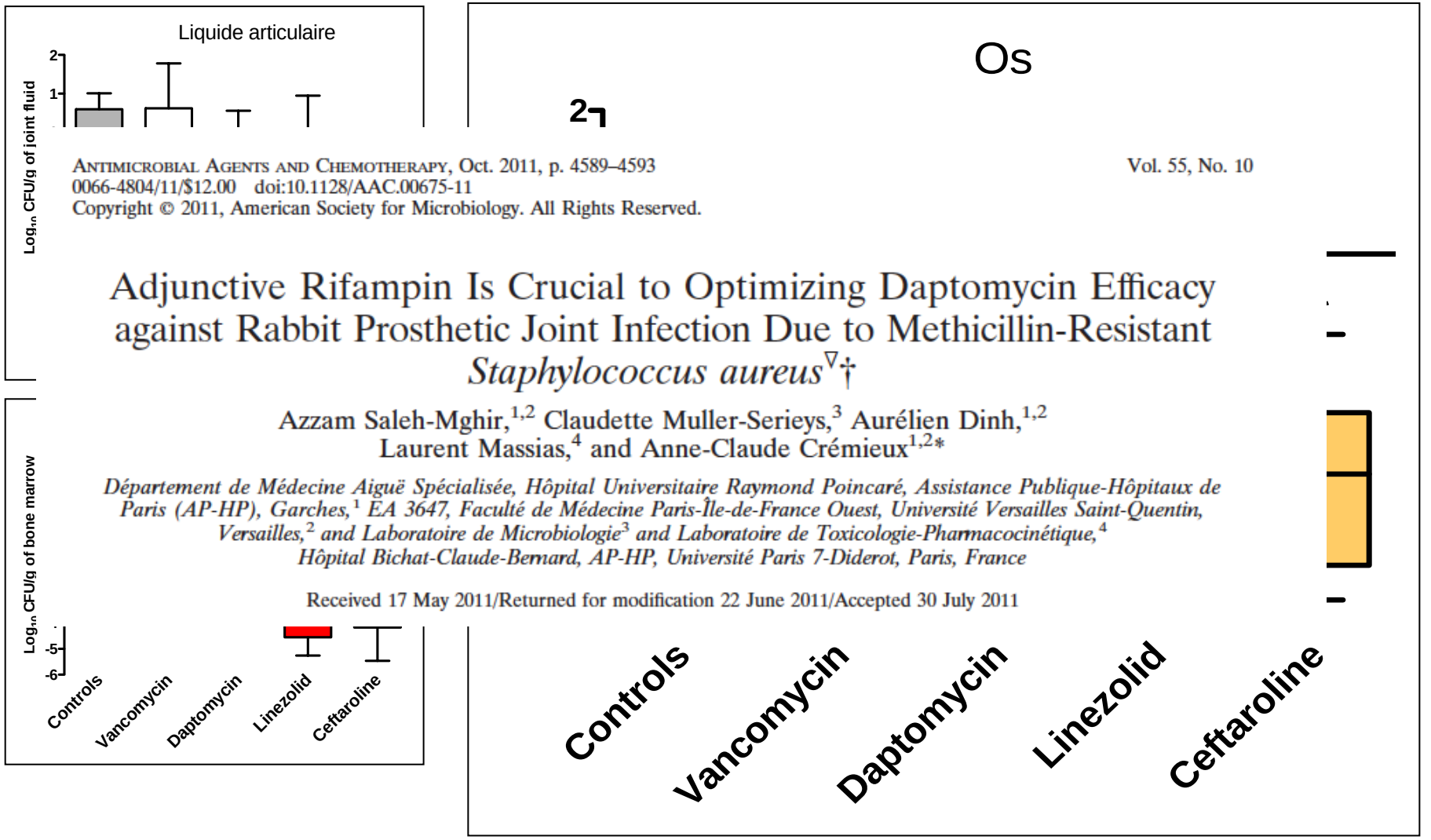






Jacqueline C et al. Efficacy of the new cephalosporin ceftaroline in the treatment of experimental methicillin-resistant *Staphylococcus aureus* acute osteomyelitis. J Antimicrob Chemother 2010; 65(8):1749-52.

Evaluation de molécules antistaphylococciques



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2011, p. 4589–4593 Vol. 55, No. 10
0066-4804/11/$12.00 doi:10.1128/AAC.00675-11

Adjunctive Rifampin Is Crucial to Optimizing Daptomycin Efficacy against Rabbit Prosthetic Joint Infection Due to Methicillin-Resistant *Staphylococcus aureus*▽†

Azzam Saleh-Mghir,[1,2] Claudette Muller-Serieys,[3] Aurélien Dinh,[1,2] Laurent Massias,[4] and Anne-Claude Crémieux[1,2]*

Département de Médecine Aiguë Spécialisée, Hôpital Universitaire Raymond Poincaré, Assistance Publique-Hôpitaux de Paris (AP-HP), Garches,[1] EA 3647, Faculté de Médecine Paris-Île-de-France Ouest, Université Versailles Saint-Quentin, Versailles,[2] and Laboratoire de Microbiologie[3] and Laboratoire de Toxicologie-Pharmacocinétique,[4] Hôpital Bichat-Claude-Bernard, AP-HP, Université Paris 7-Diderot, Paris, France

Received 17 May 2011/Returned for modification 22 June 2011/Accepted 30 July 2011

Jacqueline C et al. Efficacy of the new cephalosporin ceftaroline in the treatment of experimental methicillin-resistant *Staphylococcus aureus* acute osteomyelitis. J Antimicrob Chemother 2010; 65(8):1749-52.

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

- Registre EuCORE
- Multicentrique, rétrospectif, déclaratif
- IOA traitée par daptomycine entre Janvier 2006 et Avril 2012
- Suivi jusqu'à 24 mois après arrêt traitement

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

Table 1 Demographic and clinical characteristics (safety population)

Characteristics	Patients (*N*=638) [*n* (%)]
Osteomyelitis, non-prosthetic and prosthetic device-related infection	432 (67.7)
Non-prosthetic	224 (51.9)
Permanent prosthetic device-related	160 (37.0)
Temporary prosthetic device-related	48 (11.1)
Orthopaedic device infection [*n* (%)]	206 (32.3)
Anatomical site of infection (>5 %) [*n* (%)]	
Knee	171 (26.8)
Hip	147 (23.0)
Lower extremity	94 (14.7)
Foot/ankle	83 (13.0)
Back	65 (10.2)
Any antibiotics used for this infection prior to daptomycin [*n* (%)]	
Yes	455 (71.3)
No	166 (26.0)
Unknown	16 (2.5)
Missing	1 (0.2)

Table 2 Primary pathogens in patients with positive cultures

Primary pathogens	Patients with positive cultures (*N*=436) [*n* (%)]
Staphylococcus aureus	214 (49.1)
Methicillin-resistant	108 (24.8)
Methicillin-susceptible	88 (20.2)
Methicillin susceptibility unknown	18 (4.1)
Coagulase-negative *Staphylococcus* species	153 (35.1)
Staphylococcus epidermidis	104 (23.9)
Other	49 (11.2)
Streptococcus agalactiae or group B streptococci	5 (1.1)
Streptococcus pyogenes or group A streptococci	3 (0.7)
Viridans streptococci group	3 (0.7)
Staphylococcus species - coagulase not specified	4 (0.9)
Enterococcus faecalis	19 (4.4)
Enterococcus faecium	7 (1.6)
Vancomycin-resistant (*Enterococcus faecalis* or *Enterococcus faecium*)	5 (1.1)
Enterococcus species	3 (0.7)
Other[a]	25 (5.7)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

Table 1 Demographic and clinical characteristics (safety population)

Characteristics	Patients (*N*=638) [*n* (%)]
Osteomyelitis, non-prosthetic and prosthetic device-related infection	432 (67.7)
Non-prosthetic	224 (51.9)
Permanent prosthetic device-related	160 (37.0)
Temporary prosthetic device-related	48 (11.1)
Orthopaedic device infection [*n* (%)]	206 (32.3)
Anatomical site of infection (>5 %) [*n* (%)]	
Knee	171 (26.8)
Hip	147 (23.0)
Lower extremity	94 (14.7)
Foot/ankle	83 (13.0)
Back	65 (10.2)
Any antibiotics used for this infection prior to daptomycin [*n* (%)]	
Yes	455 (71.3)
No	166 (26.0)
Unknown	16 (2.5)
Missing	1 (0.2)

62%

Table 2 Primary pathogens in patients with positive cultures

Primary pathogens	Patients with positive cultures (*N*=436) [*n* (%)]
Staphylococcus aureus	214 (49.1)
Methicillin-resistant	108 (24.8)
Methicillin-susceptible	88 (20.2)
Methicillin susceptibility unknown	18 (4.1)
Coagulase-negative *Staphylococcus* species	153 (35.1)
Staphylococcus epidermidis	104 (23.9)
Other	49 (11.2)
Streptococcus agalactiae or group B streptococci	5 (1.1)
Streptococcus pyogenes or group A streptococci	3 (0.7)
Viridans streptococci group	3 (0.7)
Staphylococcus species - coagulase not specified	4 (0.9)
Enterococcus faecalis	19 (4.4)
Enterococcus faecium	7 (1.6)
Vancomycin-resistant (*Enterococcus faecalis* or *Enterococcus faecium*)	5 (1.1)
Enterococcus species	3 (0.7)
Other[a]	25 (5.7)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

Table 1 Demographic and clinical characteristics (safety population)

Characteristics	Patients (*N*=638) [*n* (%)]
Osteomyelitis, non-prosthetic and prosthetic device-related infection	432 (67.7)
Non-prosthetic	224 (51.9)
Permanent prosthetic device-related	160 (37.0)
Temporary prosthetic device-related	48 (11.1)
Orthopaedic device infection [*n* (%)]	206 (32.3)
Anatomical site of infection (>5 %) [*n* (%)]	
Knee	171 (26.8)
Hip	147 (23.0)
Lower extremity	94 (14.7)
Foot/ankle	83 (13.0)
Back	65 (10.2)
Any antibiotics used for this infection prior to daptomycin [*n* (%)]	
Yes	455 (71.3)
No	166 (26.0)
Unknown	16 (2.5)
Missing	1 (0.2)

Table 2 Primary pathogens in patients with positive cultures

Primary pathogens	Patients with positive cultures (*N*=436) [*n* (%)]
Staphylococcus aureus	214 (49.1)
Methicillin-resistant	108 (24.8)
Methicillin-susceptible	88 (20.2)
Methicillin susceptibility unknown	18 (4.1)
Coagulase-negative *Staphylococcus* species	153 (35.1)
Staphylococcus epidermidis	104 (23.9)
Other	49 (11.2)
Streptococcus agalactiae or group B streptococci	5 (1.1)
Streptococcus pyogenes or group A streptococci	3 (0.7)
Viridans streptococci group	3 (0.7)
Staphylococcus species - coagulase not specified	4 (0.9)
Enterococcus faecalis	19 (4.4)
Enterococcus faecium	7 (1.6)
Vancomycin-resistant (*Enterococcus faecalis* or *Enterococcus faecium*)	5 (1.1)
Enterococcus species	3 (0.7)
Other[a]	25 (5.7)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

Table 1 Demographic and clinical characteristics (safety population)

Characteristics	Patients (*N*=638) [*n* (%)]
Osteomyelitis, non-prosthetic and prosthetic device-related infection	432 (67.7)
Non-prosthetic	224 (51.9)
Permanent prosthetic device-related	160 (37.0)
Temporary prosthetic device-related	48 (11.1)
Orthopaedic device infection [*n* (%)]	206 (32.3)
Anatomical site of infection (>5 %) [*n* (%)]	
Knee	171 (26.8)
Hip	147 (23.0)
Lower extremity	94 (14.7)
Foot/ankle	83 (13.0)
Back	65 (10.2)
Any antibiotics used for this infection prior to daptomycin [*n* (%)]	
Yes	455 (71.3)
No	166 (26.0)
Unknown	16 (2.5)
Missing	1 (0.2)

Table 2 Primary pathogens in patients with positive cultures

Primary pathogens	Patients with positive cultures (*N*=436) [*n* (%)]
Staphylococcus aureus	214 (49.1)
Methicillin-resistant	108 (24.8)
Methicillin-susceptible	88 (20.2)
Methicillin susceptibility unknown	18 (4.1)
Coagulase-negative *Staphylococcus* species	153 (35.1)
Staphylococcus epidermidis	104 (23.9)
Other	49 (11.2)
Streptococcus agalactiae or group B streptococci	5 (1.1)
Streptococcus pyogenes or group A streptococci	3 (0.7)
Viridans streptococci group	3 (0.7)
Staphylococcus species - coagulase not specified	4 (0.9)
Enterococcus faecalis	19 (4.4)
Enterococcus faecium	7 (1.6)
Vancomycin-resistant (*Enterococcus faecalis* or *Enterococcus faecium*)	5 (1.1)
Enterococcus species	3 (0.7)
Other[a]	25 (5.7)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]

Table 1 Demographic and clinical characteristics (safety population)

Characteristics	Patients (*N*=638) [*n* (%)]
Osteomyelitis, non-prosthetic and prosthetic device-related infection	432 (67.7)
Non-prosthetic	224 (51.9)
Permanent prosthetic device-related	160 (37.0)
Temporary prosthetic device-related	48 (11.1)
Orthopaedic device infection [*n* (%)]	206 (32.3)
Anatomical site of infection (>5 %) [*n* (%)]	
Knee	171 (26.8)
Hip	147 (23.0)
Lower extremity	94 (14.7)
Foot/ankle	83 (13.0)
Back	65 (10.2)
Any antibiotics used for this infection prior to daptomycin [*n* (%)]	
Yes	455 (71.3)
No	166 (26.0)
Unknown	16 (2.5)
Missing	1 (0.2)

Table 2 Primary pathogens in patients with positive cultures

Primary pathogens	Patients with positive cultures (*N*=436) [*n* (%)]
Staphylococcus aureus	214 (49.1)
Methicillin-resistant	108 (24.8)
Methicillin-susceptible	88 (20.2)
Methicillin susceptibility unknown	18 (4.1)
Coagulase-negative *Staphylococcus* species	153 (35.1)
Staphylococcus epidermidis	104 (23.9)
Other	49 (11.2)
Streptococcus agalactiae or group B streptococci	5 (1.1)
Streptococcus pyogenes or group A streptococci	3 (0.7)
Viridans streptococci group	3 (0.7)
Staphylococcus species - coagulase not specified	4 (0.9)
Enterococcus faecalis	19 (4.4)
Enterococcus faecium	7 (1.6)
Vancomycin-resistant (*Enterococcus faecalis* or *Enterococcus faecium*)	5 (1.1)
Enterococcus species	3 (0.7)
Other[a]	25 (5.7)

ATB préalable 71%
Raison du switch: 30% = échec
>80% en association

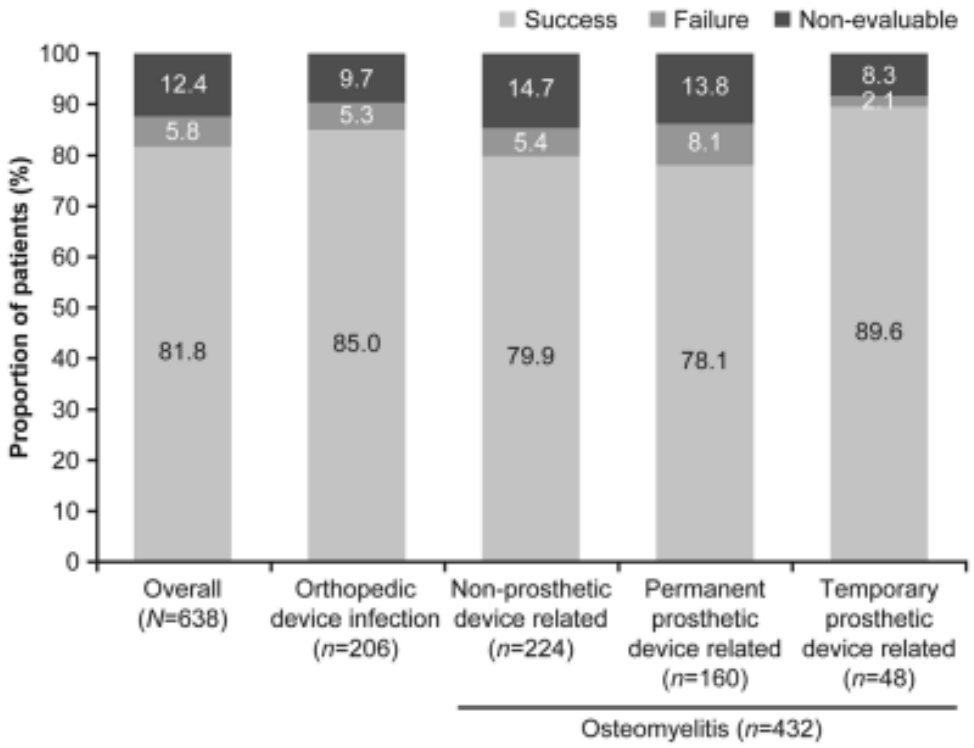
Quand le staphylocoque résiste à tout

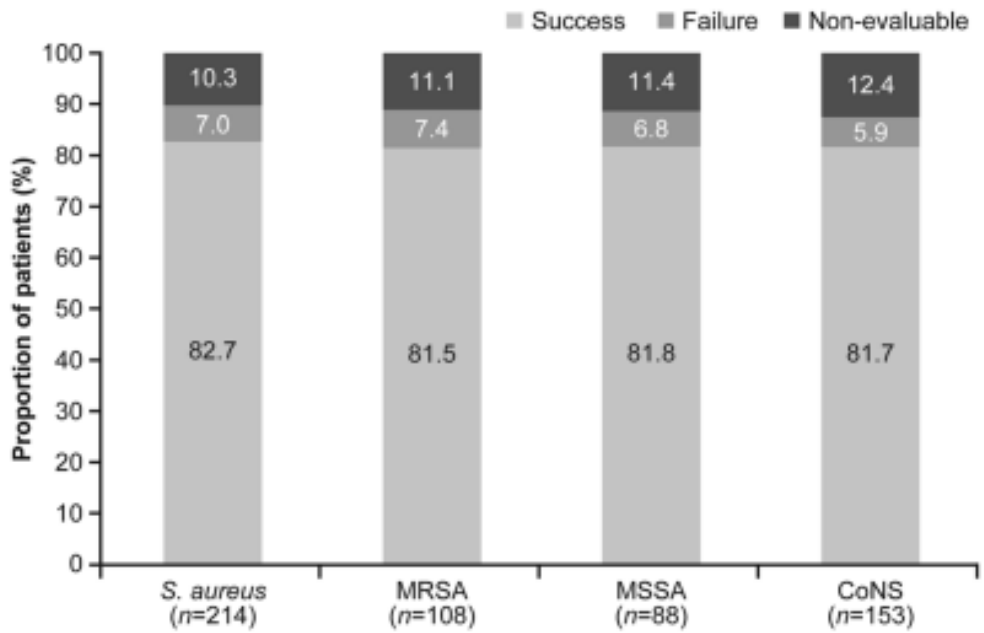
Alternatives thérapeutiques : daptomycine

Eur J Clin Microbiol Infect Dis (2016)

Daptomycin for the treatment of osteomyelitis and orthopaedic device infections: real-world clinical experience from a European registry

K. Malizos[1] · J. Sarma[2] · R. A. Seaton[3] · M. Militz[4] · F. Menichetti[5] · G. Riccio[6] · J. Gaudias[7] · U. Trostmann[8] · R. Pathan[9] · K. Hamed[10]



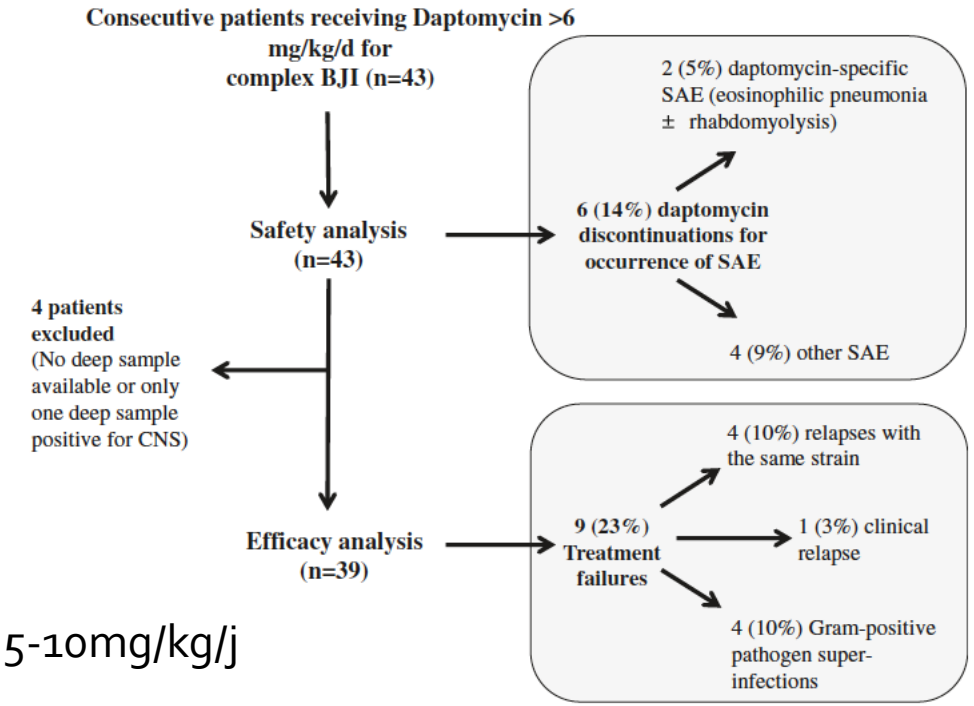


Dapto + RIF (121 patients) => 86,8% de succès

RESEARCH ARTICLE Open Access

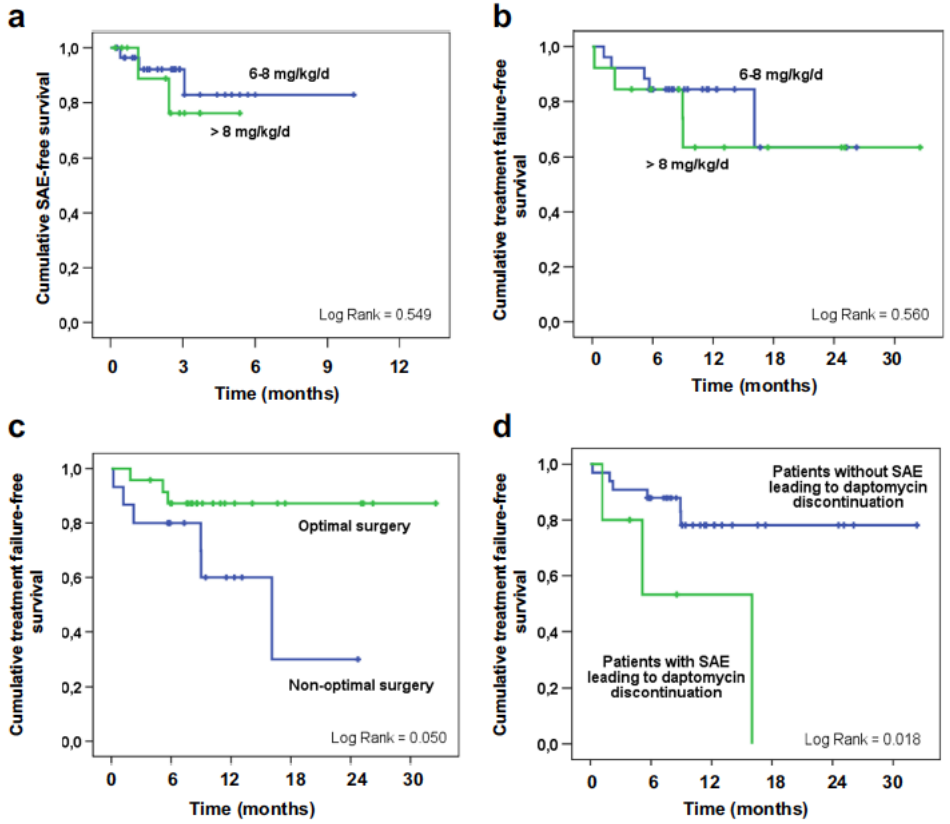
Daptomycin > 6 mg/kg/day as salvage therapy in patients with complex bone and joint infection: cohort study in a regional reference center

Roux et al. BMC Infectious Diseases (2016) 16:83



Dose: 6,5-10mg/kg/j

- SCN: 74%
- SA: 26%
- Prothèse: 53%
- Autre matériel: 33%
- 86% exposés à la vanco avant dapto
- 86% d'asso: fosfo/rif/clinda
- Chir optimale chez 62% des patients
- Echecs non en rapport avec émergence de R



Clinical Outcomes

High doses of daptomycin (10 mg/kg/d) plus rifampin for the treatment of staphylococcal prosthetic joint infection managed with implant retention: a comparative study

Lora-Tamayo et al. Diagnostic Microbiology and Infectious Disease 80 (2014) 66–71

- 18 patients: 7 PTH, 7 PTG et 4 PHI
- 10 SARM, 1 SASM, 7 SCN
- Chir = DAIR
- Durée de traitement: 42j (35-74)
- Suivi 749j (731-970)
- Succès: 9/18 (50%)
- 5 échecs microbiologiques
- Pas d'émergence de résistance

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : céphalosporines anti-SARM

International Journal of Antimicrobial Agents 50 (2017) 277–280

Salvage therapy for complex bone and joint infections with ceftaroline: a multicentre, observational study

Malandain et al

- Étude rétrospective (Nantes, Lyon, Garches)
- Janvier 2013- Janvier 2015
- Infections ostéoarticulaires traitées par au moins 48H de ceftaroline
- Description cohorte :
  - 19 patients
  - 16/19 présence de matériel orthopédique (11 prothèses, 5 ostéosynthèses)
  - *S. epidermidis* dans 15/19, dont 11 méti-R
  - Infection plurimicrobienne 16/19
  - Ceftaroline (médiane 6 semaines de ttt) en association dans 17/19 (rifampicine ++)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : céphalosporines anti-SARM

International Journal of Antimicrobial Agents 50 (2017) 277–280

Salvage therapy for complex bone and joint infections with ceftaroline: a multicentre, observational study

Malandain et al

- Effets indésirables :
  - 2 cas de neutropénie
  - 2 rash cutanés
- Évolution (médiane suivi 6 mois)
  - 7 succès
  - 7 échecs (1 récurrence et 6 « surinfections »)

ORIGINAL RESEARCH

A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Barcelone, Madrid, Lille

Morata L. *et al*. Infect Dis Ther (2014) 3:235–243

Table 2 Characteristics of patients receiving or not rifampicin concomitantly with linezolid

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Median (IQR) age	71 (63–75)	75 (66–77)	0.31
Male sex (%)	9 (41)	9 (53)	0.45
Diabetes mellitus (%)	6 (27)	3 (18)	0.37
Type of implant (%)			0.50
Hip prosthesis	7 (32)	6 (35)	
Knee prosthesis	15 (68)	10 (59)	
Shoulder prosthesis	–	1 (6)	
Age of prosthesis	30 (21–55)	24 (17–32)	
Late acute infections (%)	2 (9)	2 (12)	1
Median (IQR) days of symptoms before debridement	9 (3–25)	2 (1–22)	0.14
Fever (%)	3 (14)	2 (12)	1
Bacteremia (%)	2 (9)	1 (6)	1
Median (IQR) leukocyte count (cells/mm^3)	8,400 (6,400–9,600)	6,950 (5,750–8,125)	0.18
Median (IQR) C-reactive protein (mg/dL)	4 (2–11)	3 (1–5)	0.22
Microorganisms			
S. aureus (MR)	6 (5)	3 (0)	
CoNS (MR)	18 (13)	15 (10)	
E. faecalis	3	1	
S. viridans	1	1	
Enterobacteriaceae	2	3	
P. aeruginosa	1	–	
Polymicrobial (%)	9 (41)	6 (35)	0.50

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Adverse events	9 (41)	8 (47)	
Gastrointestinal (nausea, vomits or diarrhea)	7 (32)	3 (18)[a]	
Hematological toxicity	1 (5)	4 (24)	
Peripheral neuropathy[b]	1 (5)	1 (6)	
Outcome (%)			
Remission	14 (64)	14 (82)	0.28
Relapse	6 (27)	2 (12)	
New infection	2 (9)	1 (6)	
Median (IQR) days of follow-up from stopping antibiotics to the last visit	730 (161–1,219)	812 (618–1,362)	0.39

ORIGINAL RESEARCH

A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Barcelone, Madrid, Lille

Morata L. *et al*. Infect Dis Ther (2014) 3:235–243

Table 2 Characteristics of patients receiving or not rifampicin concomitantly with linezolid

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Median (IQR) age	71 (63–75)	75 (66–77)	0.31
Male sex (%)	9 (41)	9 (53)	0.45
Diabetes mellitus (%)	6 (27)	3 (18)	0.37
Type of implant (%)			0.50
Hip prosthesis	7 (32)	6 (35)	
Knee prosthesis	15 (68)	10 (59)	
Shoulder prosthesis	–	1 (6)	
Age of prosthesis	30 (21–55)	24 (17–32)	
Late acute infections (%)	2 (9)	2 (12)	1
Median (IQR) days of symptoms before debridement	9 (3–25)	2 (1–22)	0.14
Fever (%)	3 (14)	2 (12)	1
Bacteremia (%)	2 (9)	1 (6)	1
Median (IQR) leukocyte count (cells/mm^3)	8,400 (6,400–9,600)	6,950 (5,750–8,125)	0.18
Median (IQR) C-reactive protein (mg/dL)	4 (2–11)	3 (1–5)	0.22
Microorganisms			
S. aureus (MR)	6 (5)	3 (0)	
CoNS (MR)	18 (13)	15 (10)	
E. faecalis	3	1	
S. viridans	1	1	
Enterobacteriaceae	2	3	
P. aeruginosa	1	–	
Polymicrobial (%)	9 (41)	6 (35)	0.50

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Adverse events	9 (41)	8 (47)	
Gastrointestinal (nausea, vomits or diarrhea)	7 (32)	3 (18)[a]	
Hematological toxicity	1 (5)	4 (24)	
Peripheral neuropathy[b]	1 (5)	1 (6)	
Outcome (%)			
Remission	14 (64)	14 (82)	0.28
Relapse	6 (27)	2 (12)	
New infection	2 (9)	1 (6)	
Median (IQR) days of follow-up from stopping antibiotics to the last visit	730 (161–1,219)	812 (618–1,362)	0.39

ORIGINAL RESEARCH

A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Barcelone, Madrid, Lille

Morata L. *et al*. Infect Dis Ther (2014) 3:235–243

Table 2 Characteristics of patients receiving or not rifampicin concomitantly with linezolid

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Median (IQR) age	71 (63–75)	75 (66–77)	0.31
Male sex (%)	9 (41)	9 (53)	0.45
Diabetes mellitus (%)	6 (27)	3 (18)	0.37
Type of implant (%)			0.50
Hip prosthesis	7 (32)	6 (35)	
Knee prosthesis	15 (68)	10 (59)	
Shoulder prosthesis	–	1 (6)	
Age of prosthesis	30 (21–55)	24 (17–32)	
Late acute infections (%)	2 (9)	2 (12)	1
Median (IQR) days of symptoms before debridement	9 (3–25)	2 (1–22)	0.14
Fever (%)	3 (14)	2 (12)	1
Bacteremia (%)	2 (9)	1 (6)	1
Median (IQR) leukocyte count (cells/mm^3)	8,400 (6,400–9,600)	6,950 (5,750–8,125)	0.18
Median (IQR) C-reactive protein (mg/dL)	4 (2–11)	3 (1–5)	0.22
Microorganisms			
S. aureus (MR)	6 (5)	3 (0)	
CoNS (MR)	18 (13)	15 (10)	
E. faecalis	3	1	
S. viridans	1	1	
Enterobacteriaceae	2	3	
P. aeruginosa	1	–	
Polymicrobial (%)	9 (41)	6 (35)	0.50

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Adverse events	9 (41)	8 (47)	
Gastrointestinal (nausea, vomits or diarrhea)	7 (32)	3 (18)[a]	
Hematological toxicity	1 (5)	4 (24)	
Peripheral neuropathy[b]	1 (5)	1 (6)	
Outcome (%)			
Remission	14 (64)	14 (82)	0.28
Relapse	6 (27)	2 (12)	
New infection	2 (9)	1 (6)	
Median (IQR) days of follow-up from stopping antibiotics to the last visit	730 (161–1,219)	812 (618–1,362)	0.39

ORIGINAL RESEARCH

A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Barcelone, Madrid, Lille

Morata L. *et al*. Infect Dis Ther (2014) 3:235–243

Table 2 Characteristics of patients receiving or not rifampicin concomitantly with linezolid

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Median (IQR) age	71 (63–75)	75 (66–77)	0.31
Male sex (%)	9 (41)	9 (53)	0.45
Diabetes mellitus (%)	6 (27)	3 (18)	0.37
Type of implant (%)			0.50
Hip prosthesis	7 (32)	6 (35)	
Knee prosthesis	15 (68)	10 (59)	
Shoulder prosthesis	–	1 (6)	
Age of prosthesis	30 (21–55)	24 (17–32)	
Late acute infections (%)	2 (9)	2 (12)	1
Median (IQR) days of symptoms before debridement	9 (3–25)	2 (1–22)	0.14
Fever (%)	3 (14)	2 (12)	1
Bacteremia (%)	2 (9)	1 (6)	1
Median (IQR) leukocyte count (cells/mm^3)	8,400 (6,400–9,600)	6,950 (5,750–8,125)	0.18
Median (IQR) C-reactive protein (mg/dL)	4 (2–11)	3 (1–5)	0.22
Microorganisms			
S. aureus (MR)	6 (5)	3 (0)	
CoNS (MR)	18 (13)	15 (10)	
E. faecalis	3	1	
S. viridans	1	1	
Enterobacteriaceae	2	3	
P. aeruginosa	1	–	
Polymicrobial (%)	9 (41)	6 (35)	0.50

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Adverse events	9 (41)	8 (47)	
Gastrointestinal (nausea, vomits or diarrhea)	7 (32)	3 (18)[a]	
Hematological toxicity	1 (5)	4 (24)	
Peripheral neuropathy[b]	1 (5)	1 (6)	
Outcome (%)			
Remission	14 (64)	14 (82)	0.28
Relapse	6 (27)	2 (12)	
New infection	2 (9)	1 (6)	
Median (IQR) days of follow-up from stopping antibiotics to the last visit	730 (161–1,219)	812 (618–1,362)	0.39

ORIGINAL RESEARCH

A Retrospective Review of the Clinical Experience of Linezolid with or Without Rifampicin in Prosthetic Joint Infections Treated with Debridement and Implant Retention

Barcelone, Madrid, Lille

Morata L. *et al*. Infect Dis Ther (2014) 3:235–243

Table 2 Characteristics of patients receiving or not rifampicin concomitantly with linezolid

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Median (IQR) age	71 (63–75)	75 (66–77)	0.31
Male sex (%)	9 (41)	9 (53)	0.45
Diabetes mellitus (%)	6 (27)	3 (18)	0.37
Type of implant (%)			0.50
Hip prosthesis	7 (32)	6 (35)	
Knee prosthesis	15 (68)	10 (59)	
Shoulder prosthesis	–	1 (6)	
Age of prosthesis	30 (21–55)	24 (17–32)	
Late acute infections (%)	2 (9)	2 (12)	1
Median (IQR) days of symptoms before debridement	9 (3–25)	2 (1–22)	0.14
Fever (%)	3 (14)	2 (12)	1
Bacteremia (%)	2 (9)	1 (6)	1
Median (IQR) leukocyte count (cells/mm^3)	8,400 (6,400–9,600)	6,950 (5,750–8,125)	0.18
Median (IQR) C-reactive protein (mg/dL)	4 (2–11)	3 (1–5)	0.22
Microorganisms			
S. aureus (MR)	6 (5)	3 (0)	
CoNS (MR)	18 (13)	15 (10)	
E. faecalis	3	1	
S. viridans	1	1	
Enterobacteriaceae	2	3	
P. aeruginosa	1	–	
Polymicrobial (%)	9 (41)	6 (35)	0.50

Characteristics	Receiving rifampicin ($n = 22$)	Not receiving rifampicin ($n = 17$)	*P*
Adverse events	9 (41)	8 (47)	
Gastrointestinal (nausea, vomits or diarrhea)	7 (32)	3 (18)[a]	
Hematological toxicity	1 (5)	4 (24)	
Peripheral neuropathy[b]	1 (5)	1 (6)	
Outcome (%)			
Remission	14 (64)	14 (82)	0.28
Relapse	6 (27)	2 (12)	
New infection	2 (9)	1 (6)	
Median (IQR) days of follow-up from stopping antibiotics to the last visit	730 (161–1,219)	812 (618–1,362)	0.39

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

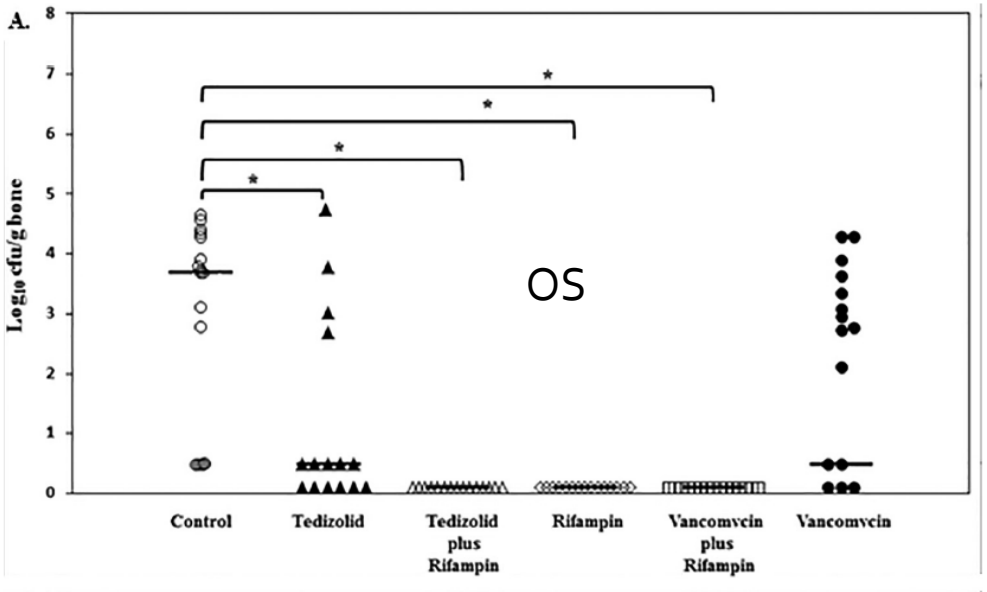
Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16

Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16



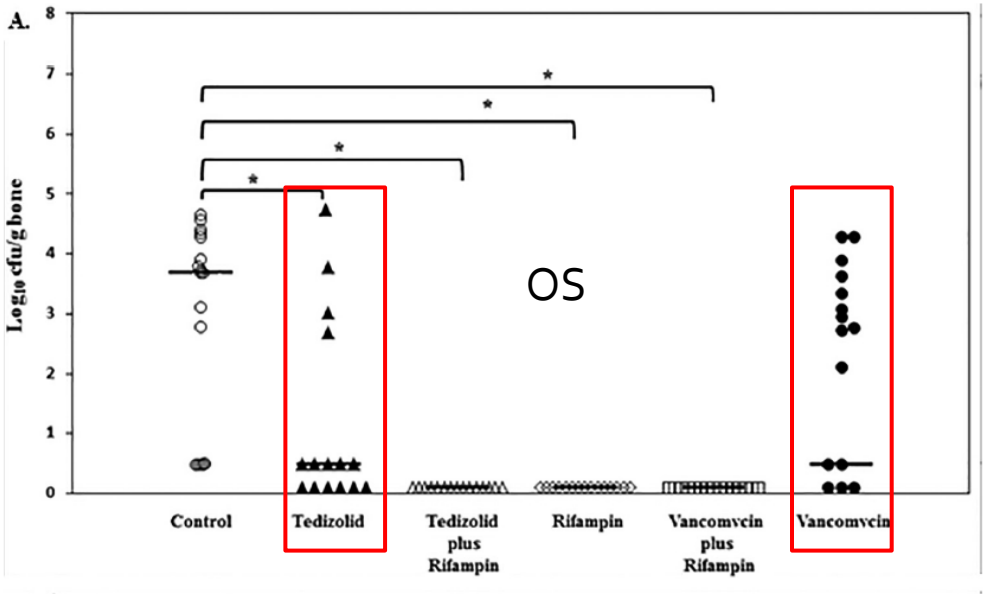
OS

Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16



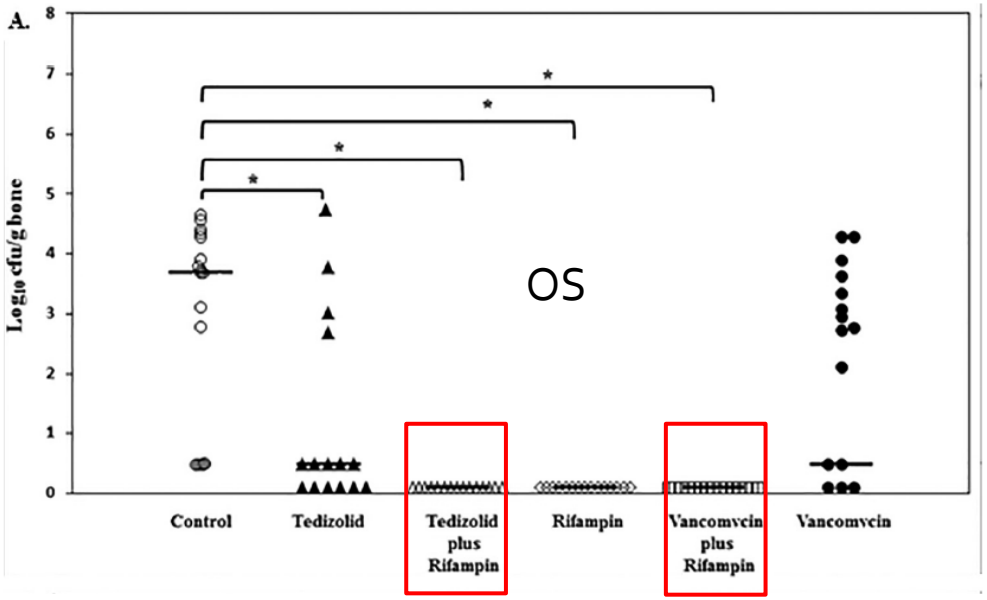
OS

Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16



OS

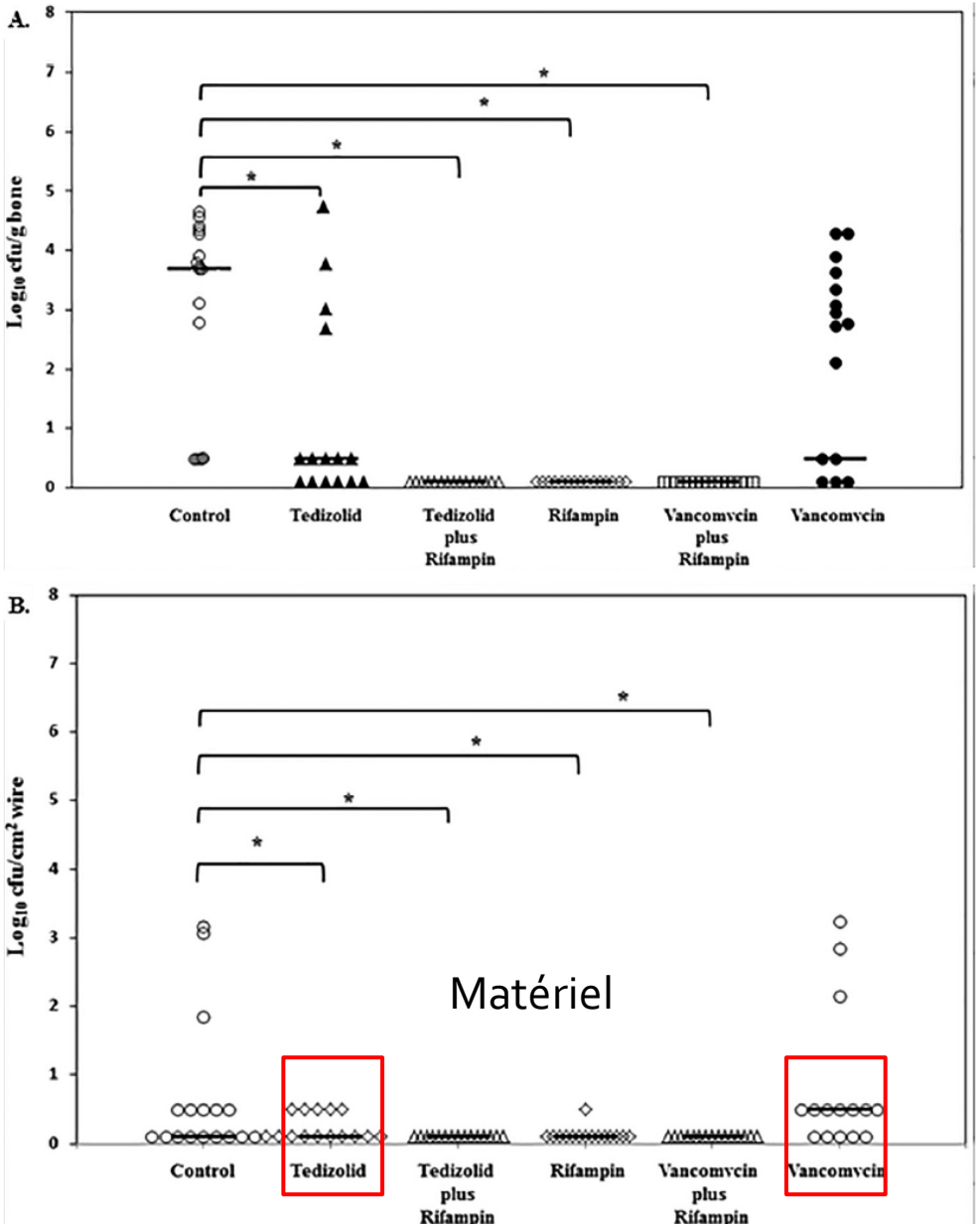
Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16

Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement

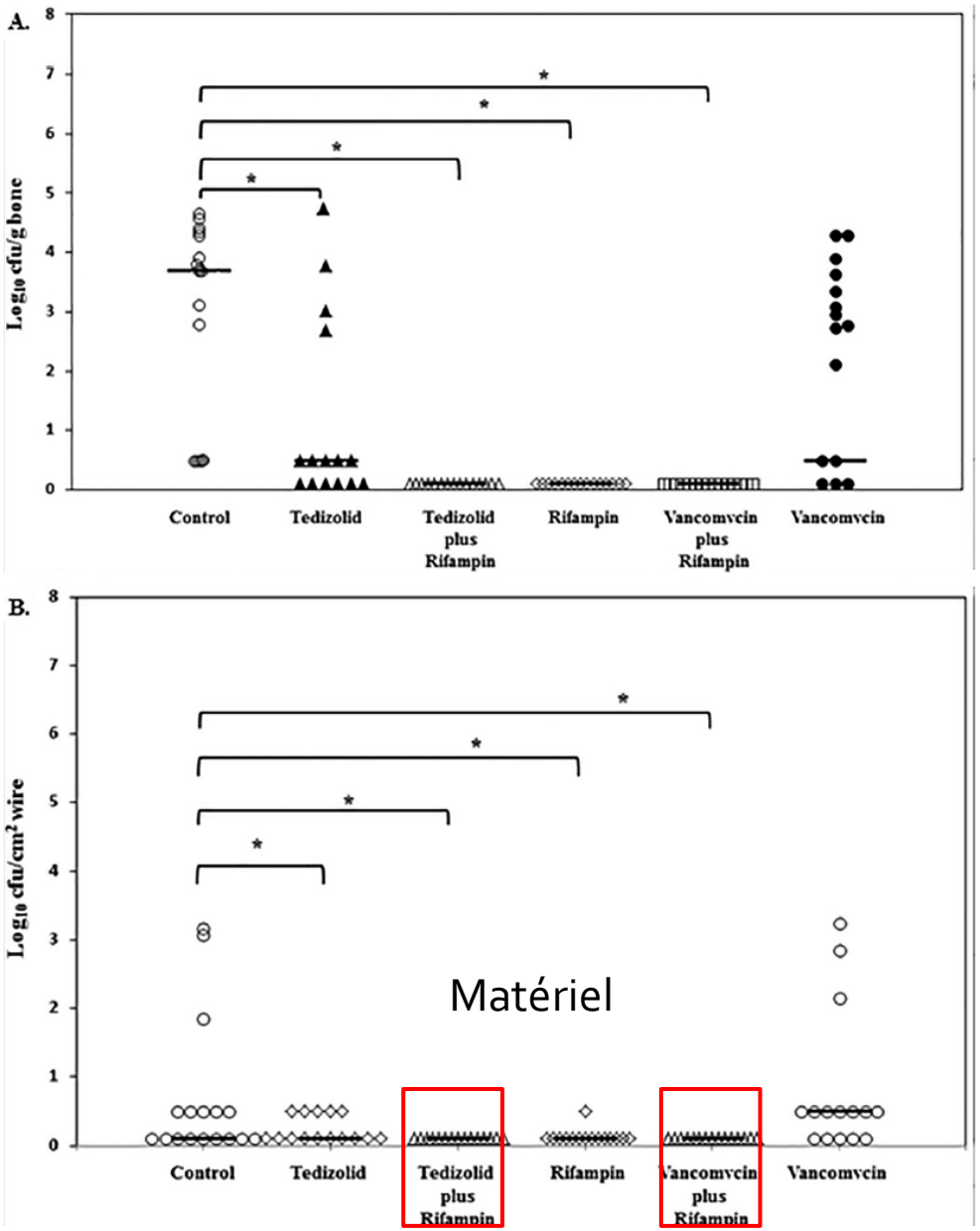


AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Activity of Tedizolid in Methicillin-Resistant *Staphylococcus epidermidis* Experimental Foreign Body-Associated Osteomyelitis

Park K-H. *et al* . Antimicrob. Agent Chemother. 2017. 2; e01644-16

Modèle d'infection sur matériel orthopédique chez le rat
N = 18/groupe
PK humanisée
Challenge puis traitement à 1 semaine (IP)
Tédizolide +/- rifampicine
Vancomycine +/- rifampicine
Sacrifice H24
Mesure de la concentration bactérienne vs contrôle sans traitement



Alternatives thérapeutiques

Sensibilité in vitro

Journal of Global Antimicrobial Resistance 13 (2018) 221–225

In vitro activity of novel anti-MRSA cephalosporins and comparator antimicrobial agents against staphylococci involved in prosthetic joint infections☆

Christophe Isnard[a,b,1], Anne Dhalluin[b,1], Damasie Malandain[a], Quentin Bruey[b], Michel Auzou[a], Jocelyn Michon[c], Jean-Christophe Giard[b], François Guérin[a,b], Vincent Cattoir[d,e,*]

Table 1
In vitro activity of ceftaroline, ceftobiprole and comparator antimicrobial agents against *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS) involved in documented prosthetic joint infections, 2011–2014.

Species (no. of isolates)/antimicrobial agent	MIC (μg/mL)			% of susceptible isolates[a]
	MIC_{50}	MIC_{90}	Range	
Staphylococcus aureus				
All isolates (n = 100)				
Oxacillin	≤0.03	2	≤0.03 to ≥32	90
Ceftaroline	0.25	0.5	0.06–1	100
Ceftobiprole	0.5	1	0.125–4	98
Daptomycin	0.25	0.5	≤0.03–1	100
Vancomycin	1	1	0.25–2	100
Teicoplanin	0.25	0.5	≤0.03–4	99
Linezolid	2	2	0.25–4	100
CoNS				
All isolates (n = 100)				
Oxacillin	≤0.03	8	≤0.03 to ≥32	86
Ceftaroline	0.06	0.25	≤0.03–1	100[b]
Ceftobiprole	0.25	1	≤0.03–2	100[b]
Daptomycin	0.12	0.5	≤0.03 to ≥32	99
Vancomycin	1	2	0.25–32	99
Teicoplanin	0.5	4	≤0.03 to ≥32	94
Linezolid	1	2	0.5–16	98
Clindamycin	0.06	2	≤0.03 to ≥32	85
Levofloxacin	0.25	4	≤0.03–16	87

Alternatives thérapeutiques

Sensibilité in vitro

Journal of Global Antimicrobial Resistance 13 (2018) 221–225

In vitro activity of novel anti-MRSA cephalosporins and comparator antimicrobial agents against staphylococci involved in prosthetic joint infections☆

Christophe Isnard[a,b,1], Anne Dhalluin[b,1], Damasie Malandain[a], Quentin Bruey[b], Michel Auzou[a], Jocelyn Michon[c], Jean-Christophe Giard[b], François Guérin[a,b], Vincent Cattoir[d,e,*]

Table 1
In vitro activity of ceftaroline, ceftobiprole and comparator antimicrobial agents against *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS) involved in documented prosthetic joint infections, 2011–2014.

Species (no. of isolates)/antimicrobial agent	MIC (μg/mL)			
	MIC[illegible]			
Staphylococcus aureus				
All isolates (n = 100)				
Oxacillin				
Ceftaroline				
Ceftobiprole				
Daptomycin				
Vancomycin				
Teicoplanin				
Linezolid				
CoNS				
All isolates (n = 100)				
Oxacillin				
Ceftaroline				
Ceftobiprole				
Daptomycin				
Vancomycin		2	0.25–32	99
Teicoplanin	0.5	4	≤0.03 to ≥32	94
Linezolid	1	2	0.5–16	98
Clindamycin	0.06	2	≤0.03 to ≥32	85
Levofloxacin	0.25	4	≤0.03–16	87

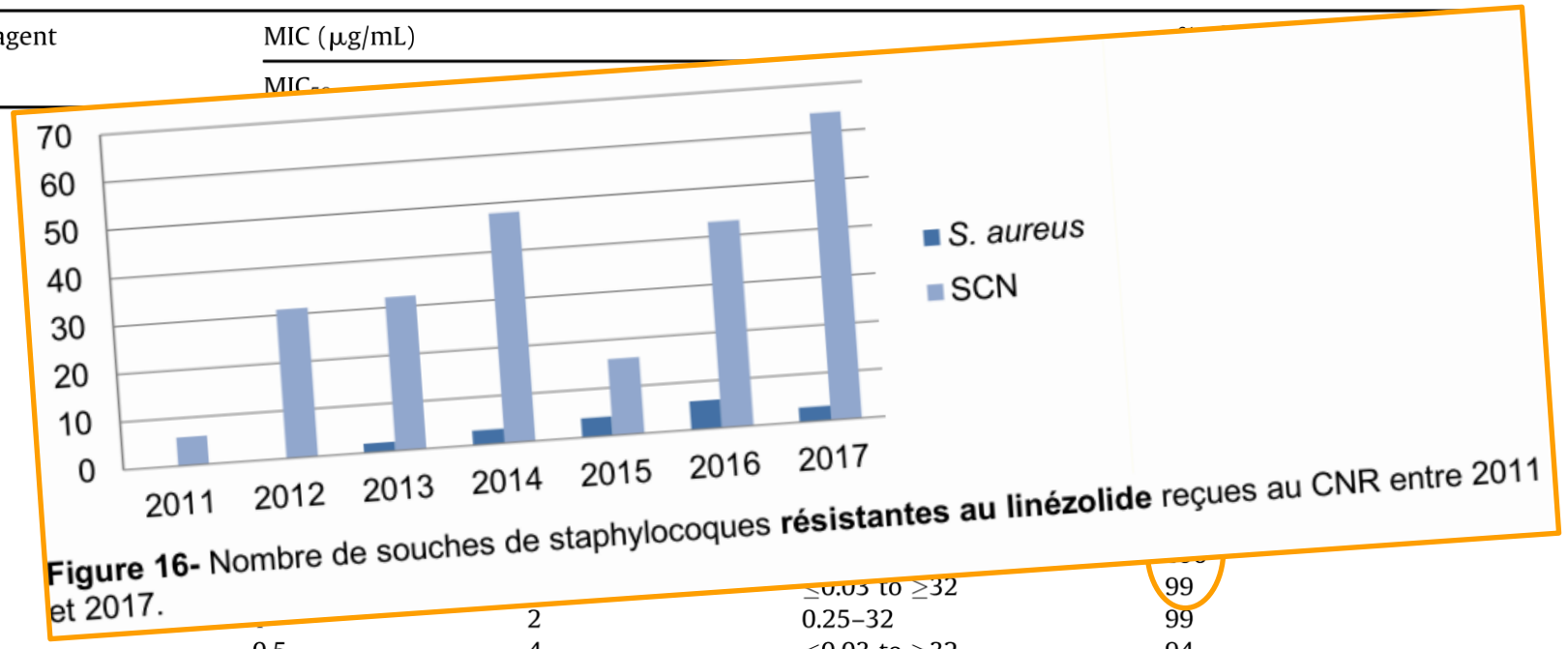


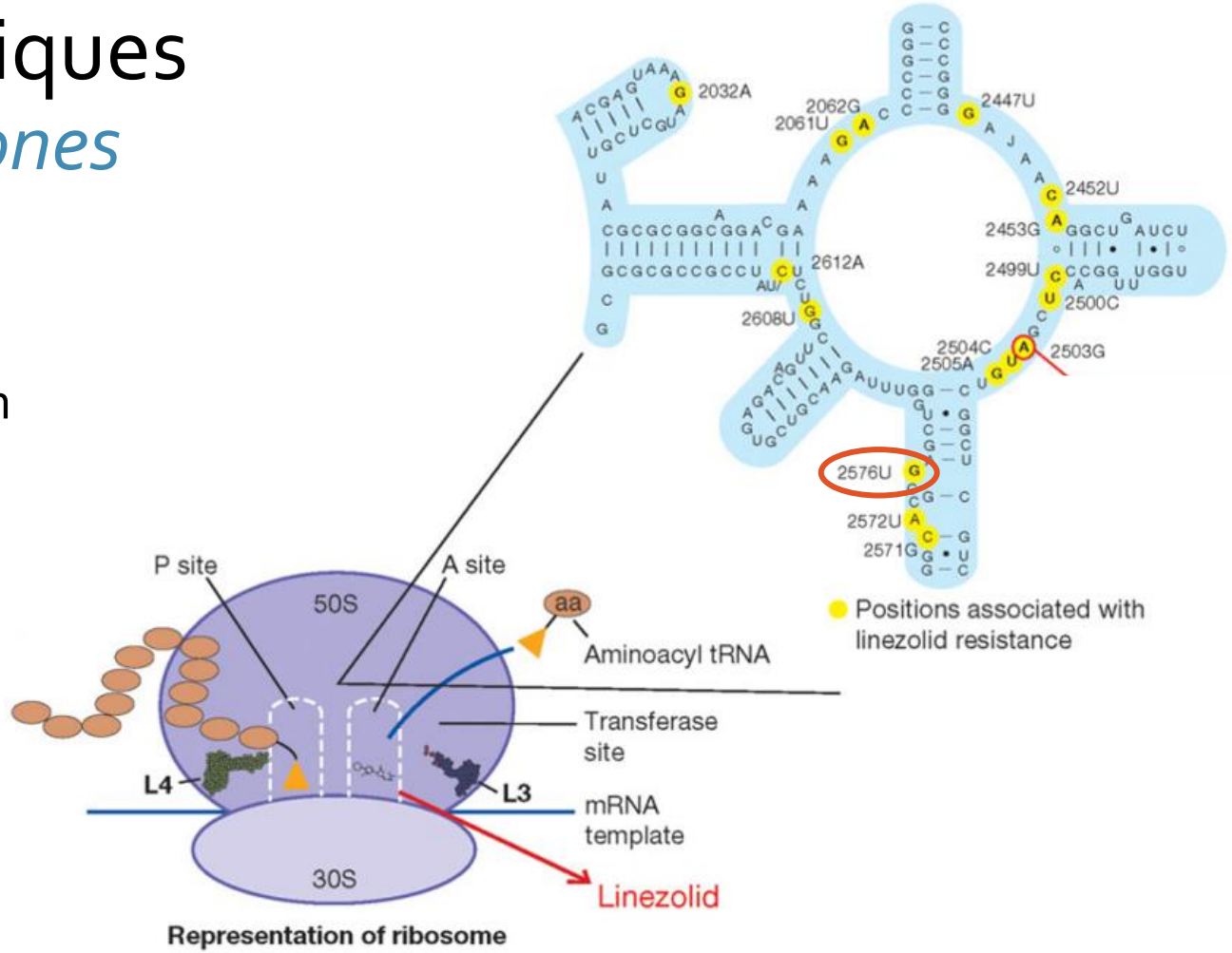
Figure 16- Nombre de souches de staphylocoques **résistantes au linézolide** reçues au CNR entre 2011 et 2017.

Alternatives thérapeutiques

Résistance aux oxazolidinones

- **Mutations ribosomales** : du gène codant l'ARNr 23S
- **Méthylation ribosomale** : acquisition du gène plasmidique *cfr* codant pour une méthyltransferase de l'ARNr 23S
- **ABC transporteurs** : acquisition du gène plasmidique *optrA*

- Mutation ARNr 23S = mécanisme le + fréquent en France
- Mais augmentation souches *cfr*+ => plasmidique => fort potentiel de transmission et de dissémination



Evolving resistance among Gram + pathogens ; Munita et al; CID 2015

Alternatives thérapeutiques

Résistance aux oxazolidinones

CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

Tous prélèvements confondus	% de souches R liné en 2017	% de souches R liné en 2018
S. aureus	0,3	0,3
S. epidermidis	8,5	8,2
S. lugdunensis	0	0
S. capitis	0	0

Alternatives thérapeutiques

Résistance aux oxazolidinones

CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

Isolées d'IOA	% de souches R liné en 2017	% de souches R liné en 2018
S. aureus	0	0
S. epidermidis	5,3	0
S. lugdunensis	0	0
S. capitis	0	0

Au total : 1,1% de l'ensemble des staphylocoques responsables d'IOA R liné en 2017

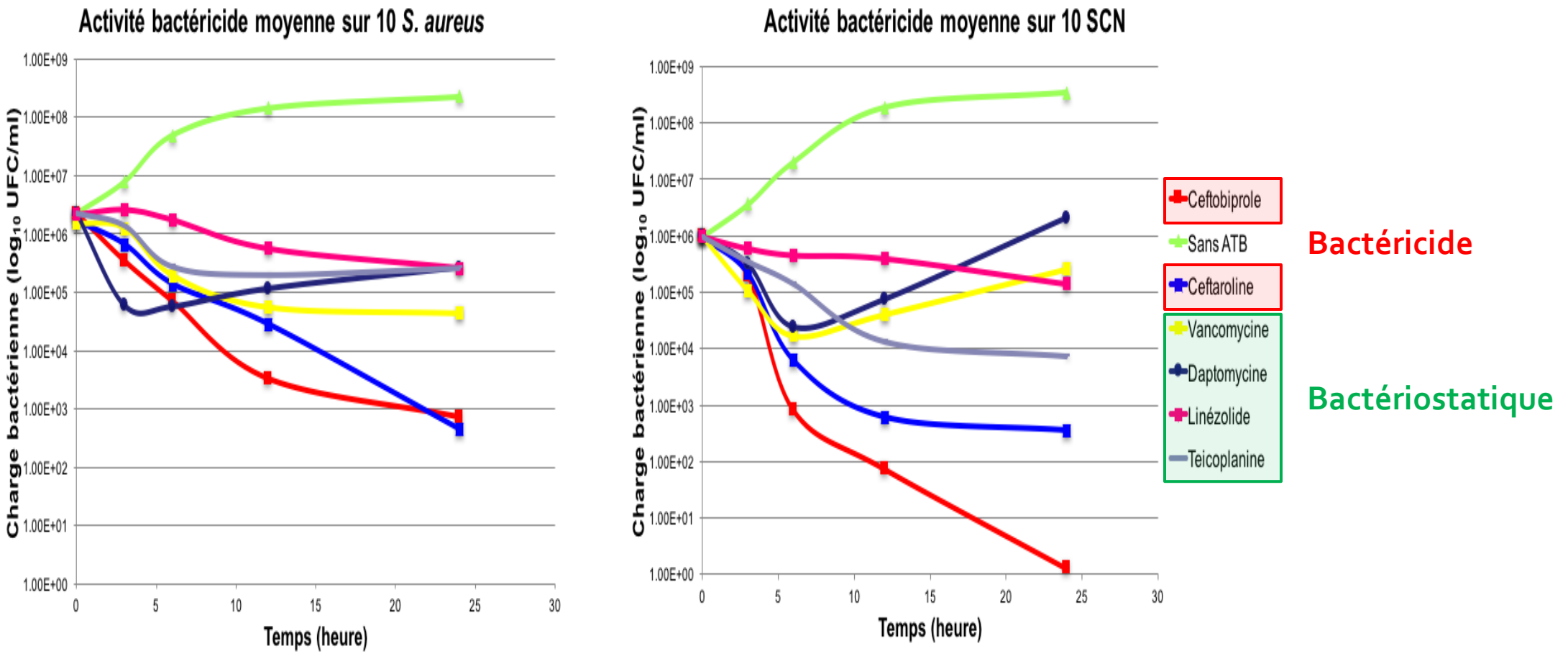
0% en 2018

3/57 souches de *S. epidermidis* responsables d'IOA :

- Mutation ARN 23s (3/3)
- Associée au gène *cfr* (1/3)

Alternatives thérapeutiques

Activité bactéricide in vitro



Manlandain et al., RICAI 2015

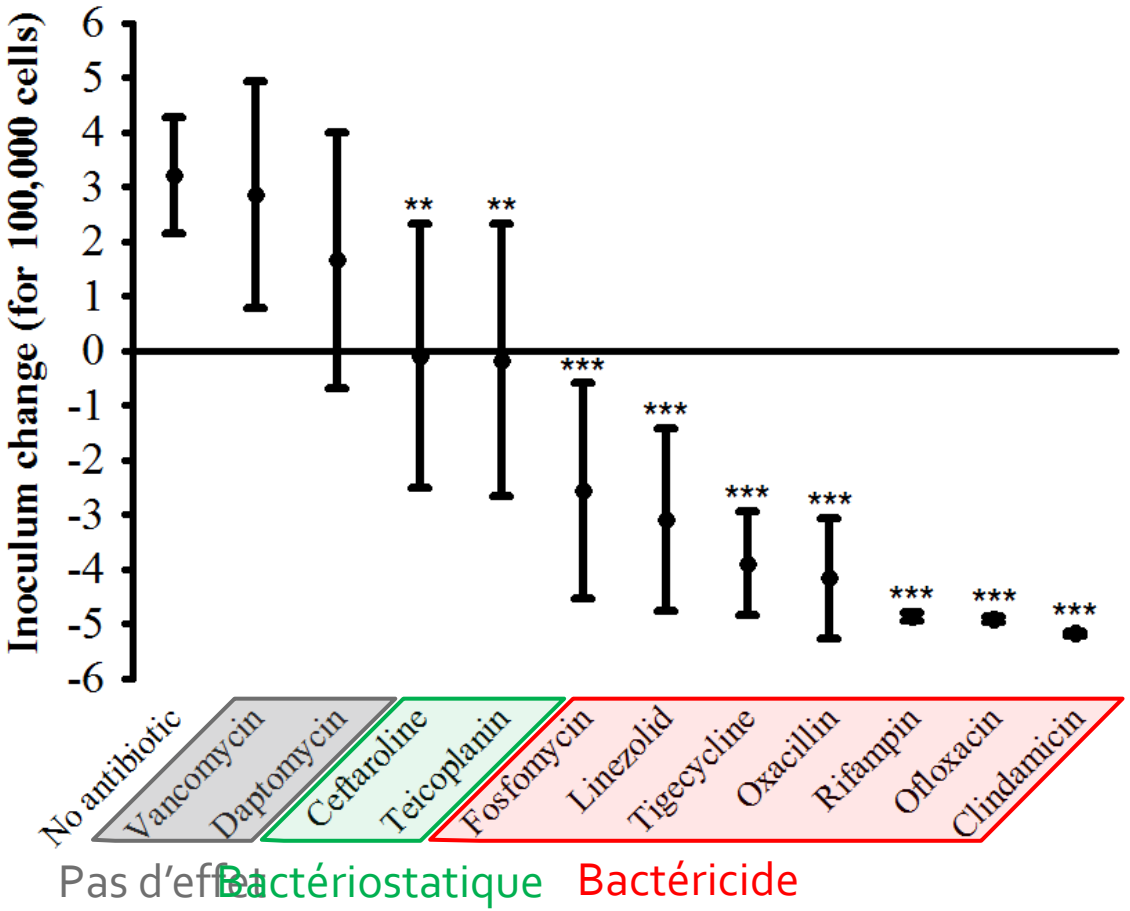
Alternatives thérapeutiques

Activité intraostéoblastique

AAC Journals.ASM.org

Antimicrobial Activity against Intraosteoblastic *Staphylococcus aureus*

Florent Valour,[a,b] Sophie Trouillet-Assant,[b] Natacha Riffard,[b] Jason Tasse,[b] Sacha Flammier,[b] Jean-Philippe Rasigade,[b,c] Christian Chidiac,[a,b] François Vandenesch,[b,c,d] Tristan Ferry,[a,b] Frédéric Laurent,[b,c,d] on behalf of the Lyon Bone and Joint Infection Study Group



- Modèle *ex-vivo* infection ostéoblastes
- SASM
- Concentrations ATB = concentrations osseuses

Alternatives thérapeutiques

Dalbavancine

- *S. aureus* : S = 100 %
- SCN : S = 99,4 %

International Journal of Antimicrobial Agents 51 (2018) 608–611

Dalbavancin in-vitro activity obtained against Gram-positive clinical isolates causing bone and joint infections in US and European hospitals (2011–2016)

Michael A. Pfaller [a,b], Robert K. Flamm [a], Mariana Castanheira [a], Helio S. Sader [a,*], Rodrigo E. Mendes [a]

Table 1
Antimicrobial activity of dalbavancin tested against the main organisms and organism groups of isolates (mg/L)

Organism/organism group (no. of isolates)	No. of isolates at MIC (mg/L; cumulative %)								MIC_{50}	MIC_{90}
	≤0.03	0.06	0.12	0.25	0.5	1	2	>2		
Staphylococcus aureus (801)	412 (51.4)	342 (94.1)	47 (100.0)						≤0.03	0.06
MSSA (534)	280 (52.4)	224 (94.4)	30 (100.0)						≤0.03	0.06
MRSA (267)	132 (49.4)	118 (93.6)	17 (100.0)						0.06	0.06
Coagulase-negative staphylococci (160)	110 (68.8)	43 (95.6)	6 (99.4)	1 (100.0)					≤0.03	0.06
S. epidermidis (97)	62 (63.9)	30 (94.8)	5 (100.0)						≤0.03	0.06
S. lugdunensis (21)	18 (85.7)	3 (100.0)							≤0.03	0.06
Other CoNS (42)[a]	30 (71.4)	10 (95.2)	1 (97.6)	1 (100.0)					≤0.03	0.06
Enterococcus faecalis (82)	38 (46.3)	35 (89.0)	5 (95.1)	1 (96.3)	0 (96.3)	0 (96.3)	0 (96.3)	3 (100.0)	0.06	0.12
β-haemolytic streptococci (164)	148 (90.2)	11 (97.0)	5 (100.0)						≤0.03	≤0.03
S. agalactiae (80)	69 (86.2)	7 (95.0)	4 (100.0)						≤0.03	0.06
S. disgalactiae (36)	36 (100.0)								≤0.03	≤0.03
S. pyogenes (48)	43 (89.6)	4 (97.9)	1 (100.0)						≤0.03	0.06
Viridans group streptococci (45)[b]	41 (91.1)	4 (100.0)							≤0.03	≤0.03

BP EUCAST

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : dalbavancine

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections

L. Morata,[a] J. Cobo,[b] M. Fernández-Sampedro,[c] P. Guisado Vasco,[d] E. Ruano,[e] J. Lora-Tamayo,[f] M. Sánchez Somolinos,[g] P. González Ruano,[h] A. Rico Nieto,[i] A. Arnaiz,[j] M. Estébanez Muñoz,[k] M. E. Jiménez-Mejías,[l] A. B. Lozano Serrano,[m] E. Múñez,[n] D. Rodriguez-Pardo,[o] R. Argelich,[p] A. Arroyo,[q] J. M. Barbero,[r] F. Cuadra,[s] A. Del Arco,[t] M. D. del Toro,[u,v] L. Guio,[w] D. Jimenez-Beatty,[x] N. Lois,[y] O. Martin,[z] R. M. Martínez Alvarez,[aa] F. J. Martinez-Marcos,[bb] L. Porras,[cc] M. Ramírez,[dd] J. Vergas García,[ee] A. Soriano[a]

- Étude multicentrique (30 centres Espagne), rétrospective (2016-2018)
- Infection ostéoarticulaire traitée par au moins une dose de dalbavancine

TABLE 1 Etiology according to type of infection

Microorganism(s)	No. (%) of patients with: Implant-associated infection (n = 45)	Bone or joint infection (n = 19)
Staphylococcus epidermidis	26 (57.7)	4 (21)
Staphylococcus aureus	4 (8.9)	10 (52.6)
Staphylococcus lugdunensis	2 (4.4)	0
Staphylococcus capitis	1 (2.2)	0
Streptococcus pneumoniae	1 (2.2)	0
Enterococcus faecalis	4 (8.9)	1 (5.2)
Enterococcus faecium	3 (6.6)	1 (5.2)
Corynebacterium striatum	2 (4.4)	1 (5.2)
Streptococcus spp.[a]	0	3 (15.7)
Anaerobes[b]	2 (4.4)	1 (5.2)
Gram negatives[c]	2 (4.4)	0
Polymicrobial	5 (11.1)	3 (15.7)
Negative culture	3 (6.6)	1 (5.2)

[a]*Streptococcus* spp. included one *S. agalactiae*, one *S. pyogenes*, and one *S. sanguinis*.
[b]Anaerobes included one *Clostridium celerecrescens* and two *Propionibacterium acnes*.
[c]Gram negatives included one *Escherichia coli* and one *Pseudomonas aeruginosa* (both were isolated with a Gram-positive microorganism).

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : dalbavancine

Antimicrobial Agents and Chemotherapy

Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections

L. Morata,[a] J. Cobo,[b] M. Fernández-Sampedro,[c] P. Guisado Vasco,[d] E. Ruano,[e] J. Lora-Tamayo,[f] M. Sánchez Somolinos,[g] P. González Ruano,[h] A. Rico Nieto,[i] A. Arnaiz,[j] M. Estébanez Muñoz,[k] M. E. Jiménez-Mejías,[l] A. B. Lozano Serrano,[m] E. Múñez,[n] D. Rodríguez-Pardo,[o] R. Argelich,[p] A. Arroyo,[q] J. M. Barbero,[r] F. Cuadra,[s] A. Del Arco,[t] M. D. del Toro,[u,v] L. Guio,[w] D. Jimenez-Beatty,[x] N. Lois,[y] O. Martín,[z] R. M. Martínez Alvarez,[aa] F. J. Martínez-Marcos,[bb] L. Porras,[cc] M. Ramírez,[dd] J. Vergas García,[ee] A. Soriano[a]

TABLE 1 Etiology according to type of infection

Microorganism(s)	No. (%) of patients with: Implant-associated infection (n = 45)
Staphylococcus epidermidis	26 (57.7)
Staphylococcus aureus	4 (8.9)
Staphylococcus lugdunensis	2 (4.4)
Staphylococcus capitis	1 (2.2)
Streptococcus pneumoniae	1 (2.2)
Enterococcus faecalis	4 (8.9)
Enterococcus faecium	3 (6.6)
Corynebacterium striatum	2 (4.4)
Streptococcus spp.[a]	0
Anaerobes[b]	2 (4.4)
Gram negatives[c]	2 (4.4)
Polymicrobial	5 (11.1)
Negative culture	3 (6.6)

[a]*Streptococcus* spp. included one *S. agalactiae*, one *S. pyogenes*, and one *S. sanguinis*.
[b]Anaerobes included one *Clostridium celerecrescens* and two *Propionibacterium acnes*.
[c]Gram negatives included one *Escherichia coli* and one *Pseudomonas aeruginosa* (both were isolate
Gram-positive microorganism).

Type of implant, no. (%)		
Joint prosthesis	26 (57.8)	
Hip	13	
Knee	10	
Shoulder	3	
Other implant	19 (42.2)	
Spine	11	
Long bone	5	
Other	3	

Median (IQR) no. of dalbavancin doses	5 (3–8)

Other concomitant antibiotic, no. (%)		
Rifampin	8 (17.7)	
Other	7 (15.5)	

Outcome, no. (%)[d]		
Implant retention	23 (52.3)	
Success	15	
Improvement	8	
Failure	0	
Implant removal	21 (47.7)	
Success	16	
Improvement	4	
Failure	1	

TABLE 2 Characteristics and outcomes of patients with implant-associated infections (n = 45)

Variable[f]	Value
Age (yrs), mean (SD)	64 (15)
Male sex, no. (%)	24 (53.3)
Comorbidity, no. (%)	
Diabetes mellitus	7 (15.5)
Rheumatoid arthritis	3 (6.6)
Chronic renal failure	5 (11.1)
Cancer	5 (11.1)
COPD	4 (8.8)
Liver cirrhosis	2 (4.4)
Cardiac disease	3 (6.6)
Type of implant, no. (%)	
Joint prosthesis	26 (57.8)
Hip	13
Knee	10
Shoulder	3
Other implant	19 (42.2)
Spine	11
Long bone	5
Other	3
Median (IQR) no. of days from implantation to infection diagnosis	115 (27–424)
Fever, no. (%)	13 (28.8)
Local signs of infection at admission, no. (%)	31 (68.8)
Wound drainage, no. (%)	21 +(46.6)
Fistula, no. (%)	11 (24.4)
Median (IQR) leukocyte count (cells/mm^3)	7,300 (5,750–9,925)
Median (IQR) SCr (mg/dl) before dalbavancin treatment[a]	1 (0.6–1)
Median (IQR) highest SCr (mg/dl) during dalbavancin[a]	1 (0.6–1)
Baseline CRP (mg/dl)[b]	5 (2.7–11.7)
Last control CRP (mg/dl)[c]	1 (0.3–1.3)
Median (IQR) no. of days of antibiotics prior to dalbavancin treatment	41 (21–87)
Reason for starting dalbavancin, no. (%)	
Failure to prior antibiotic	12 (26.6)
Simplification	23 (51.1)
Toxicity to prior antibiotic	10 (22.2)
Median (IQR) no. of dalbavancin doses	5 (3–8)
Other concomitant antibiotic, no. (%)	
Rifampin	8 (17.7)
Other	7 (15.5)
Outcome, no. (%)[d]	
Implant retention	23 (52.3)
Success	15
Improvement	8
Failure	0
Implant removal	21 (47.7)
Success	16
Improvement	4
Failure	1
Death, no. (%)[e]	1 (2.2)
Median (IQR) no. of days of follow-up	157 (75.5–273.5)

Quand le staphylocoque résiste à tout

Alternatives thérapeutiques : dalbavancine

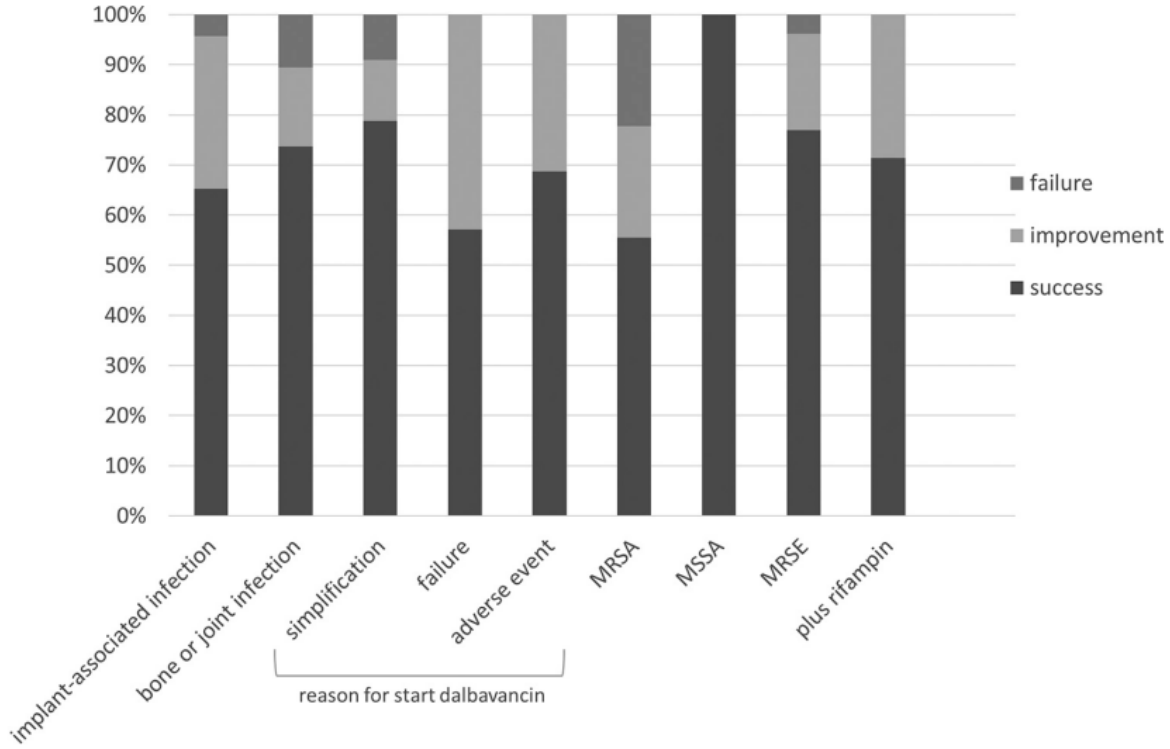


FIG 1 Outcome of patients according to the type of infection, the reason for starting dalbavancin, etiology, and concomitant use of rifampin.

Antimicrobial Agents and Chemotherapy

Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections

L. Morata,[a] J. Cobo,[b] M. Fernández-Sampedro,[c] P. Guisado Vasco,[d] E. Ruano,[e] J. Lora-Tamayo,[f] M. Sánchez Somolinos,[g] P. González Ruano,[h] A. Rico Nieto,[i] A. Arnaiz,[j] M. Estébanez Muñoz,[k] M. E. Jiménez-Mejías,[l] A. B. Lozano Serrano,[m] E. Múñez,[n] D. Rodríguez-Pardo,[o] R. Argelich,[p] A. Arroyo,[q] J. M. Barbero,[r] F. Cuadra,[s] A. Del Arco,[t] M. D. del Toro,[u,v] L. Guio,[w] D. Jimenez-Beatty,[x] N. Lois,[y] O. Martín,[z] R. M. Martínez Álvarez,[aa] F. J. Martínez-Marcos,[bb] L. Porras,[cc] M. Ramírez,[dd] J. Vergas García,[ee] A. Soriano[a]

TABLE 2 Characteristics and outcomes of patients with implant-associated infections ($n = 45$)

Variable[f]	Value
Age (yrs), mean (SD)	64 (15)
Male sex, no. (%)	24 (53.3)
Comorbidity, no. (%)	
Diabetes mellitus	7 (15.5)
Rheumatoid arthritis	3 (6.6)
Chronic renal failure	5 (11.1)
Cancer	5 (11.1)
COPD	4 (8.8)
Liver cirrhosis	2 (4.4)
Cardiac disease	3 (6.6)
Type of implant, no. (%)	
Joint prosthesis	26 (57.8)
Hip	13
Knee	10
Shoulder	3
Other implant	19 (42.2)
Spine	11
Long bone	5
Other	3
Median (IQR) no. of days from implantation to infection diagnosis	115 (27–424)
Fever, no. (%)	13 (28.8)
Local signs of infection at admission, no. (%)	31 (68.8)
Wound drainage, no. (%)	21 +(46.6)
Fistula, no. (%)	11 (24.4)
Median (IQR) leukocyte count (cells/mm^3)	7,300 (5,750–9,925)
Median (IQR) SCr (mg/dl) before dalbavancin treatment[a]	1 (0.6–1)
Median (IQR) highest SCr (mg/dl) during dalbavancin[a]	1 (0.6–1)
Baseline CRP (mg/dl)[b]	5 (2.7–11.7)
Last control CRP (mg/dl)[c]	1 (0.3–1.3)
Median (IQR) no. of days of antibiotics prior to dalbavancin treatment	41 (21–87)
Reason for starting dalbavancin, no. (%)	
Failure to prior antibiotic	12 (26.6)
Simplification	23 (51.1)
Toxicity to prior antibiotic	10 (22.2)
Median (IQR) no. of dalbavancin doses	5 (3–8)
Other concomitant antibiotic, no. (%)	
Rifampin	8 (17.7)
Other	7 (15.5)
Outcome, no. (%)[d]	
Implant retention	23 (52.3)
Success	15
Improvement	8
Failure	0
Implant removal	21 (47.7)
Success	16
Improvement	4
Failure	1
Death, no. (%)[e]	1 (2.2)
Median (IQR) no. of days of follow-up	157 (75.5–273.5)

Outcome, no. (%)[d]
Implant retention 23 (52.3)
Success 15
Improvement 8
Failure 0
Implant removal 21 (47.7)
Success 16
Improvement 4
Failure 1

« Nouveaux » antibiotiques anti staph MR

Caractéristiques	Oxazilodinones		Céphalosporines		Lipopeptides	Lipoglycopeptides
	Linézolide	Tédizolide	Ceftaroline	Ceftobiprole	Daptomycine	Dalvabancine
Administration	IV/PO	IV/PO	IV	IV	IV	IV
Biodisponibilité PO	>90%	>90%	-	-	-	-
T1/2	5-7h	12h	2.5h	3.3h	9h	14j
Posologie	200 mg/j	600 mgx2/j	600 mgx2/j	500 mgx3/j	10-12 mg/kg/j	1500 mg/15j
EI potentiels	Tox mitochodries	Moins de tox ?	Neutropénie		Rhabdomyolyse (CPK+++) Pneumopathie éo	Transaminases
% sensibilité	100	92-100	100	98	86-98	100
Breakpoints EUCAST	4 mg/l	≤ 0.5 mg/l	≤ 1 mg/l (SA) SCN (ND)	≤ 2 mg/l (SA) SCN (ND)	≤ 1 mg/l	≤ 0,125 mg/l
Etudes PK os	Oui	Non	Non	Non	Oui	Oui
Etudes exp os	Oui	Oui	Oui			
Etudes cliniques os	Oui	Non	+/-	Non	Oui	Oui

Take home messages

- Diagnostic microbiologique :
  - 4 prélèvements font aussi bien que 5, 6, 7, …
  - 3 milieux font aussi bien que 4
- Alternatives potentielles : très bonne sensibilité mais attention risque d'émergence de résistance aux oxazolidinones par mécanisme plasmidique
- Place des nouvelles molécules reste à préciser (peu d'études)
- Quid de la vancomycine ?
- Avis centre de référence +++

DIAPO EN PLUS POUR DISCUSSION

ORIGINAL ARTICLE INFECTIOUS DISEASES

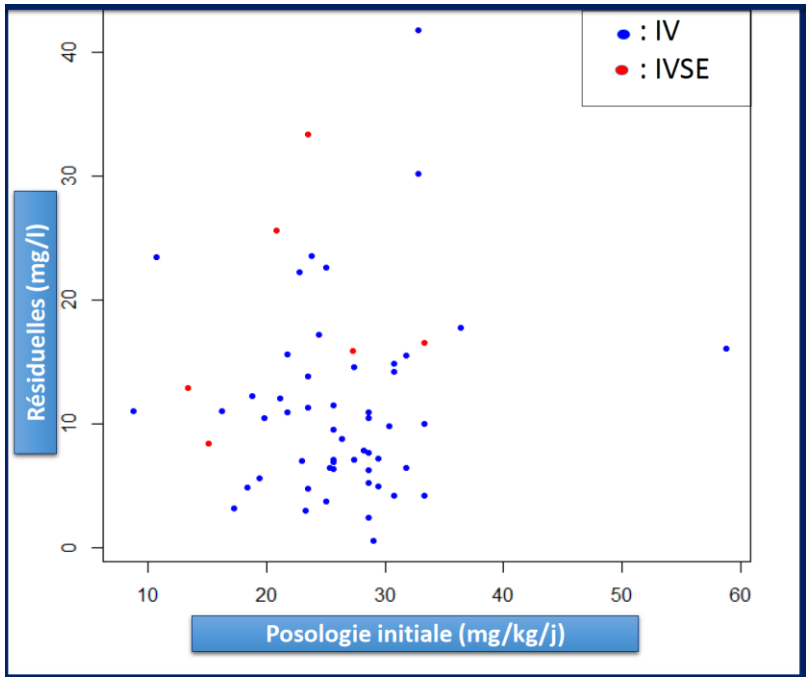
Continuous high-dose vancomycin combination therapy for methicillin-resistant staphylococcal prosthetic hip infection: a prospective cohort study

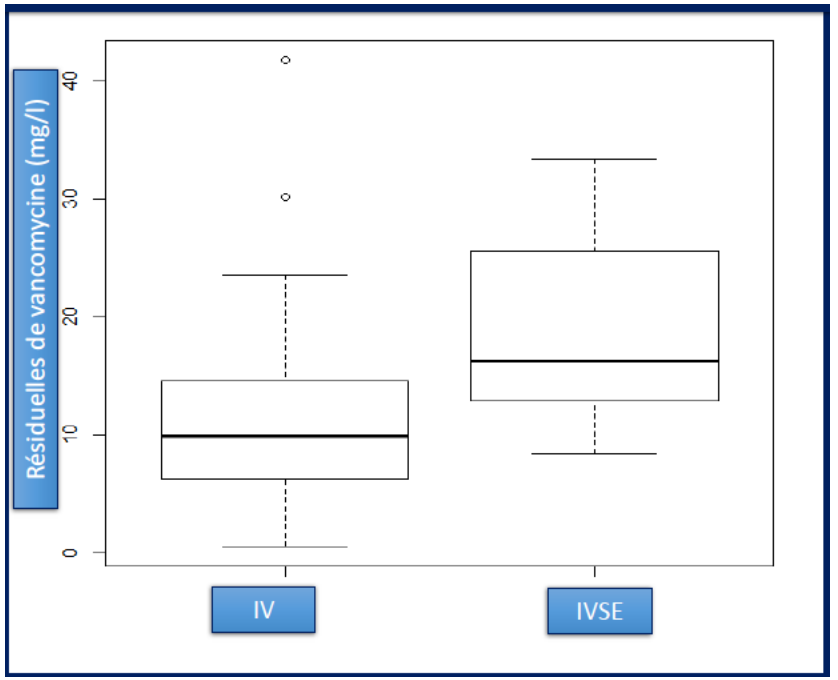
Dubée et al. Clin Microbiol Infect 2013; 19: E98–E105

- Prospectif, observationnel, monocentrique
- PTH (n = 60)
- SCN (n = 53 dont 20 GIS), SA (n = 9 dont 1GIS)
- Chirurgie: changement 1T (n = 32), 2T (n = 26), résection (n = 2)
- Antibiothérapie:
  - Phase 1: 6 semaines: vancomycine IVSE 30-40mg/L + une autre molécule
  - Phase 2: 6 semaines de traitement oral
- Succès à 2 ans: 68%
- I rénale: 38%

De la complexité de l'utilisation de la vancomycine dans une unité d'orthopédie

	HAS 2014	PILLY 2014	IDSA 2009
Posologie	1000 mg/12h (<80 kg) 1250 mg/12h (80-100 kg) 1500 mg/12h (> 100 Kg)	20-30 mg/kg/12h	15-20 mg/kg/8-12h
Résiduelle	20-30 mg/l (72h)	30-40 mg/l	15-20 mg/l





Dosages réalisés en moyenne 36h après le début de la vancomycine

C Galimard[1], J Michon[1], G Rochcongar[2], C Hulet[2], R Verdon[1]
[1]SMIT, CHU CAEN; [2] Service de Chirurgie Orthopédique, CHU CAEN

RESEARCH ARTICLE Open Access

Teicoplanin-based antimicrobial therapy in *Staphylococcus aureus* bone and joint infection: tolerance, efficacy and experience with subcutaneous administration

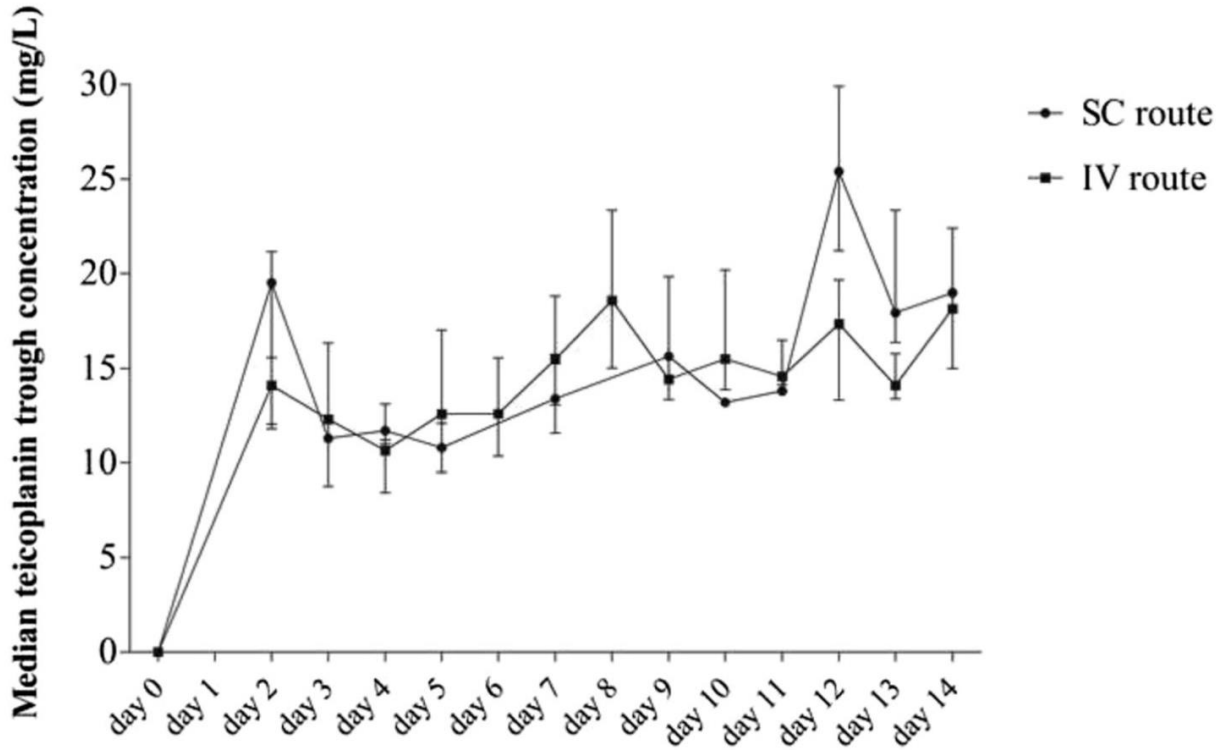
Peeters et al. BMC Infectious Diseases (2016) 16:622

- Rétrospectif, monocentrique
- IOA à SA (n = 65).
  - Prothèse (n = 34)
  - ostéosynthèses (n = 11)
- Chirurgie: lavage (n = 24), changement 1T (n = 3), 2T (n = 15),
- Antibiothérapie:
  - teicoplanine 6mg/kg/12h 5 fois puis 6mg/kg/24h, plus un compagnon
  - Objectif: 15-25mg/l
- Succès à 1 ans: 60%

RESEARCH ARTICLE Open Access

Teicoplanin-based antimicrobial therapy in *Staphylococcus aureus* bone and joint infection: tolerance, efficacy and experience with subcutaneous administration

Peeters et al. BMC Infectious Diseases (2016) 16:622



Sensibilité aux céphalosporines anti-SARM

Activité *in vitro* de la ceftaroline et du ceftobiprole sur des souches de *S. aureus* (n = 100) et SCN (n = 100) impliquées dans des IOA sur prothèse (CHU de Caen, 2011-2014)

Espèces (nombre d'isolats) Antibiotiques	MIC (mg/l)			% of susceptible isolates
	MIC_{50}	MIC_{90}	Range	
S. aureus				
All isolates (n = 100)				
Ceftaroline	0.25	0.5	0.06-1	100
Ceftobiprole	0.5	1	0.125-4	98
MSSA (n = 81)				
Ceftaroline	0.25	0.5	0.06-1	100
Ceftobiprole	0.5	1	0.125-4	99
MRSA (n = 19)				
Ceftaroline	0.5	1	0.25-1	100
Ceftobiprole	1	2	1-4	95
CoNS				
All isolates (n = 100)				
Ceftaroline	0.06	0.25	≤0.03-1	100
Ceftobiprole	0.25	1	≤0.03-2	100
MS-CoNS (n = 73)				
Ceftaroline	0.06	0.25	≤0.03-1	100
Ceftobiprole	0.125	0.5	≤0.03-1	100
MR-CoNS (n = 27)				
Ceftaroline	0.25	0.5	0.06-1	100
Ceftobiprole	0.5	1	0.125-2	100

Manlandain et al., RICAI 2015

Staphylocoques et résistance aux oxazolidinones

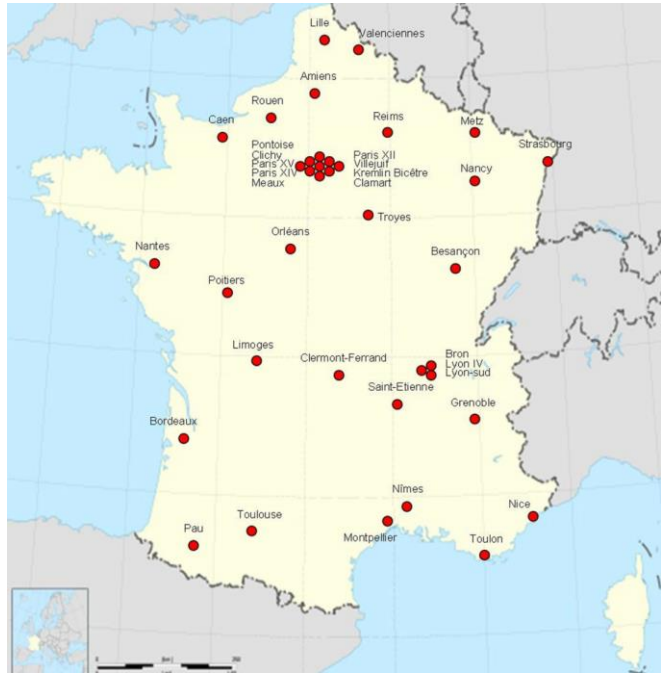
Résistance : incidence

International Journal of Antimicrobial Agents 46 (2015) 622–630

Susceptibility trends including emergence of linezolid resistance among coagulase-negative staphylococci and meticillin-resistant *Staphylococcus aureus* from invasive infections☆

Jean-Winoc Decousser[a,b,*,1], Marine Desroches[a,b,1], Nadège Bourgeois-Nicolaos[a,c], Julien Potier[a], François Jehl[d], Gérard Lina[e,f], Vincent Cattoir[g], François Vandenesh[e,f], Florence Doucet-Populaire[a,c], on behalf of the Microbs Study Group[2]

- Octobre 2011 – Février 2012
- 367 SARM, 695 SCN responsables d'infections invasives (29% d'IOA)
- 37 centres en France



Staphylocoques et résistance aux oxazolidinones

Résistance : incidence

International Journal of Antimicrobial Agents 46 (2015) 622–630

Susceptibility trends including emergence of linezolid resistance among coagulase-negative staphylococci and meticillin-resistant *Staphylococcus aureus* from invasive infections☆

Jean-Winoc Decousser[a,b,*,1], Marine Desroches[a,b,1], Nadège Bourgeois-Nicolaos[a,c], Julien Potier[a], François Jehl[d], Gérard Lina[e,f], Vincent Cattoir[g], François Vandenesch[e,f], Florence Doucet-Populaire[a,c], on behalf of the Microbs Study Group[2]

Table 1
Minimum inhibitory concentrations (MICs) and percent susceptibility (%S) of meticillin-resistant *Staphylococcus aureus* (MRSA) according to the clinical origin of the isolates.

Origin/antimicrobial agent	MIC (mg/L)			%S[a,b]
	MIC_{50}	MIC_{90}	Range	
All origins (*N* = 367)				
Vancomycin	1	1	0.5–2	100
Daptomycin	0.5	0.5	0.25–1	100
Teicoplanin	0.5	1	≤0.06–4	99.5
Linezolid	2	4	0.06–4	100
Gentamicin	0.5	2	≤0.25 to >2	86.4
Levofloxacin	8	8	0.06 to >8	18
Fusidic acid	0.25	2	≤0.03 to >2	86.4
Rifampicin	0.015	0.015	≤0.008 to >4	93.5
Tigecycline	0.12	0.12	≤0.03–0.5	100
Bone and joint infection (*N* = 136)				
Vancomycin	1	1	0.5–2	100
Daptomycin	0.5	0.5	0.25–1	100
Teicoplanin	0.5	1	0.12–4	99.3
Linezolid	2	4	0.06–4	100
Gentamicin	0.5	2	≤0.25 to >2	86.8
Levofloxacin	8	8	0.06 to >8	19.1
Fusidic acid	0.25	2	≤0.03 to >2	86.8
Rifampicin	0.015	0.06	<0.008 to >4	91.2
Tigecycline	0.12	0.12	<0.03–0.5	100

Staphylocoques et résistance aux oxazolidinones

Résistance : incidence

International Journal of Antimicrobial Agents 46 (2015) 622–630

Susceptibility trends including emergence of linezolid resistance among coagulase-negative staphylococci and meticillin-resistant *Staphylococcus aureus* from invasive infections☆

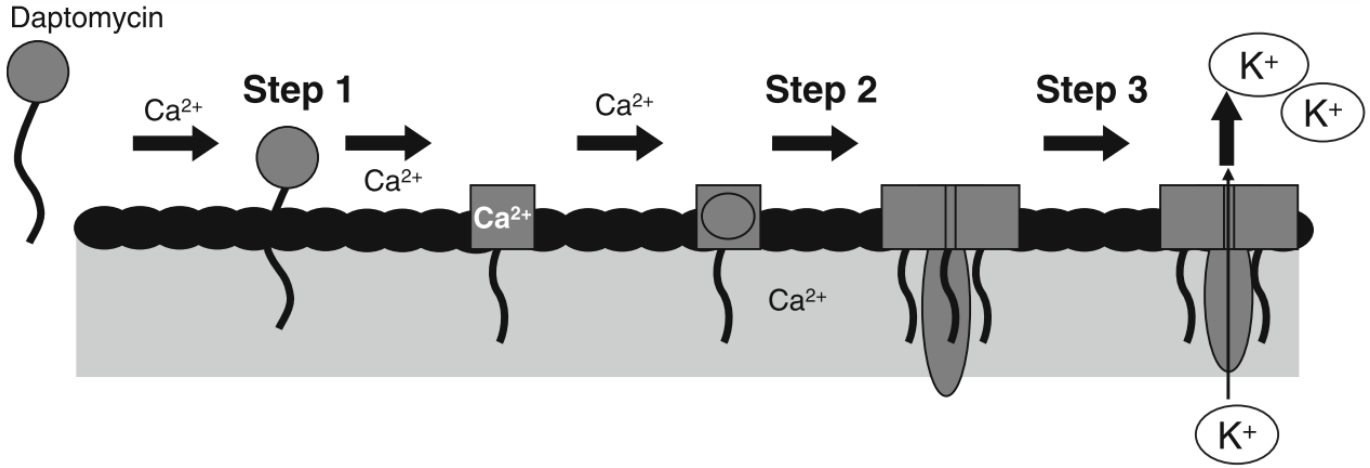
Jean-Winoc Decousser[a,b,*,1], Marine Desroches[a,b,1], Nadège Bourgeois-Nicolaos[a,c], Julien Potier[a], François Jehl[d], Gérard Lina[e,f], Vincent Cattoir[g], François Vandenesh[e,f], Florence Doucet-Populaire[a,c], on behalf of the Microbs Study Group[2]

Table 4
Minimum inhibitory concentrations (MICs) and percent susceptibility (%S) of coagulase-negative staphylococci (CoNS) according to the clinical origin of the isolates.

Origin/antimicrobial agent	MIC (mg/L)			%S[a,b]
	MIC_{50}	MIC_{90}	Range	
All origins ($N = 695$)				
Meticillin	N/D	N/D	N/D	28.9
Vancomycin	2	2	0.5–4	100
Daptomycin	0.5	1	0.06–2	99.7
Teicoplanin	4	8	0.12–64	77
Linezolid	1	2	0.12 to >32	98.6
Gentamicin	2	2	≤0.25 to >2	47.2
Levofloxacin	4	8	0.06 to >8	42.4
Fusidic acid	2	2	≤0.03 to >2	45.6
Rifampicin	0.015	4	≤0.008 to >4	82.6
Tigecycline	0.12	0.25	≤0.03 to >2	99.6
Bone and joint infection ($N = 172$)				
Meticillin	N/D	N/D	N/D	46.7 ($P < 0.05$)
Vancomycin	2	2	0.5–4	100
Daptomycin	0.5	1	0.12–2	99.4
Teicoplanin	2	8	0.12–16	85.6 ($P < 0.05$)
Linezolid	1	2	0.25 to >32	99.4
Gentamicin	0.25	2	≤0.25 to >2	62.9 ($P < 0.05$)
Levofloxacin	0.5	8	0.12 to >8	57.5($P < 0.05$)
Fusidic acid	0.5	2	≤0.03 to >2	55.1($P < 0.05$)
Rifampicin	0.015	4	≤0.008 to >4	84.4
Tigecycline	0.06	0.25	≤0.03–0.5	100

Staphylocoques et résistance à la daptomycine

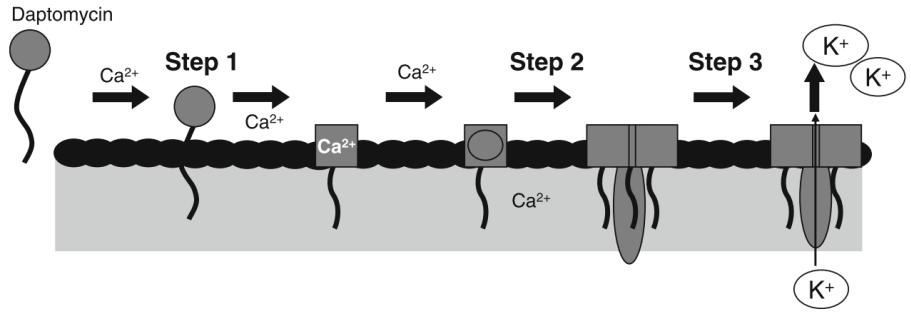
Mécanisme d'action

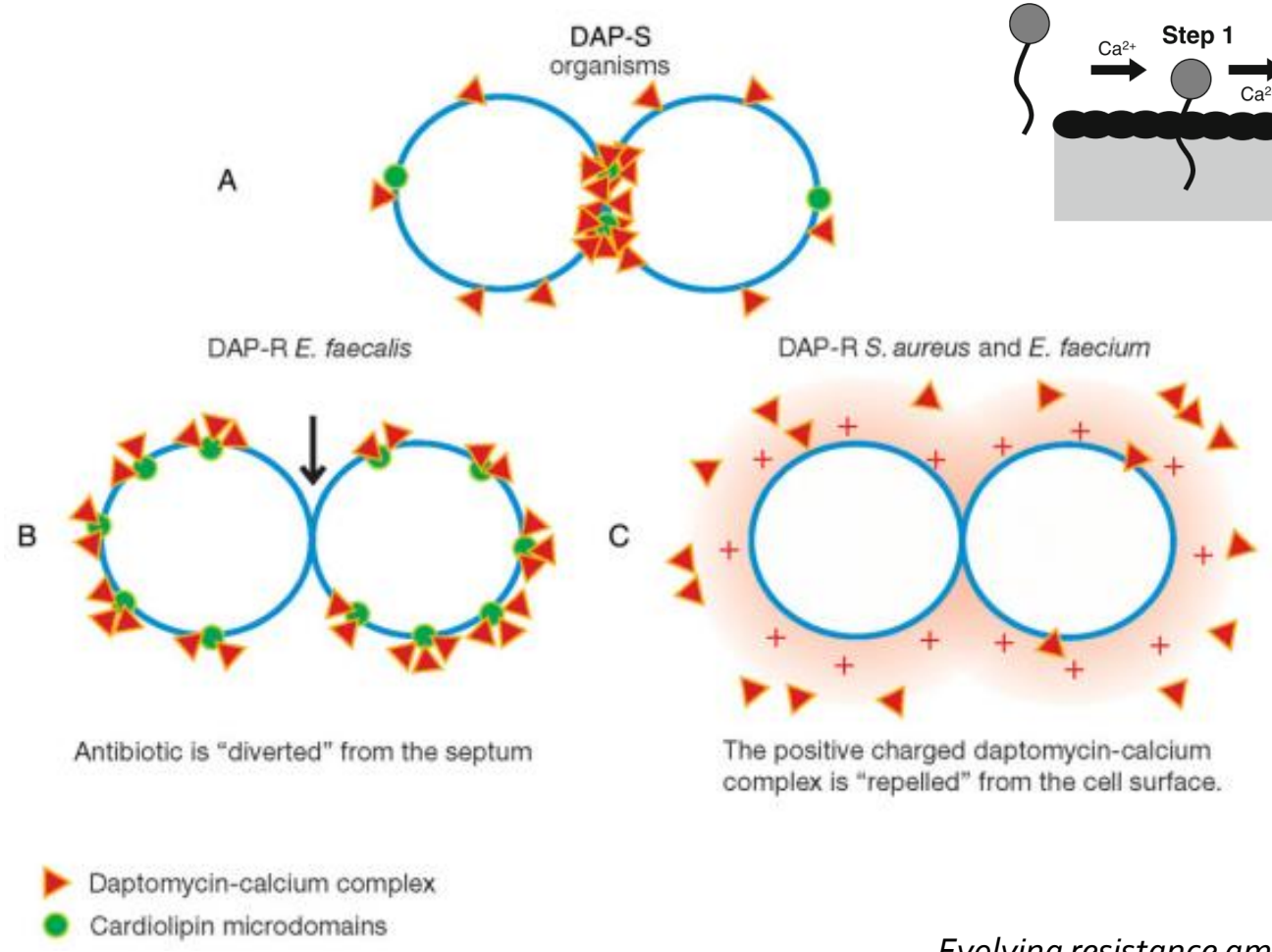


Daptomycin ; Tedesco et al; Pharmacotherapy 2004

Staphylocoques et résistance à la daptomycine

Résistance : mécanismes



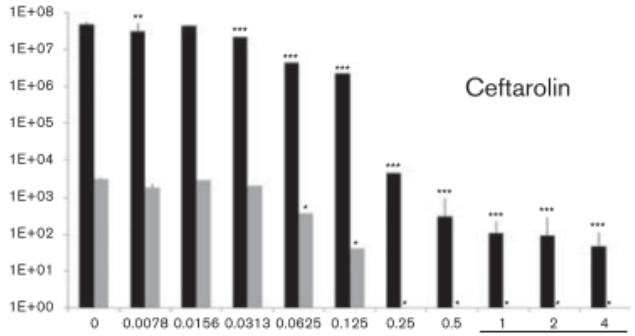


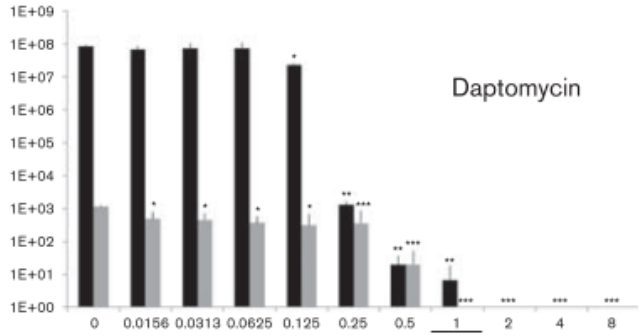
Evolving resistance among Gram + pathogens ; Munita et al; CID 2015

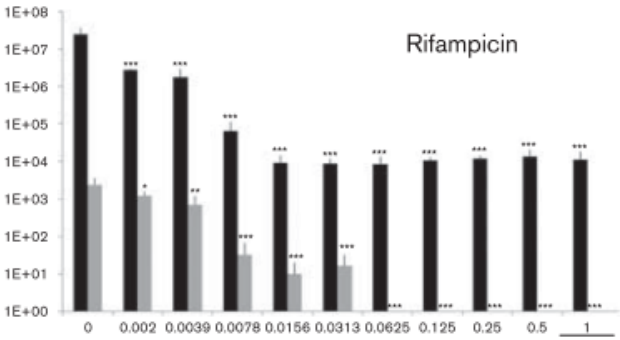
Journal of Medical Microbiology (2015)

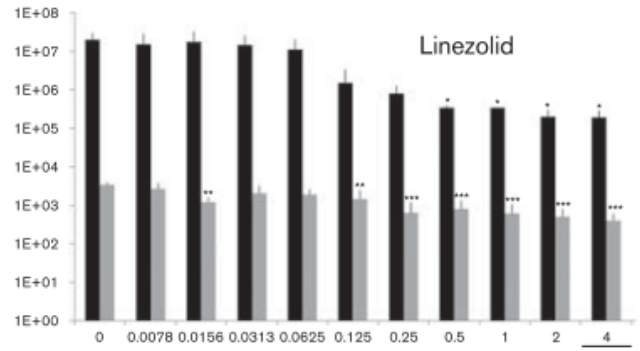
Effects of antibiotics on biofilm and unattached cells of a clinical *Staphylococcus aureus* isolate from bone and joint infection

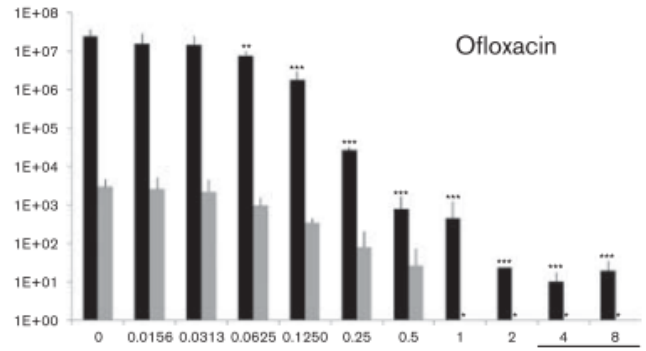
Claire Marquès,[1,2] Jason Tasse,[3,4] Anne Pracros,[2] Valérie Collin,[1] Christine Franceschi,[1] Frédéric Laurent,[3,4] Sonia Chatellier[1] and Christiane Forestier[2]







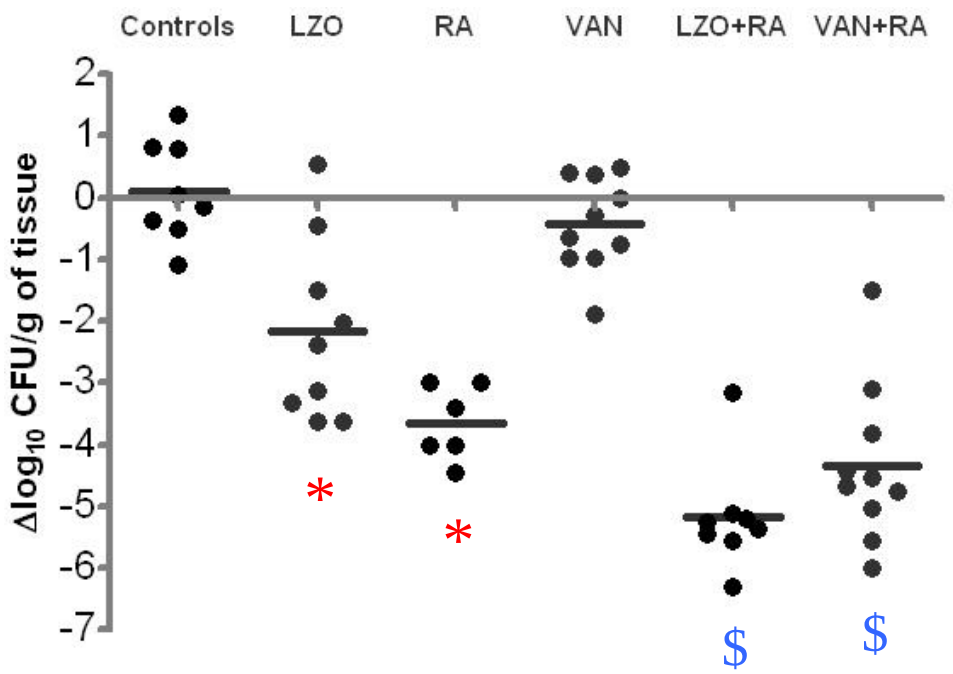




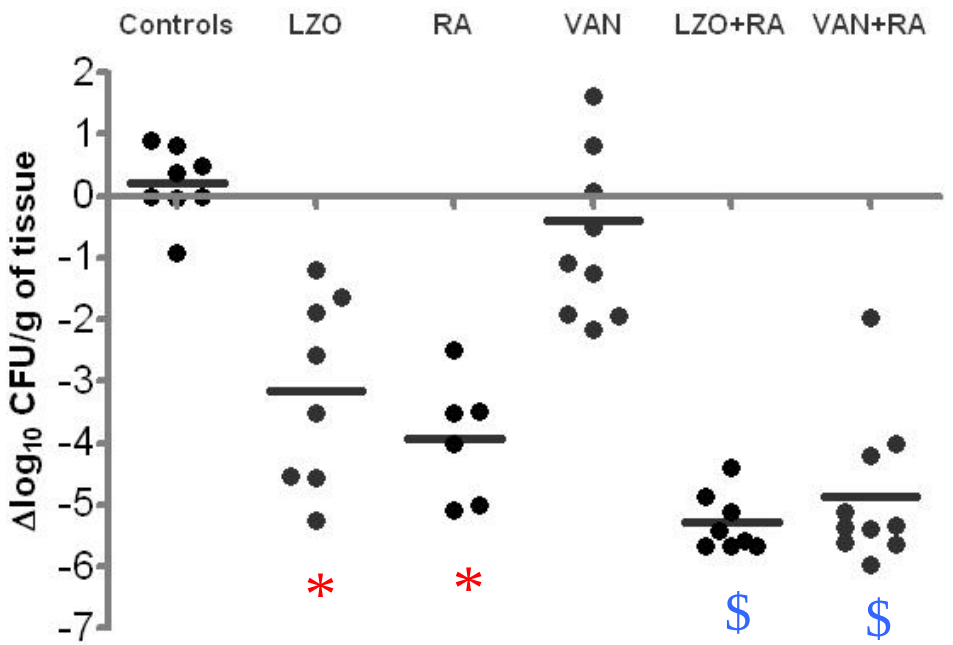
Associations : linézolide-rifampicine vs vancomycine-rifampicine

Associations : linézolide-rifampicine vs vancomycine-rifampicine

Moelle osseuse



Os



Associations : linézolide-rifampicine vs vancomycine-rifampicine