

Best of 2010-2011 : les infections ostéo-articulaires

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Études expérimentales: quoi de neuf ?

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

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Title: Daptomycin, Fosfomycin, or Both for Treatment of Methicillin-Resistant

Staphylococcus aureus Osteomyelitis in an Experimental Rat Model

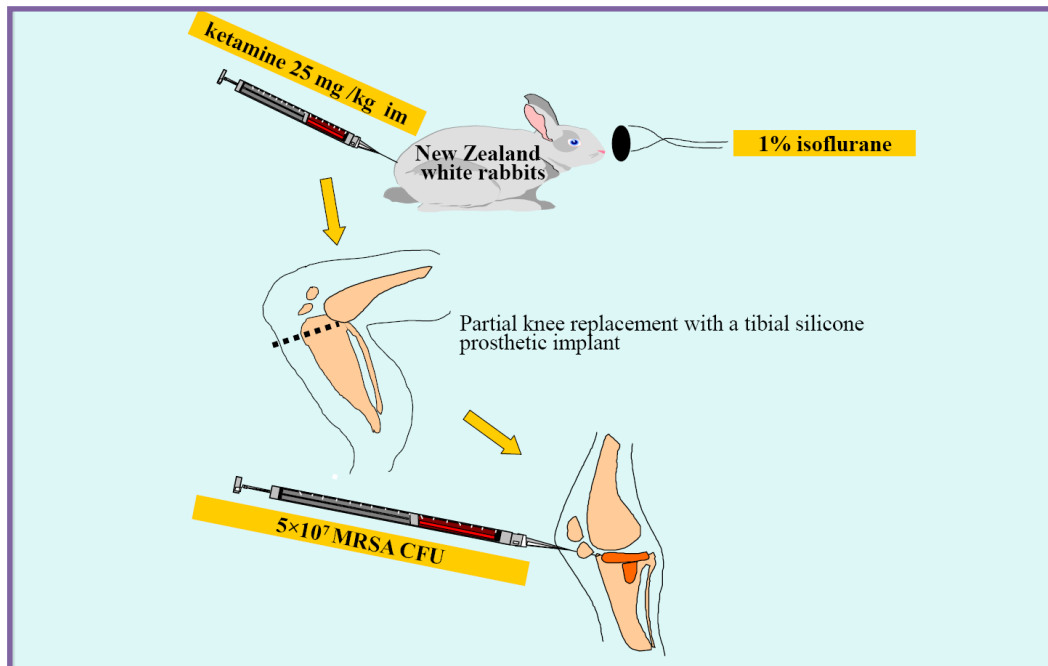
Running title: Daptomycin and fosfomycin in experimental MRSA osteomyelitis

W. Poeppl,¹ S. Tobudic,¹ T. Lingscheid,¹ R. Plasenzotti,² N. Kozakowski,³ H. Lagler,¹ A.

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J1 : Inoculation intra-articulaire de SARM (5×10^7) cfu

J7 : 4 bras de traitement

- DAP 22 mg/kg/j IV (équivalent à 8 mg/kg/j chez l'homme)
- VAN 60 mg/kg/j en 2 injections IM
- DAP + RIF 10 mg/kg/j en 2 injections IM
- VAN + RIF 10 mg/kg/j en 2 injections IM

Traitement pendant 7 jours

J17 : sacrifice des animaux, prélèvements de tibia mis en culture

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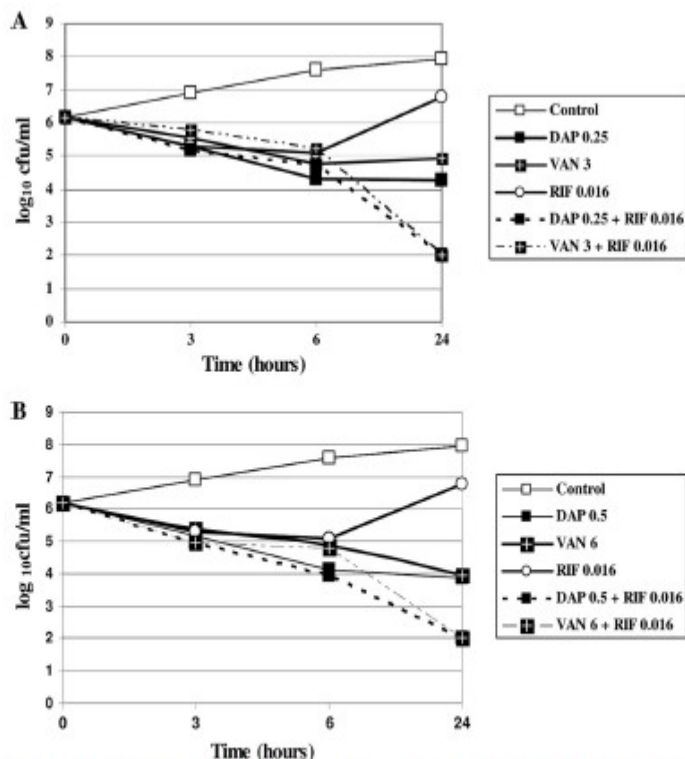


FIG. 1. *In vitro* killing curves for methicillin-resistant *Staphylococcus aureus* strain S271, using different antibacterial agents and combinations: 2x MIC (A) or 4x MIC, except rifampin (2x MIC) (B). DAP, daptomycin; VAN, vancomycin; RIF, rifampin.

TABLE 1. Effects of antibiotic treatment on experimental MRSA prosthetic knee infection in rabbits

Treatment ^a	No. of rabbits with sterile bone/total	Log ₁₀ CFU/g of bone (mean ± SD)	No. of rabbits with daptomycin mutant strain/no. infected
None	0/9	5.93 ± 1.15	2/9
Daptomycin	2/12	4.23 ± 1.44 ^b	6/10 ^c
Vancomycin	0/12	4.63 ± 1.08 ^b	3/12
Daptomycin + rifampin	11/11	1.47 ± 0.04 ^{d,e}	0/2 ^d
Vancomycin + rifampin	6/8	1.50 ± 0.12 ^d	0/2 ^d

^a For 7 days, rabbits were injected with daptomycin (22 mg/kg i.v. o.d.) or vancomycin (60 mg/kg i.m. b.i.d.) alone or combined with rifampin (10 mg/kg i.m. b.i.d.).

^b Significantly different from results with untreated controls ($P < 0.01$).

^c Other rabbits had sterile bones.

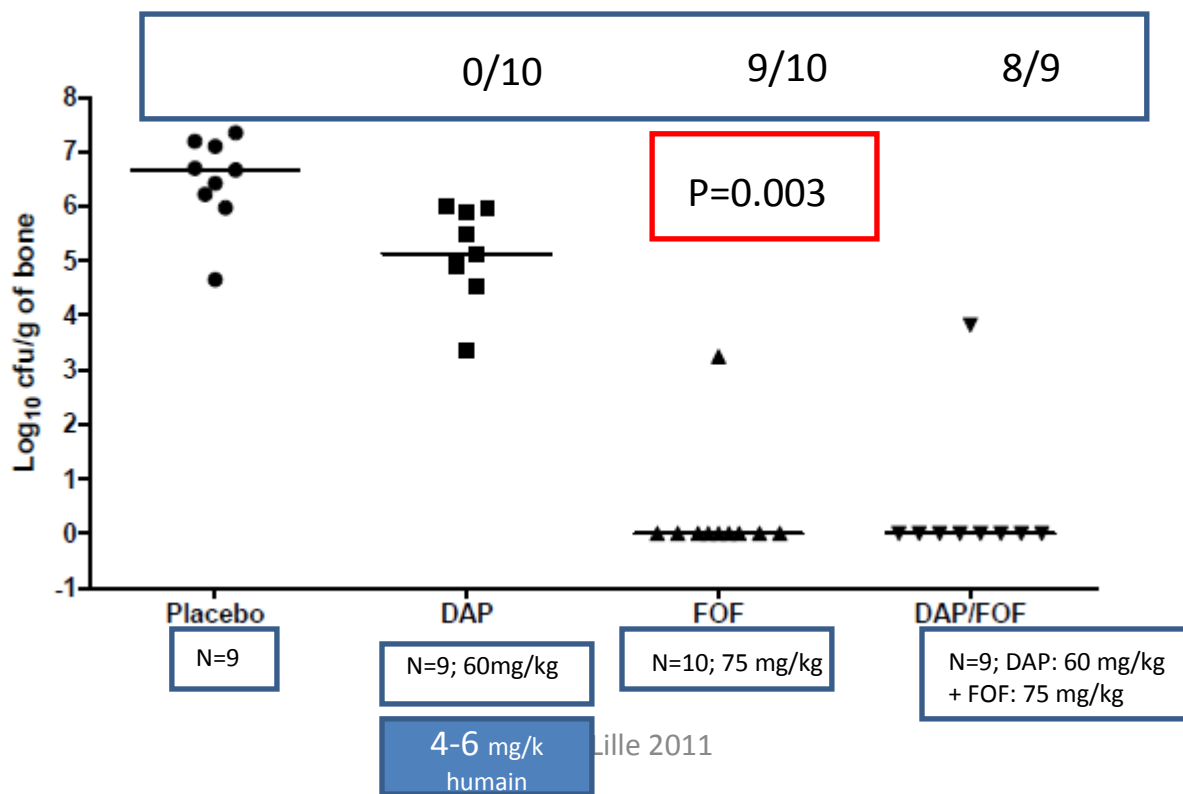
^d Significantly different from results with monotherapy ($P < 0.01$).

^e This value, the limit of detection, was accorded to sterile bone (see Materials and Methods), explaining the absence of a value in the last column.

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Running title: Daptomycin and fosfomycin in experimental MRSA osteomyelitis

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Quid des études cliniques ?

Outcome and Predictors of Treatment Failure in Total Hip/Knee Prosthetic Joint Infections Due to *Staphylococcus aureus*

Eric Senneville, Donatienne Joulie, Laurence Legout, Michel Valette, Hervé Dezèque, Eric Beltrand, Bernadette Roselé, Thibaud d'Escrivan, Caroline Loïez, Michèle Caillaux, Yazdan Yazdanpanah, Carlos Maynou, and Henri Migaud

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334 • CID 2011:53 (15 August)

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- 98 patients inclus dans l'étude porteur d'un IPOA à SA
- Définition de l'IPOA et prise en charge selon l'algorithme de Zimmerli et al. et follow-up > 3 ans.
- Comorbidités:
 - diabète (n=32; 32.6%), corticothérapie (n=11; 11.2%), cancer (n=5; 5.1%), bactériémie concomittante (n=18; 18.4%)
 - Délai: 1/3 IPOA précoce; 2/3 IPOA retardée ou tardive.
 - MSSA était observé dans 81 cas et MRSA dans 17 cas. Dans 27 cas l'infection à staphylocoque doré était associée à un autre germe, SCN (n=14) ou autres (n=13).

Table 1. Baseline Characteristics of 98 Patients With Total Hip or Knee Prosthesis Infection Due to *Staphylococcus aureus* According to Outcome

Characteristic	Remission (n = 77)	Failure (n = 21)	P
Age, mean years ± SD	66.3 ± 14.7	70.0 ± 13.4	.29
Male sex	32 (41.6)	11 (52.4)	.38
Body mass index, mean ± SD	28.4 ± 5.7	28.3 ± 7.9	.95
Diabetes mellitus	24 (31.2)	8 (38.1)	.54
Use of steroid therapy	10 (12.9)	1 (4.8)	.29
Ongoing cancer treatment	4 (5.2)	1 (4.8)	.63
Concomitant <i>Staphylococcus aureus</i> bacteremia	15 (19.5)	3 (14.3)	.82
Acute infection (<4 weeks duration)	14 (19.7)	6 (28.5)	.36
Time to infection			
Median months ± SD	74.1 ± 83.4	63.3 ± 91.5	.20
Early (≤3 months)	26 (33.8)	11 (52.4)	.12
Delayed (>3–24 months)	17 (22.1)	4 (19.1)	.76
Late (≥24 months)	34 (44.1)	6 (28.5)	.20
No. of operations since implantation, mean ± SD	1.10 ± 1.95	1.71 ± 2.88	.94
Fever (temperature, >38°C) at admission	10 (12.9)	3 (14.3)	.87
Presence of sinus tract	27 (35.1)	11 (52.4)	.14
White blood cell count, mean ×10 ⁹ cells/L ± SD	9276.7 ± 3647.7	8950.5 ± 3452.1	.71
CRP level, mean mg/L ± SD			
At first presentation	98.5 ± 87.3	81.0 ± 66.2	.39
Prior to reimplantation	18.8 ± 5.9	24.1 ± 37.1	.69
ASA score >2 ^a	23 (29.9)	13 (61.9)	.02
Methicillin-susceptible <i>S. aureus</i>	65 (84.4)	16 (76.2)	.38
Methicillin-resistant <i>S. aureus</i>	12 (15.6)	5 (23.8)	.38
Polymicrobial infection	18 (25.4)	9 (42.8)	.08
Coagulase-negative staphylococci	9 (11.7)	5 (23.8)	.16
Other bacteria ^b	9 (11.7)	4 (19.1)	.42

NOTE. Data are no. (%) of patients unless otherwise indicated. ASA, American Society of Anesthesiologists; CRP, C-reactive protein; SD, standard deviation.

^a Chronic diseases of the heart (n = 2), liver (n = 17), or kidney (n = 4), and respiratory insufficiency (n = 6) mostly related to chronic obstructive pulmonary disease.

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^b *Streptococcus viridans* (n = 5), *Enterococcus faecalis* (n = 2), *Escherichia coli* (n = 3), *Pseudomonas aeruginosa* (n = 2), *Propionibacterium acnes* (n = 1).

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

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

NOTE. Data are no. (%) of patients unless otherwise indicated. SD, standard deviation.

^a Including 26 patients with 2-stage replacement and 8 with arthrodesis.

^b At least 1 antibiotic agent active against intraoperative pathogen(s).

Table 3. Characteristics of Treatment and Outcome of 98 Patients With Total Hip or Knee Prosthesis Infection Due to *Staphylococcus aureus*

Variable	Rifampin treatment (<i>n</i> = 68)		No Rifampin treatment (<i>n</i> = 30)		<i>P</i>
	Fluoroquinolone combinations (<i>n</i> = 39)	Other rifampin combinations (<i>n</i> = 29)	Linezolid monotherapy (<i>n</i> = 11)	Other treatment (<i>n</i> = 19)	
Debridement-retention (<i>n</i> = 41)	15/16 (93.8)	10/15 (66.7)	3/3 (100)	4/7 (57.1)	.11
One-stage replacement (<i>n</i> = 14)	6/6 (100)	5/5 (100)	1/1 (100)	2/2 (100)	...
Two-stage replacement (<i>n</i> = 26)	12/12 (100)	6/9 (66.7)	4/4 (100)	0/1 (0)	.01
Arthroplastic resection (<i>n</i> = 9)	1/1 (100)	0	1/3 (33.3)	2/5 (40)	...
Arthrodesis (<i>n</i> = 8)	3/4 (75)	0	0	2/4 (50)	...
Total	37/39 (94.8)	21/29 (72.4)	9/11 (81.8)	10/19 (52.6)	.002

NOTE. Data are no. (%) of patients with remission.

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En analyse multivariée:

Variable / rémission	OR (95%, IC)	p
Score ASA > 2	6.87 (1.45-32.45)	0.04
RIF-FQ	0.4 (0.17-0.97)	0.01

• Confirmation de l'Intérêt du traitement à base de RIF démontré dans d'autres études cliniques et expérimentales

• MRSA associé à échec ?

- Dans l'étude : MRSA (29.7%) vs MSSA (19.7%) (Taille ?)
- Segado et al. : Vanco oui pas vrai si RIF + autre ATB

Et quoi d'autre ?

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Serial measurement of the C-reactive protein is a poor predictor of treatment outcome in prosthetic joint infection

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Periprosthetic joint infection following *Staphylococcus aureus* bacteremia

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