# Monothérapie dans les infections ostéo-articulaires staphylococciques : une hérésie ?

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CENTRES DE RÉFÉRENCE POUR LES INFECTIONS OSTÉO-ARTICULAIRES COMPLEXES DU GRAND OUEST
CRIOGO

# Pourquoi la bithérapie

# Emergence de Résistance FQ/RMP

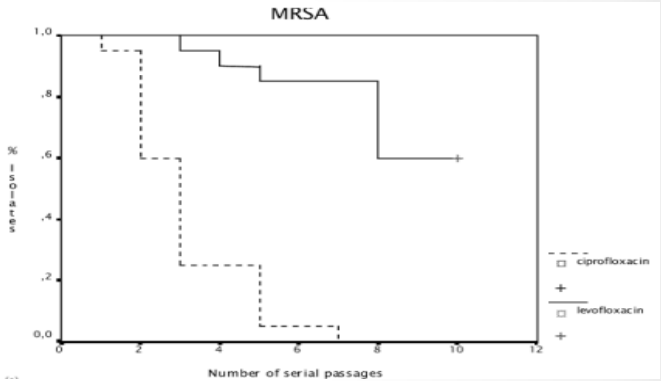
Emergence de résistance défini :
Risque d'émergence R QI > 10 ou AUIC > 100 [1]

Fluoroquinolones

- Facteur de risque indépendant d'acquisition SARM [2]
- Sélection de résistance *S. aureus* quand sous dosé, surtout sur cipro +++ moins sur la levofloxacine [3,4]

Rifampicine:

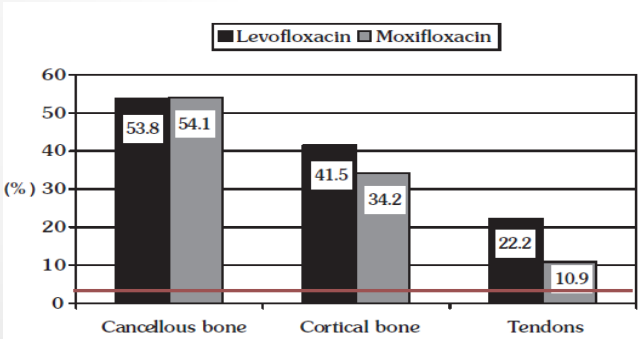
- Sélection rapide de résistance monothérapie de Rifampicine [5,6]
- Chez l'animal : 63% de R monoT rifam [7]




[1] Rapport spilf 2015
[2] Scaefler *et al.*, 1989,
[2] Shalit *et al.*, 1989
[3] Limoncu *et al.*, 2003;
[3] Blumberg *et al.*, 1991
[4] Wilson *et al.*, 2014
[5] O'Reilly *et al.*, 1992
[6] Zimmerli *et al.*, 1994
[7] Goetz *et al.*, 2022

# Nouvelles FQ, nouvel état d'esprit

- Moins de Résistance pour moxiflo même à dose suboptimale [1, 2, 3, 4]
- Moxiflo et levoflo: in vitro 18h > MPC90 [5], dans les PJI [6]




CMI90

FIGURE 1 - Penetration of levofloxacin and moxifloxacin in osteoarticular tissues of patients undergoing total hip arthroplasty.

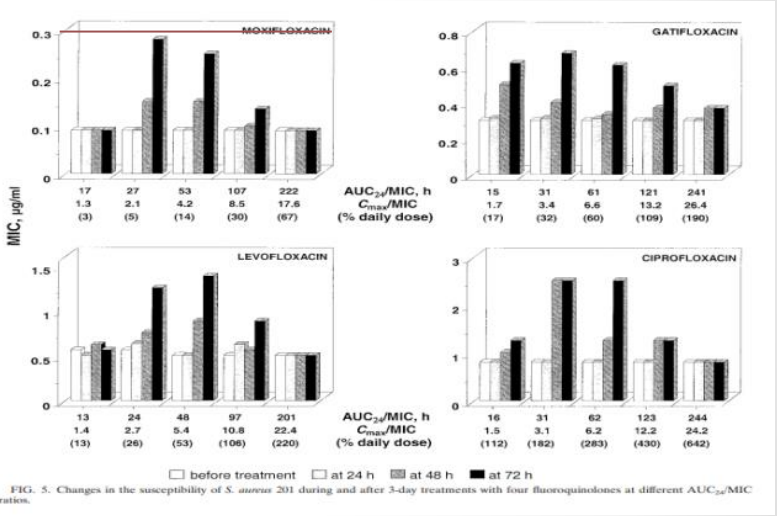



FIG. 5. Changes in the susceptibility of *S. aureus* 201 during and after 3-day treatments with four fluoroquinolones at different $AUC_{24}$/MIC ratios.

[1] Firsov *et al.*, 2003
[2] Lister *et al.*, 2001
[3] Pong *et al.*, 1999
[4] Bogdanovich *et al.*, 2005
[5] Metzler *et al.*, 2004
[6] Metallidis *et al.*, 2007

# *Staphylococcus aureus*: Pro biT

## Role of Rifampin for Treatment of Orthopedic Implant–Related Staphylococcal Infections

### A Randomized Controlled Trial

Werner Zimmerli, MD; Andreas F. Widmer, MD, MSc; Marianne Blatter, MD; R. Frei, MD;
Peter E. Ochsner, MD; for the Foreign-Body Infection (FBI) Study Group

- n=33
- Gpe rifam (75%) précoce vs (50%) gpe placebo
- 9 arrêts de l'essai ?
- Arrêté précoce : succès biT
- Emergence de résistance (5/6 des échecs)

Petit effectif avec 33%, perdus de vue
Infection précoce <2 mois…
Ciprofloxacine sur *S. aureus*
Émergence de résistance

**Table 3:** Details on the therapeutic outcome in 38 evaluable patients with chronic osteomyelitis treated with three quinolones.

| Osteomyelitis | Pefloxacin (n = 14) | Ofloxacin (n = 17) | Ciprofloxacin (n = 7) | Overall |
|---|---|---|---|---|
| Gram-positive pathogen | | | | |
| Number evaluated | 5 | 11 | 5 | 21 |
| Satisfactory response | 5 | 7 | 2 | 14 |
| Failure | 0 | 4 | 3 | 7 |
| *Enterobacteriaceae* | | | | |
| Number evaluated | 4 | 4 | 1 | 9 |
| Satisfactory response | 3 | 4 | 1 | 8 |
| Failure | 1 | 0 | 0 | 1 |
| *Pseudomonas aeruginosa* | | | | |
| Number evaluated | 5 | 2 | 1 | 8 |
| Satisfactory response | 4 | 2 | 1 | 7 |
| Failure | 1 | 0 | 0 | 1 |
| No foreign body | | | | |
| Number evaluated | 6 | 9 | 4 | 19 |
| Satisfactory response | 5 | 7 | 3 | 15 |
| Failure | 1 | 2 | 1 | 4 |
| Foreign body | | | | |
| Number evaluated | 8 | 8 | 3 | 19 |
| Satisfactory response | | | | |
| With surgery | 3 | 2 | 0 | 5 |
| Without surgery | 4 | 4 | 1 | 9 |
| Failure | 1 | 2 | 2 | 5 |

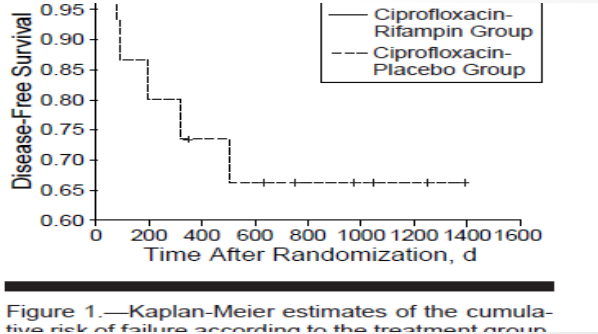
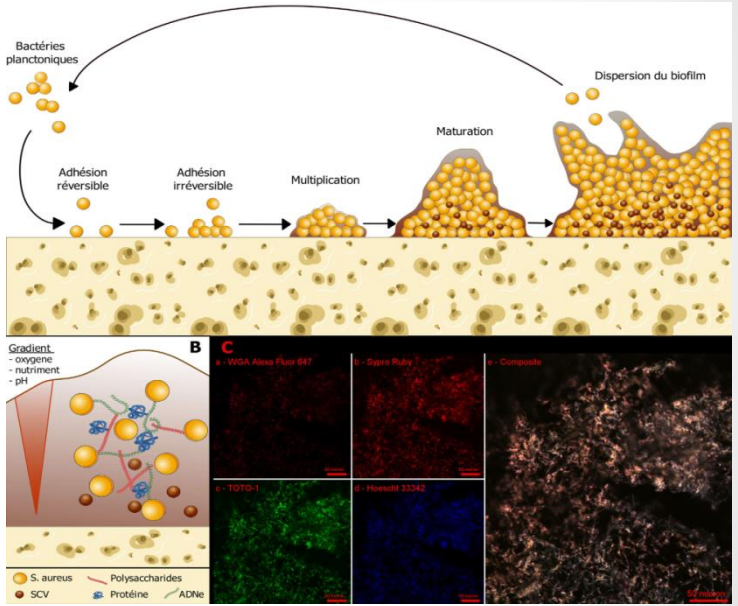



Figure 1.—Kaplan-Meier estimates of the cumulative risk of failure according to the treatment group

# Physiopathologie des IOA: biofilm

- Rôle barrière
- Échappement au système immunitaire= activité diminuée des neutrophiles activés (NET)
  - Dégradation partielle des Dnases staph
  - Neutralisation effet bactéricide par adhésines et effet inducteur du biofilm
- Diffusion ATB → tolérance
  - Absorption atb par PNAG
  - Inactivation atb par enz
  - Dormance
  - Effet inoculum
  - Induction gene R (pompe à efflux)
  - Diversité génétique
  - SCV
  - Persisters

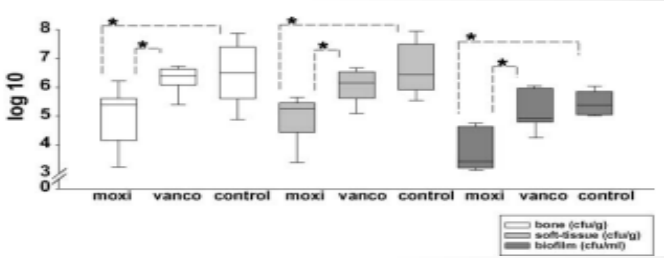



Jamard *et al.*, 2022
Mooney *et al.*, 2018
Lebeaux *et al.*, 2014

# Antibiotique antibiofilm

- Fluoroquinolones:
  - In vitro: SASM SARM [1]
  - In vivo: cage lapin SASM, moxiflo bonne pénétration biofilm [2]

- Rifampicine/doxycycline:
  - In vitro: doxy rifam dapto [3,4,5]
  - In vivo: restaure activité atbf daptomycine [6]



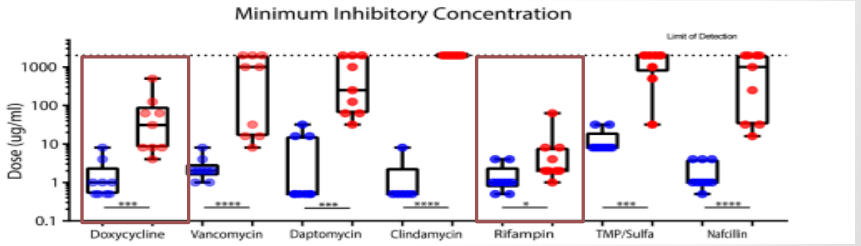



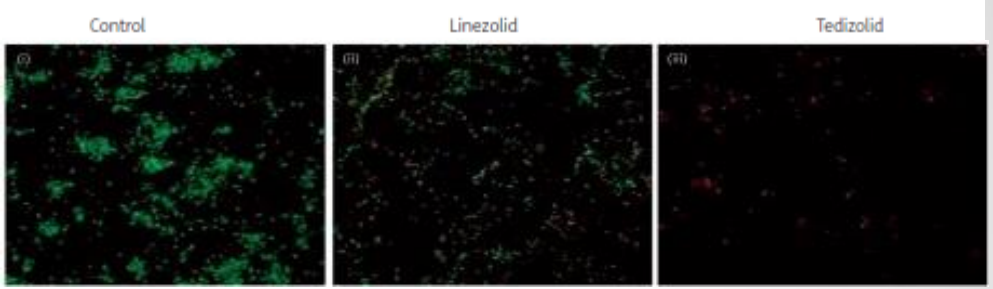

**Table 1.** Major characteristics of antibiotics active against staphylococcal biofilm

| Antibiotics | Inhibition of biofilm formation (adhesion) | Biofilm penetration | Bactericidal activity in biofilm |
|---|---|---|---|
| Vancomycin | + | ++[16,17] | +[16,17] |
| Linezolid | + | ++[24,29] | +[24] |
| Daptomycin | + | +++[15] | ++[21,24] |
| Rifampicin | + | +++[8,16,18] | ++[16,30] |
| Moxifloxacin | + | ++[31] | ++[21,31] |
| Rifampicin + daptomycin | + | +++[2,30] | +++[28,30] |
| Rifampicin + vancomycin | + | ++[16,18] | ++[16,27,32] |
| Rifampicin + linezolid | + | +++[16,29] | +++[27,32] |

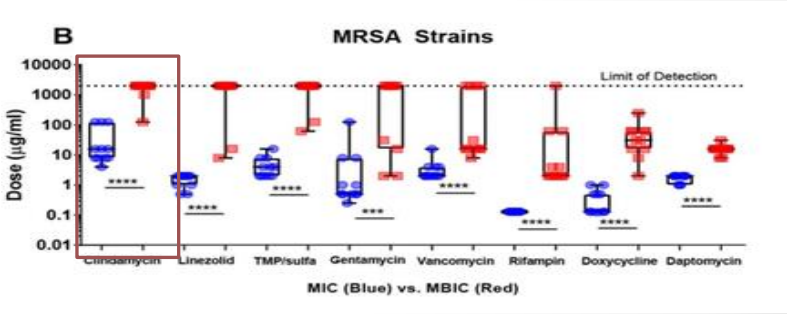
[1] Bauer et al., 2013
[2] Kaltéis *et al.*, 2006
[3] Mandell *et al.*, 2019
[4] Perez-Alba *et al.*, 2023
[5] Koch *et al.*, 2022
[6] Tasse *et al.*, 2016

# Antibiotique antibiofilm

- Linézolide:
  - In vitro: mauvaise [1] / bonne [2] activité biofilm, bonne activité anti adhérente, bonne activité intracellulaire [1]
  - In vivo: inhibe adhérence biofilm [3]




- Clindamycine :
  - In vitro: bonne activité anti adhérence [4,5] peu d'activité antibiofilm [6]




1 Abad *et al.*, 2019
2 Delpech *et al.*, 2018
3 Wu *et al.*, 2014

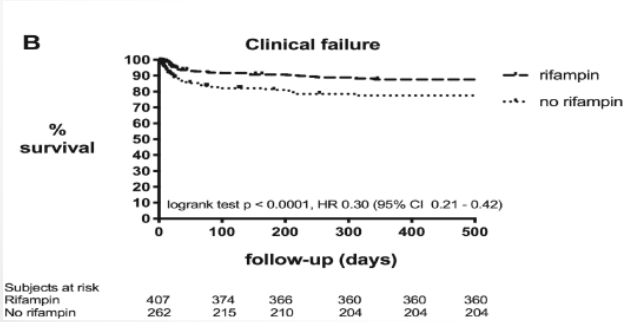
4 Tasse *et al.*, 2016
5 Schilcher *et al.*, 2016
6 Mandell *et al.*, 2019
7 Smith *et al.*, 2009

# *S. aureus* : Pro biT

## 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]

- n=669 PJI.
- Rifam :
  - succès (32,2% vs 54,2%)
  - échec : Rifam (5 jours post DAIR)




| | Rifampin (n = 407) | No rifampin (n = 262) | *P* value |
|---|---|---|---|
| Baseline characteristics | | | |
| Male sex | 43.5% (177/407) | 43.9% (115/262) | .92 |
| Age >80 years | 23.4% (95/406) | 18.3% (47/257) | .12 |
| BMI >30 kg/m$^2$ | 48.1 % (177/368) | 55.6% (138/248) | .07 |
| Characteristics implant | | | |
| Primary | 83% (338/407) | 80.5% (206/256) | .40 |
| Cemented | 77.3% (310/401) | 64.7% (152/235) | .001 |
| Fracture as indication prosthesis | 15.5% (63/407) | 16.5% (42/254) | .72 |
| Late acute PJI | 3.2% (13/406) | 15.4% (39/253) | <.001 |
| Identified micro-organism | | | |
| *Staphylococcus aureus* | 61.9% (252/407) | 56.9% (149/262) | .19 |
| Polymicrobial | 37.8% (154/407) | 37.8% (99/262) | .98 |
| Surgical treatment | | | |
| Exchange modular components | 45.6% (182/399) | 45.2% (104/230) | .92 |
| DAIR >4 wks after surgery[a] | 18.6% (73/393) | 19.6% (42/214) | .75 |

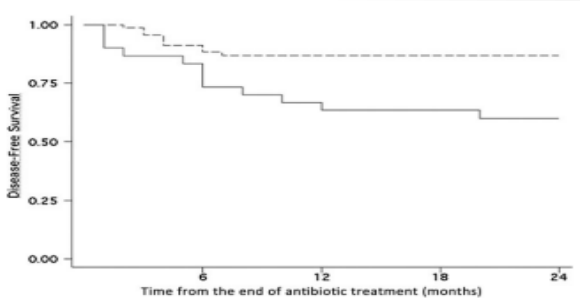
# *S. aureus*: Pro biT

Lora-Tamayo J, *et al.*, 2012: rétrospective multicentrique
345 PJI - 45% échecs (90 jours)
DAIR: rifam effet protecteur

Tornero *et al.*, 2014
160 PJI précoce (25 > 30 jours)
Échecs : 27% cirrhotique + crp
monoT *p*=0,067

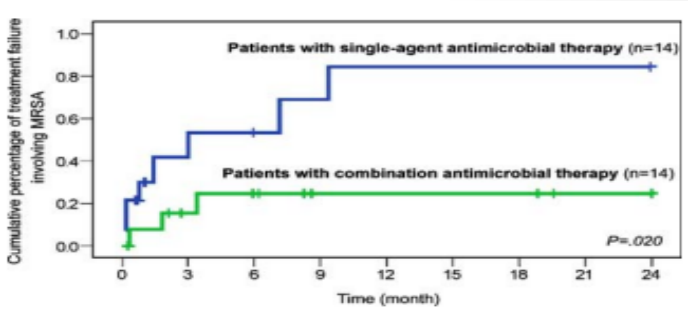
Senneville E, *et al.*, 2011
98 PJI ; rifam = succès
NS sur SARM ou monoT

Ferry *et al.*, 2010
52 dont 23 PJI et 29 OS SARM
50% monoT bactrim, vanco, linézolide
Échecs: rétention implant, monoT




RMP + FQ

autres



# Pourquoi pas la monothérapie

# *S. aureus*: Pro monoT sur matériel

Rifampin combination therapy in staphylococcal prosthetic joint infections: a randomized controlled trial

Øystein Espeland Karlsen[1,2*], Pål Borgen[3], Bjørn Bragnes[4], Wender Figved[5], Bjarne Grøgaard[1], Jonas Rydinge[1], Lars Sandberg[6], Finnur Snorrason[1], Helge Wangen[7], Eivind Witsøe[8] and Marianne Westberg[1]

- n=48 PJI infection aigue
- Cloxa + vanco proba puis
  - Méti S :gpe rifam (J1) + cloxa IV 2 semaines puis relai oral cloxa + rifam 4 semaines
  - Meti R vanco + rifam 6 sm
- Pas de différence pour les échecs entre les 2 gpes
- Peu de résistance

Atb à débattre cloxa PO et vanco …
Durée à débattre 6 semaines..
Petit effectif

**Table 1** Baseline characteristics of the 48 patients

| Characteristics | Rifampin group (*n* = 23) | Monotherapy group (*n* = 25) | Total (*n* = 48) |
|---|---|---|---|
| Age, year, median (range) | 70 (37–92) | 66 (39–84) | 68.5 (37–92) |
| Sex, male (%) | 15 (65) | 17 (68) | 32 (67) |
| ASA scores 1–2, no (%) | 16 (70) | 21 (84) | 37 (77) |
| BMI, mean (SD) | 30.1 (1.3) | 27 (1.0) | 28.4 (0.8) |
| Diabetes mellitus | 3 | 3 | 6 |
| Immunosuppressive medication | 2 | 2 | 4 |
| Smoking | 3 | 4 | 7 |
| Time from index surgery to revision, median, days (range) | 19 (7–912) | 17 (8–122) | 18 (7–912) |
| Hip prosthesis | | | |
| Primary hip prosthesis | 17 | 14 | 31 |
| Revision hip prostehesis | 3 | 5 | 8 |
| Knee prosthesis | | | |
| Primary knee prosthesis | 3 | 6 | 9 |
| CRP pre surgery, mean (SD) | 135 (21.1) | 167 (26.4) | 151 (16.9) |
| Creatinin pre surgery, mean (SD) | 78 (5.7) | 79 (4.4) | 79 (3.5) |
| Type of prosthesis[a] | | | |
| Cemented prosthesis | 14 | 16 | 30 |
| Non cemented | 4 | 5 | 9 |
| Reverse hybrid | 4 | 4 | 8 |

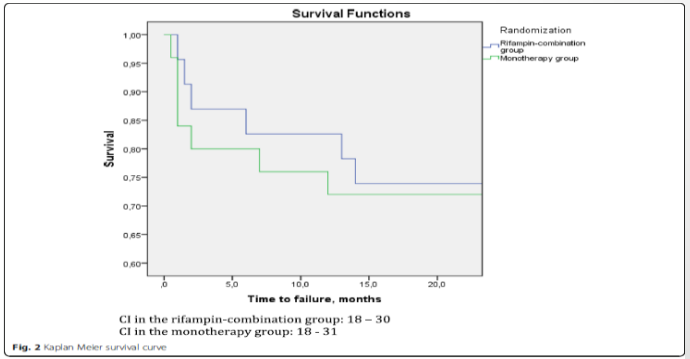



**Fig. 2** Kaplan Meier survival curve

# *S. aureus*: Pro monoT

**Importance of selection and duration of antibiotic regimen in prosthetic joint infections treated with debridement and implant retention**

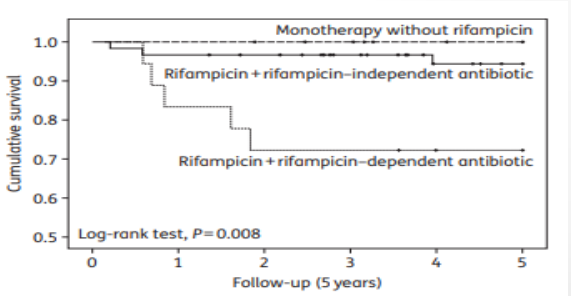
Eduard Tornero[1]*, Laura Morata[2], Juan C. Martínez-Pastor[1], Silvia Angulo[1], Andreu Combalia[1], Guillem Bori[1], Sebastián García-Ramiro[1], Jordi Bosch[3], Josep Mensa[2] and Alex Soriano[2]

- n=143 PJI aigues – DAIR
- Échecs 11,8%
- 11 monothérapies – 0 échecs
- FdR : bithérapie avec atb interagissant avec la rifam → clindamycine (mais 300 mg), bactrim, linézolide)

Attention aux interactions

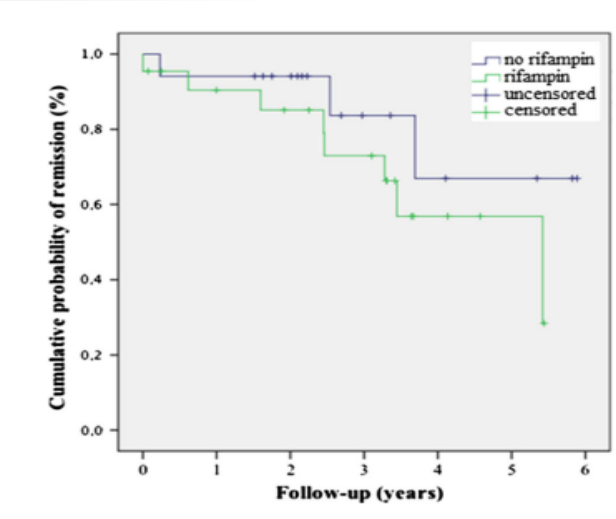
**Table 1.** Outcome (failure or relapse) of PJIs due to Gram-positive microorganisms according to the pattern of susceptibility and antibiotic treatment received

| | Number (%) of patients, remission (*N*=79) | Number (%) of patients, failure (*N*=10) | *P* | | Number (%) of patients, relapse (*N*=4) | *P* | |
|---|---|---|---|---|---|---|---|
| Type of antibiotic treatment received | | | | | | | |
| levofloxacin + rifampicin | 49 (62.0) | 4 (40.0) | 0.305 | | 1 (25.0) | 0.299 | |
| amoxicillin + rifampicin | 6 (7.6) | 1 (10.0) | 0.579 | | 0 (0) | 1.000 | |
| linezolid + rifampicin | 5 (6.3) | 3 (30.0) | **0.043** | | 1 (25.0) | 0.319 | |
| co-trimoxazole + rifampicin | 3 (3.8) | 1 (10.0) | 0.385 | 0.279[c] | 1 (25.0) | 0.171 | 0.262[c] |
| clindamycin + rifampicin | 5 (6.3) | 1 (10.0) | 0.522 | | 1 (25.0) | 0.247 | |
| linezolid | 9 (11.4) | 0 (0) | 0.590 | | 0 (0) | 1.000 | |
| co-trimoxazole | 1 (1.3) | 0 (0) | 1.000 | | 0 (0) | 1.000 | |
| ciprofloxacin | 1 (1.3) | 0 (0) | 1.000 | | 0 (0) | 1.000 | |
| Category | | | | | | | |
| rifampicin + rifampicin-independent antibiotic[a] | 55 (69.6) | 5 (50.0) | 0.284 | | 1 (25.0) | 0.100 | |
| rifampicin + rifampicin-dependent antibiotic[b] | 13 (16.5) | 5 (50.0) | **0.026** | **0.033**[d] | 3 (75.0) | **0.025** | **0.020**[d] |
| monotherapy without rifampicin | 11 (13.9) | 0 (0) | 0.352 | | 0 (0) | 1.000 | |



# Linézolide

- Morata *et al.*, 2014: rétro
  - 22 PJI liné+ rifam vs 17 liné




- Legout *et al.*, 2010: rétrospective
  - 49 PJI – 24 OS – 19 OM – 12 pied diab
  - Pas de différence entre mono ou bithérapie
- Bassetti *et al.*, 2005 : prospective
  - 20 PJI dont 15 bithérapie 80% réussite
  - 4 rechutes sans variation de la CMI liné
- Gomez *et al.*, 2011: prospective
  - 49 PJI – infection < 3 mois – échec DAIR
  - 69% succès biT

Theil *et al.*, 2020 : revue

Monothérapie liné = option

# Clindamycine

Courjon *et al.*, 2017: rétro
- 133 patients dont 21 monoT
- 41% sur matériel
- FQ = protecteur mais monoT
- pas de FdR d'échec

| Characteristic | Success (%), $n = 111$ (83) | Failure (%), $n = 22$ (17) | *p-value* | AOR [95%CI] |
|---|---|---|---|---|
| Age (years)[a] | 64 ± 17 | 63 ± 16 | 0.634 | |
| Sex-ratio (M/F) | 1.84 | 1 | 0.188 | |
| **Diagnosis** | | | | |
| Septic arthritis | 19 (17) | 5 (23) | 0.531 | |
| Osteomyelitis | 45 (41) | 5 (23) | 0.115 | |
| Vertebral osteomyelitis | 26 (23) | 0 (0) | **0.025** | |
| With surgical device | 46 (41) | 11 (50) | 0.458 | |
| Chronic infection | 77 (69) | 20 (91) | 0.037 | |
| **Bacterial species** | | | | |
| *Staphylococcus spp.* | 93 (84) | 17 (77) | 0.460 | |
| Methicillin-resistant | 20 (19) | 5 (33) | 0.488 | |
| *Streptococcus spp.* | 16 (14) | 4 (19) | 0.899 | |
| Others | 2 (18) | 1 (5) | 0.990 | |
| Positive blood samples | 21 (19) | 2 (9) | 0.624 | |
| **Antibiotic regimen** | | | | |
| Clindamycin + fluroquinolones | 44 (40) | 2 (9) | **0.012** | 5.35 [1.16–24.55] |
| Clindamycin + rifampicin | 22 (25) | 5 (23) | 0.804 | |
| Clindamycin + others[b] | 15 (13) | 6 (27) | 0.138 | |
| Clindamycin + amoxicillin | 8 (7) | 3 (14) | 0.563 | |
| Clindamycin alone | 15 (13) | 6 (27) | 0.105 | |
| **Duration of therapy** (weeks)[a] | 7.4 ± 2.5 | 10.1 ± 5.5 | **0.013** | |
| Six weeks of antibiotic therapy | 80 (72) | 9 (41) | **0.010** | 3.01 [1.14–7.97] |

Zeller *et al.*, 2009: rétro
- 70 patients (44 PJI)
- biT dim concentration mais 92% guéri dont 4 sous suppressif

Czekaj *et al.*, 2011 : rétro
- 20 IOA biT avec rifam
- Dosages, 100% guérisons

- Pontiflex *et al.*, 1973: rétro
  - 12 OM
  - clindamycine monothérapie
  - 2 échecs

El Samad *et al.*, 2008: rétro
- 61 patients (50% PJI)
- 88,5% bithérapie
- 91% guérison

| Efficacité n = 56 | IOA sur prothèse $n = 28$ | IOA non prothétique $n = 28$ |
|---|---|---|
| Âge | 66,2 (44–85) | 54,25 (26–82) |
| Sex-ratio H/F | 0,65 | 1,8 |
| Première infection | 21/28 (75 %) | 23/28 (82,1 %) |
| Infection chronique | 15/28 (53,7 %) | 14/28 (50 %) |
| Infection polymicrobienne | 2/28 (7,1 %) | 5/28 (17,9 %) |
| Infection à SA | 15/28 (53,6 %) | 23/28 (82,1 %) |
| Infection à SCN | 7/28 (25 %) | 5/28 (17,9 %) |
| Antibiotique associé | | |
| Rifampicine | 15/28 (53,6 %) | 9/28 (32,1 %) |
| Ofloxacine | 5/28 (17,9 %) | 7/28 (25 %) |
| Acide fusidique | 2/28 (7,1 %) | 5/28 (17,9 %) |
| Teicoplanine | 2/28 (7,1 %) | 1/28 (3,6 %) |
| Vancomycine | 2/28 (7,1 %) | 1/28 (3,6 %) |
| Amoxicilline | | 1/28 (3,6 %) |
| Monothérapie | 2/28 (7,1 %) | 4/28 (14,3 %) |
| Durée moyenne du traitement (j) | 110,4 | 91,1 |
| Efficacité à 18 mois | 27/28 (96,43 %) | 24/28 (85,7 %) |
| Rechute | 1/28 (3,57 %) | 4/28 (14,3 %) |

# Evaluation of clindamycin use in bone and joint infections: is a monotherapy a safe option ? A monocentric observational study

S. Jamard *et al.*, via le CRIOGO

- 88 monoT clinda / 49 biT
- Charlson 6 →Plus de cirrhotique gpe biT *
- 61% sur matériel
- 74% infections chroniques

- Échec 30%
  → 51 % en biT et 18% monoT

Monothérapie clindamycine apparait safe
Effet intracellulaire, moins d'interaction

| | Success (n=96) | Failure (n=41) | Univariate OR (IC95, p) | Multivariate adjusted on AIC OR (IC95, p) | IPTW OR (IC95, p) |
|---|---|---|---|---|---|
| Sex (Male) | 71 (74.0) | 28 (68.3) | 0.76 (0.34-1.72, p=0.5) | - | - |
| Malnutrition | 2 (2.1) | 5 (12.2) | 6.53 (1.34-47.03, p=0.03) | 11.83 (1.74-112.31, p=0.02) | - |
| Diabetes mellitus | 41 (42.7) | 23 (56.1) | 1.71 (0.82-3.62, p=0.15) | - | - |
| Malignant Neoplasm | 17 (17.7) | 11 (26.8) | 1.70 (0.70-4.03, p=0.23) | 2.43 (0.80-7.47, p=0.12) | - |
| Chronic alcoholic intoxication | 29 (30.2) | 19 (46.3) | 2.00 (0.94-4.25, p=0.07) | - | - |
| Device related infection | 59 (61.5) | 25 (61.0) | 0.98 (0.47-2.10, p=0.96) | - | - |
| Fever | 30 (31.2) | 24 (58.5) | 3.11 (1.47-6.71, p=0.003) | 3.26 (1.30-8.56, p=0.01) | - |
| Polymicrobial infection | 29 (30.2) | 10 (24.4) | 0.75 (0.31-1.68, p=0.49) | - | - |
| Staphylococcus aureus | 54 (56.2) | 27 (65.9) | 1.50 (0.71-3.27, p=0.3) | - | - |
| Monotherapy | 72 (75.0) | 16 (39.0) | 0.21 (0.10-0.46, p<0.001) | 0.18 (0.07-0.46, p<0.001) | 0.36 (0.17-0.76, p=0.008) |
| Duration of treatment (days) Median (IQR) | 42.0 (3.0) | 42.0 (3.0) | 1.00 (0.99-1.02, p=0.57) | - | - |

# *S. aureus*: Pro monoT sur matériel FQ

Safety and Efficacy of Moxifloxacin Monotherapy for Treatment of Orthopedic Implant-Related Staphylococcal Infections▽

Rafael San Juan,[1]* Ana Garcia-Reyne,[1] Pedro Caba,[2] Fernando Chaves,[3] Carlos Resines,[2] Fernando Llanos,[2] Francisco López-Medrano,[1] Manuel Lizasoain,[1] and Jose Maria Aguado[1]

- n=48. IOA
- ttt: post op vanco + cloxa/céfazo puis moxiflo 3 mois
- Infection chronique chez 36 patients (75%) et n=21 (43%) implant gardé
- 82,6% succès et 71 % avec la rétention de matériel

TABLE 1. Characteristics of the 48 patients included in the study

| Characteristic | Value |
|---|---|
| Sex (% male/% female) | 52.1/47.9 |
| Mean ± SD age (yr) | 58.8 ± 2.6 |
| Mean ± SD Charlson comorbidity index | 0.8 ± 0.2 |
| No. (%) of patients with the following type of orthopedic implant: | |
| Osteosynthesis material[b] | 28 (58.3 |
| Hip prosthesis | 9 (18.8 |
| Knee prosthesis | 10 (20.8 |
| Shoulder prosthesis | 1 (2.1) |
| No. (%) of patients with the following timing of infection: | |
| Early infection | 6 (12.5 |
| Late chronic infection | 33 (68.8 |
| Late hematogenous infection | 3 (6.3) |
| Finding in prosthetic joint revision | 6 (12.5 |
| No. (%) of patients with the following etiology of infection: | |
| *Staphylococcus aureus* | 33 (68.8 |
| CoNS | 15 (31.2 |
| Median (range) no. of days of i.v. antibiotic treatment[c] | 12.6 (1– |
| Median (range) no. of days of oral moxifloxacin treatment | 78 (24–2 |
| No. (%) of patients with global cure | |
| Per ITT | 38 (79.1) |
| All patients ($n$ = 46) | 38 (82.6) |
| Patients with implant retention[d] ($n$ = 20) | 15 (71.3) |
| Patients with *S. aureus* infection ($n$ = 33) | 26 (78.8) |
| Patients with CoNS infection with global cure ($n$ = 14) | 12 (86) |

Pas d'émergence de résistance aux quinolones sur les échecs

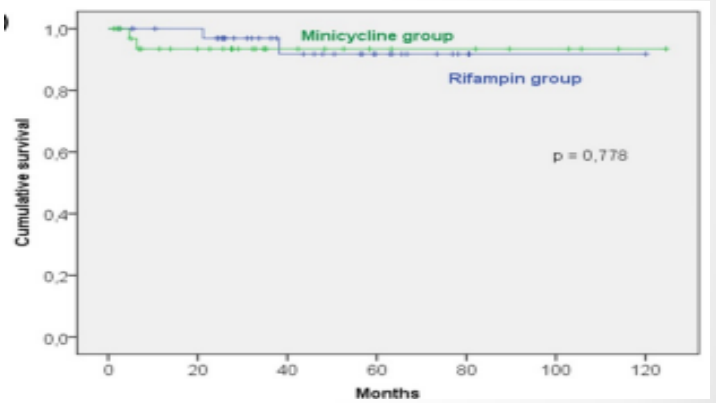
Lombes *et al.*, 2024:
ISO post op chir rachis: 20 patients
11 monoT vs 9 biT: pas de différence (5 sous FQ seule)

# Cycline

**Minocycline Combined with Vancomycin for the Treatment of Methicillin-Resistant Coagulase-Negative Staphylococcal Prosthetic Joint Infection Managed with Exchange Arthroplasty**

Géraldine Bart[1], Valérie Zeller[1,2✉], Younes Kerroumi[2], Beate Heym[2,3], Vanina Meyssonnier[1,2], Nicole Desplaces[2], Marie Dominique Kitzis[5], Jean Marc Ziza[1,2], Simon Marmor[2,4]

- 70 PJI SCN méti-R : IV 6 semaines par
  - Vancomycine + rifam puis minocycline rifam
  - Vancomycine + minocycline puis mino seule
- 36 CMI Vanco > 2 (50% des effectifs dont 71% mino)
- Pas de différence : 80 % réussite sur IOAC
- 8 souches tétra R mais mino S pas de rechute (mécanisme d'efflux)

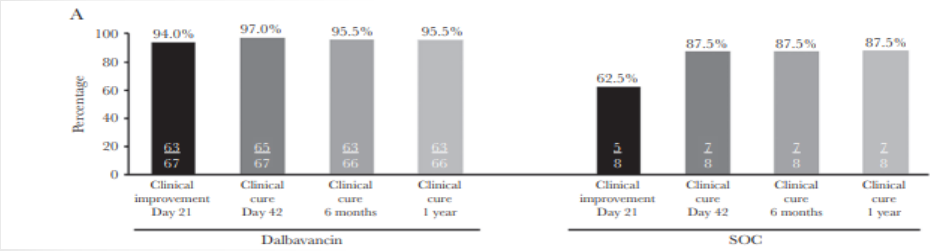



Tigécycline: alternative dans 2 séries de cas :
- 19 ostéomyélites Griffin *et al.*, 2013
- 36 IOAC Wach *et al.*, 2018

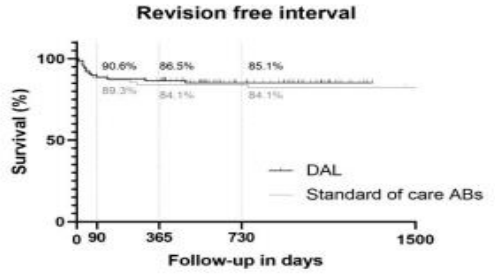
Cycline: alternative en monothérapie
Bonne diffusion des cyclines

# Dalbavancine

Rappo *et al.*, 2019: Randomisé
70 ostéomyélites dalba (monoT) vs 10 OM SOC




Simon *et al.*, 2022: rétro biT
89 PJI dalba/89 SOC




Morata *et al.*, 2019 : rétro
45 IOA matériel et 19 IOA natives
biT dalba vs SOC

Wunsch *et al.*, 2019: rétro
32PJI - 30 OM 39 autres (64 biT)

Dimopoulou *et al.*, 2023 : revue

Dalbavancine alternative
Bonne tolérance

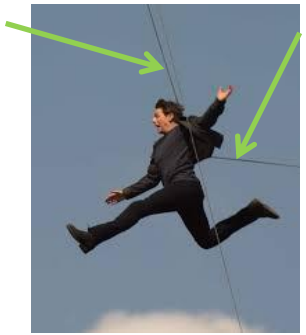
# Conclusion

- Avec matériel : la première intention reste la bithérapie quinolone + rifam. En cas d'impossibilité sur la tolérance ou la résistance la monothérapie peut s'envisager, privilégier la clindamycine, doxy, dalbavancine…

- A l'avenir: études à faire sur la monothérapie
  - Clindamycine en cours de publication
  - Dalbavancine en cours

# Infectiologue aventurier?

OUI

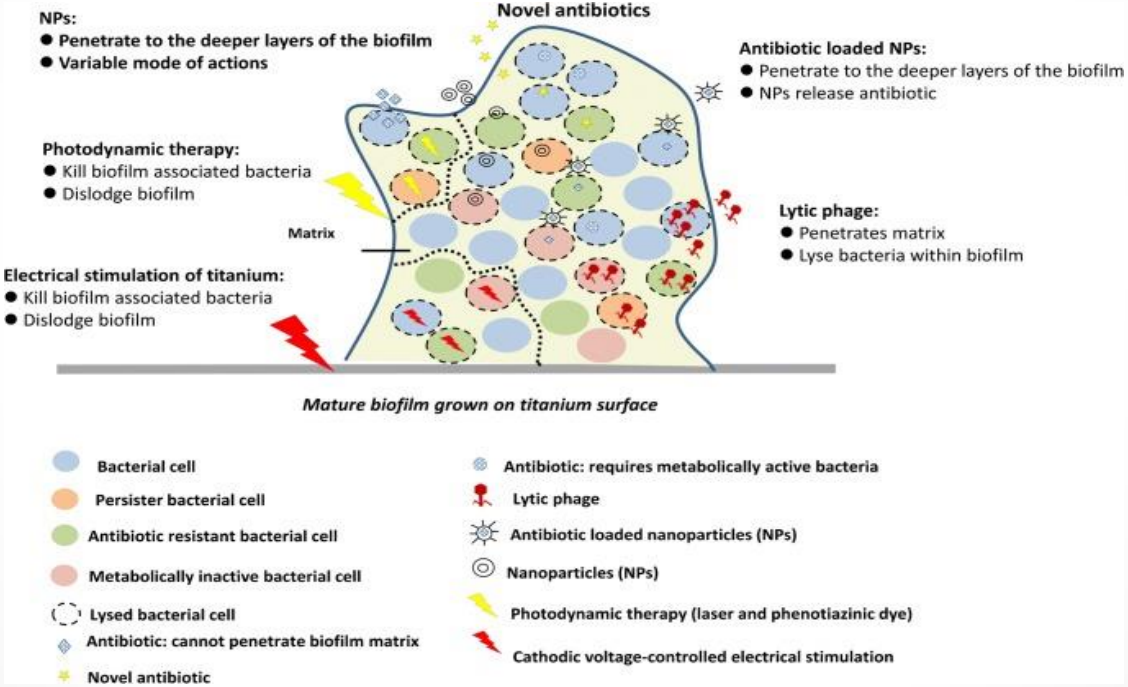


MAIS

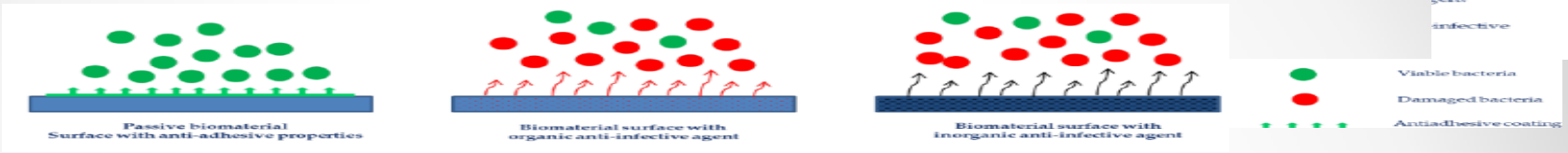
# Merci de votre attention

CENTRES DE RÉFÉRENCE POUR LES INFECTIONS OSTÉO-ARTICULAIRES COMPLEXES DU GRAND OUEST
CRIOGO

CHRU
HÔPITAUX DE TOURS


NPs:
Penetrate to the deeper layers of the biofilm
Variable mode of actions
Novel antibiotics
Antibiotic loaded NPs:
Penetrate to the deeper layers of the biofilm
NPs release antibiotic
Photodynamic therapy:
Kill biofilm associated bacteria
Dislodge biofilm
Matrix
Lytic phage:
Penetrates matrix
Lyse bacteria within biofilm
Electrical stimulation of titanium:
Kill biofilm associated bacteria
Dislodge biofilm
Mature biofilm grown on titanium surface
Bacterial cell
Persister bacterial cell
Antibiotic resistant bacterial cell
Metabolically inactive bacterial cell
Lysed bacterial cell
Antibiotic: cannot penetrate biofilm matrix
Novel antibiotic
Antibiotic: requires metabolically active bacteria
Lytic phage
Antibiotic loaded nanoparticles (NPs)
Nanoparticles (NPs)
Photodynamic therapy (laser and phenotiazinic dye)
Cathodic voltage-controlled electrical stimulation

# Techniques innovantes

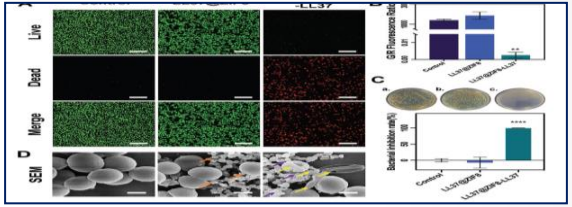


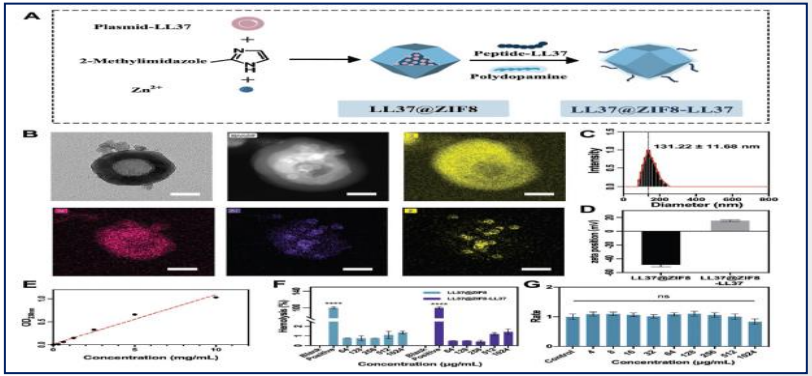

**Surfaces passives** : présente des modification chimiques ou structurelles empêchant l'adhésion sans relarguer d'agent anti microbien

- Anti adhésive: 5 propriétés:
  - répulsion stérique,
  - répulsion électrostatique
  - faible énergie de surface
  - interactions superhydrophobes et hydrophobes
  - Interaction physique substrat-microorganisme
- Polyethylène glycol, hydrogel, poly zwitterionic materiau…
- Ajouter sur la surface du serum ou plasma ou des protéines

**Surfaces actives**: relargue un agent antimicrobien

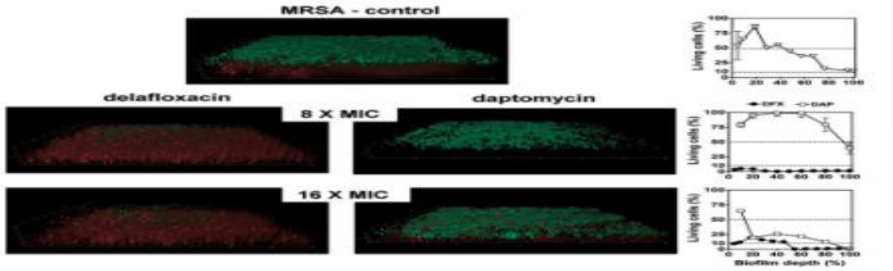
- Organic (antibiotiques, PAM, phages)
- Inorganique: métaux ou ions (nanoparticules)

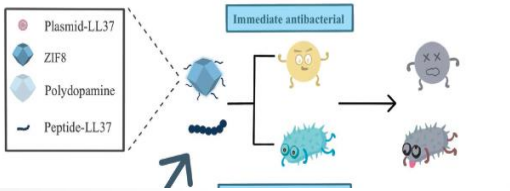


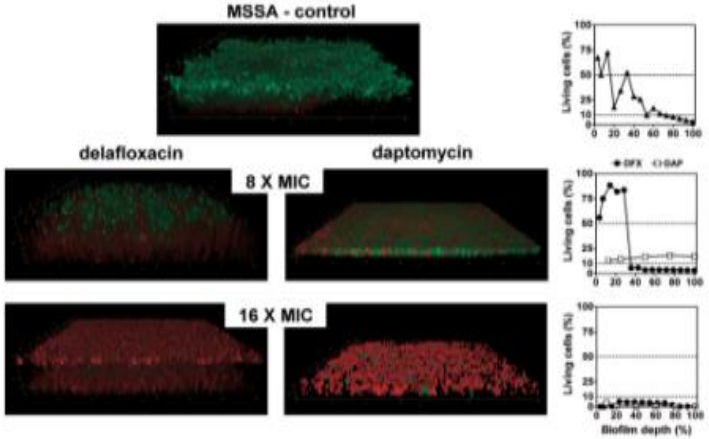




PAM: coûteux et sensible au pH et protéase
Inhibiteur de QS: desintégration de biofilm mais spectre étroit, Résistance
Nanoparticules de métaux

# Exemple de technique innovante PAM




RESEARCH ARTICLE

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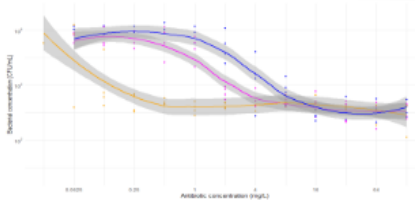
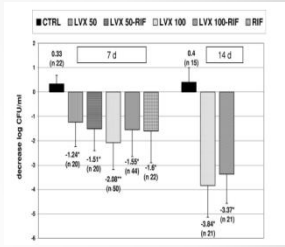
## Multi-Mode Antibacterial Strategies Enabled by Gene-Transfection and Immunomodulatory Nanoparticles in 3D-Printed Scaffolds for Synergistic Exogenous and Endogenous Treatment of Infections

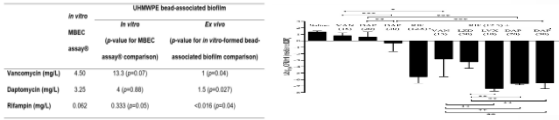
*Xinhua Qu, Minqi Wang,* Miaochen Wang, Haozheng Tang, Shutao Zhang, Hongtao Yang, Weien Yuan, You Wang, Jianping Yang,* and Bing Yue**

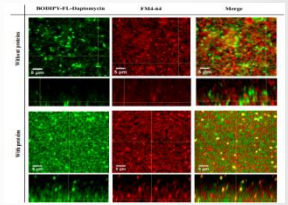
# Antibiotiques antibiofilm

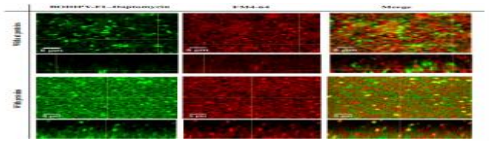
- Daptomycine :
  - In vitro ok SASM [1]
  - In vivo: ok SASM [2,3]
  - Moins vrai sur SARM [1,2]
- Fluoroquinolones:
  - In vitro: SASM SARM
  - In vivo: cage lapin SASM, moxiflo bonne pénétration biofilm [4]

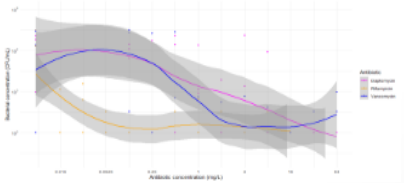


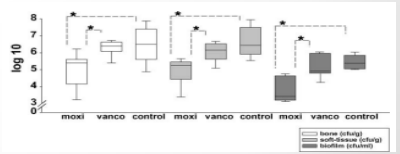











[1] Bauer *et al.*, 2013; Boudjemaa *et al.*, 2016
[2] John *et al.*, 2009 ; Jamard *et al.*, 2023
[3] Jacqueline *et al.*, 2014
[4] Kaltéis *et al.*, 2006