

JNI

24^{es} Journées
Nationales
d'Infectiologie

Grenoble

et la région Auvergne-Rhône-Alpes

ALPEXPO

du mercredi 7 au vendredi 9 juin 2023



Nouveaux concepts dans les infections sur matériel

Florent VALOUR



Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : VALOUR Florent

Titre : *Nouveaux concepts dans les infections sur matériel*

L'orateur ne souhaite pas répondre

- Consultant ou membre d'un conseil scientifique OUI NON
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents : MSD, Pfizer OUI NON
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès : MSD, Pfizer, Correvio, Ménarini OUI NON
- Investigateur principal d'une recherche ou d'une étude clinique OUI NON

DAIR / 1 temps / 2 temps

Immunothérapie

Biomarqueurs

Nouveaux antibiotiques

Protéomique

Phages

Durées de traitement

Prophylaxie

Coating

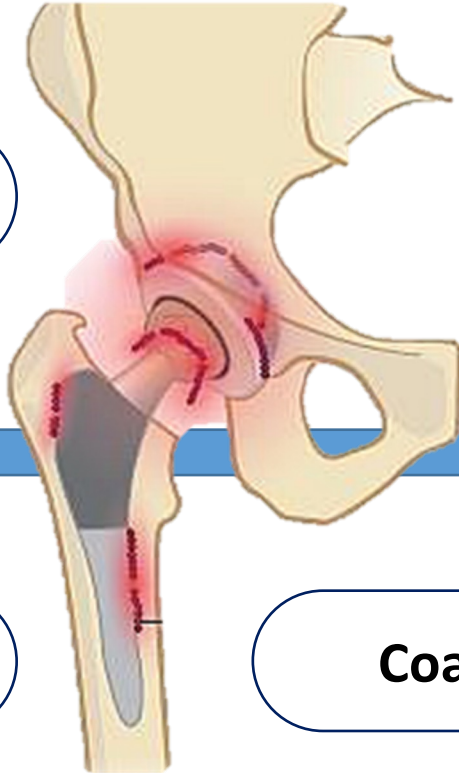
Antibiothérapie locale

Biomatériaux

Substituts osseux

Persisters

Biologie moléculaire



DAIR / 1 temps / 2 temps

Immunothérapie

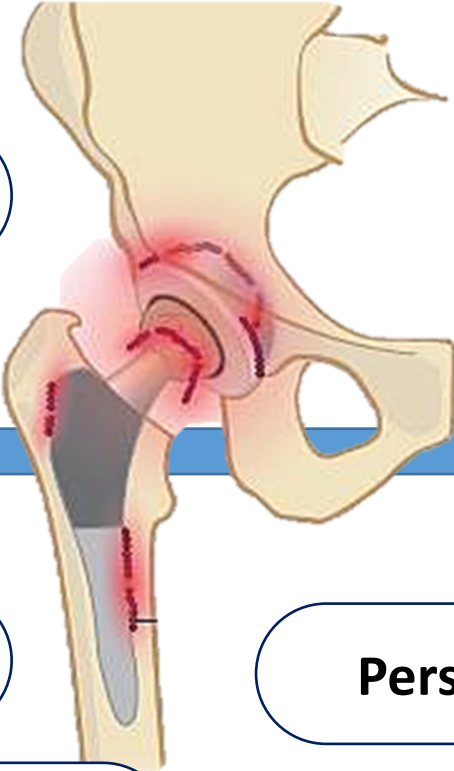
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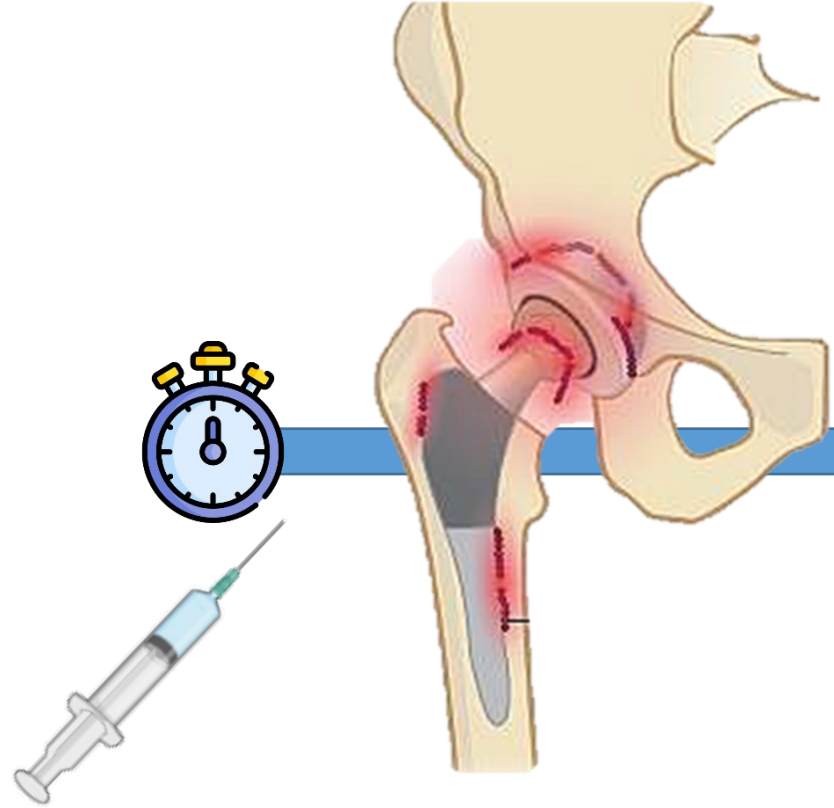
Coating

Biomatériaux

Biologie moléculaire

Laboratoire

**DON'T
MAKE ME
USE MY
ORTHOPEDIC
SURGEON
VOICE**



1 – Nouvelle stratégie antibiotique : long acting



Dalbavancine : quel rationnel ?



Demi-vie : 372h (15 jours)

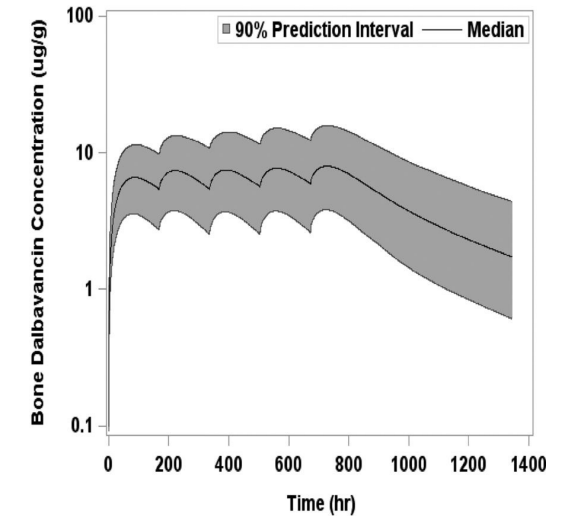
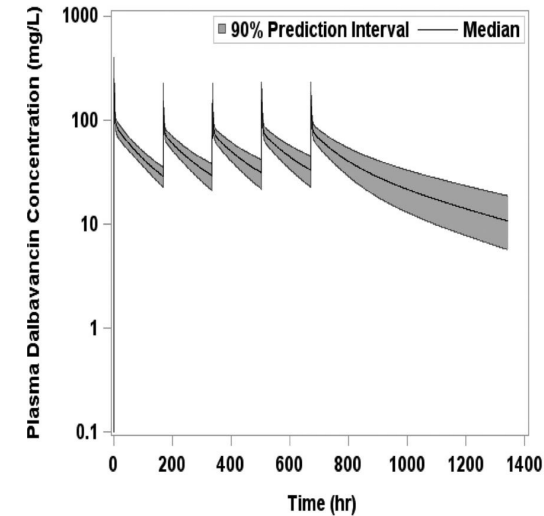


Diffusion osseuse

- Concentration constantes
- Ration AUC os/plasma \approx 13%

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

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



1,000 mg i.v. on day 1 and 500 mg i.v. weekly

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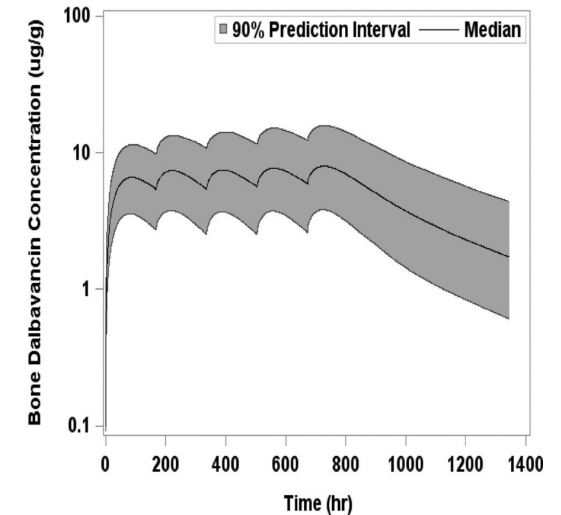
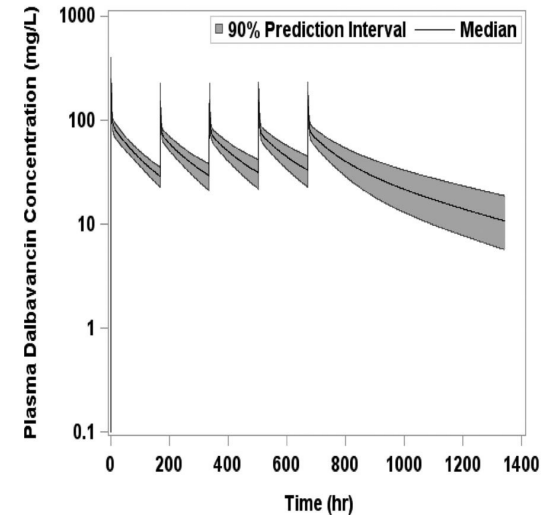
Activité anti-biofilm

- *in vitro* et *in vivo*
- *S. aureus* et *S. epidermidis* +++
Effet additif/syn avec RMP
- *E. faecalis* et *E. faecium*

El Haj et al, IJAA 2022
Jacob et al, Sci rep 2021
Silva et al, J Chemother 2021
Silva et al, JAC 2020
Di Pilato et al, DMID 2020
Knafl et al, EJCMID 2017
Fernandez et al, DMID 2016
Baldoni et al, IJAA 2013
Díaz-Navarro et al, IDT 2022
Neudorfer et al, DMID 2018

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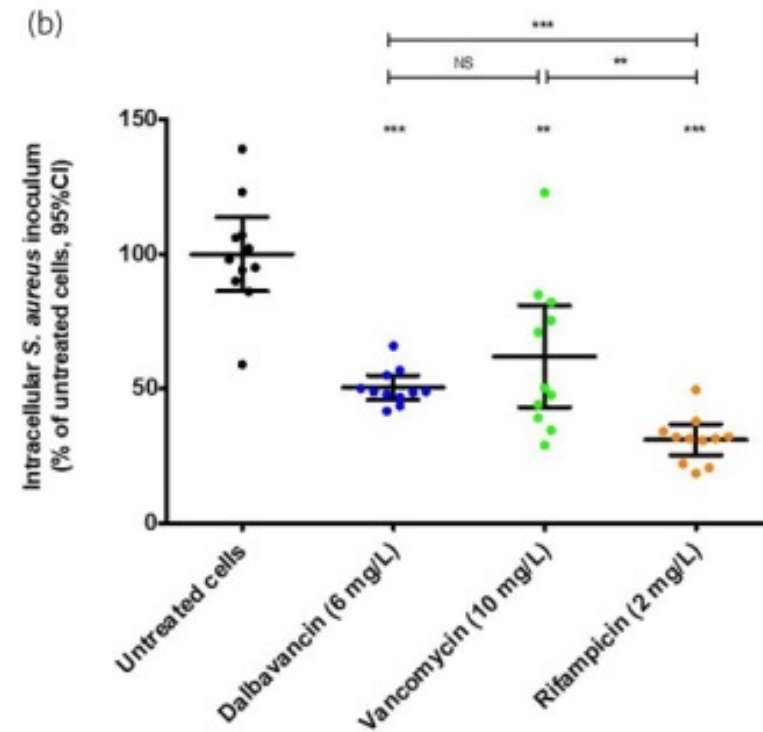
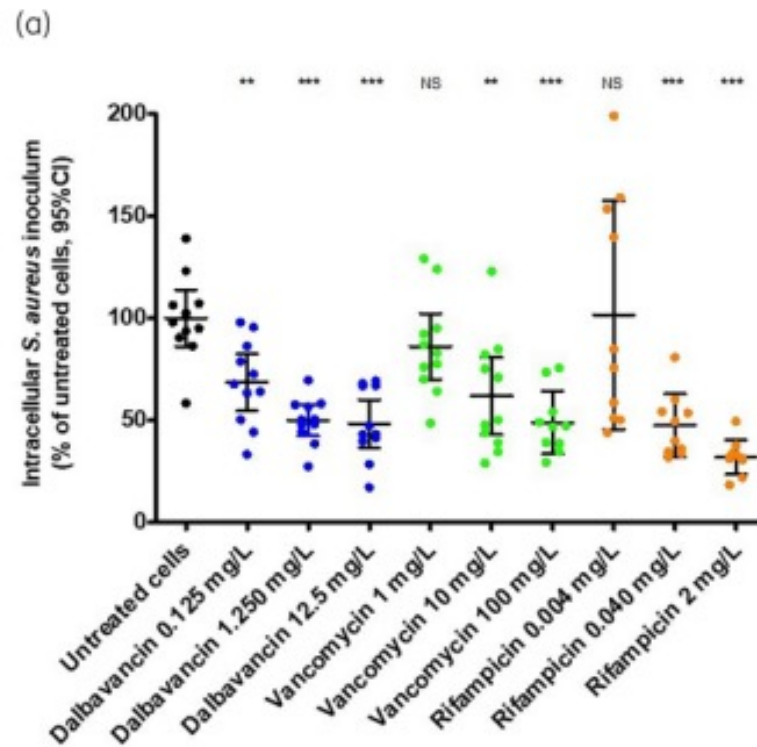
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Activité intracellulaire moyenne

Evaluation of intraosteoblastic activity of dalbavancin against *Staphylococcus aureus* in an ex vivo model of bone cell infection

Pierre Chauvelot^{1,2,3}, Céline Dupieux-Chabert^{1,2,4,5}, Lélia Abad¹, Aubin Souche^{1,2,4,5}, Tristan Ferry^{1,2,3,4}, Jérôme Josse^{1,2,4}, Frédéric Laurent^{1,2,4,5†} and Florent Valour^{1,2,3,4**†} on behalf of the Lyon BJI Study Group†



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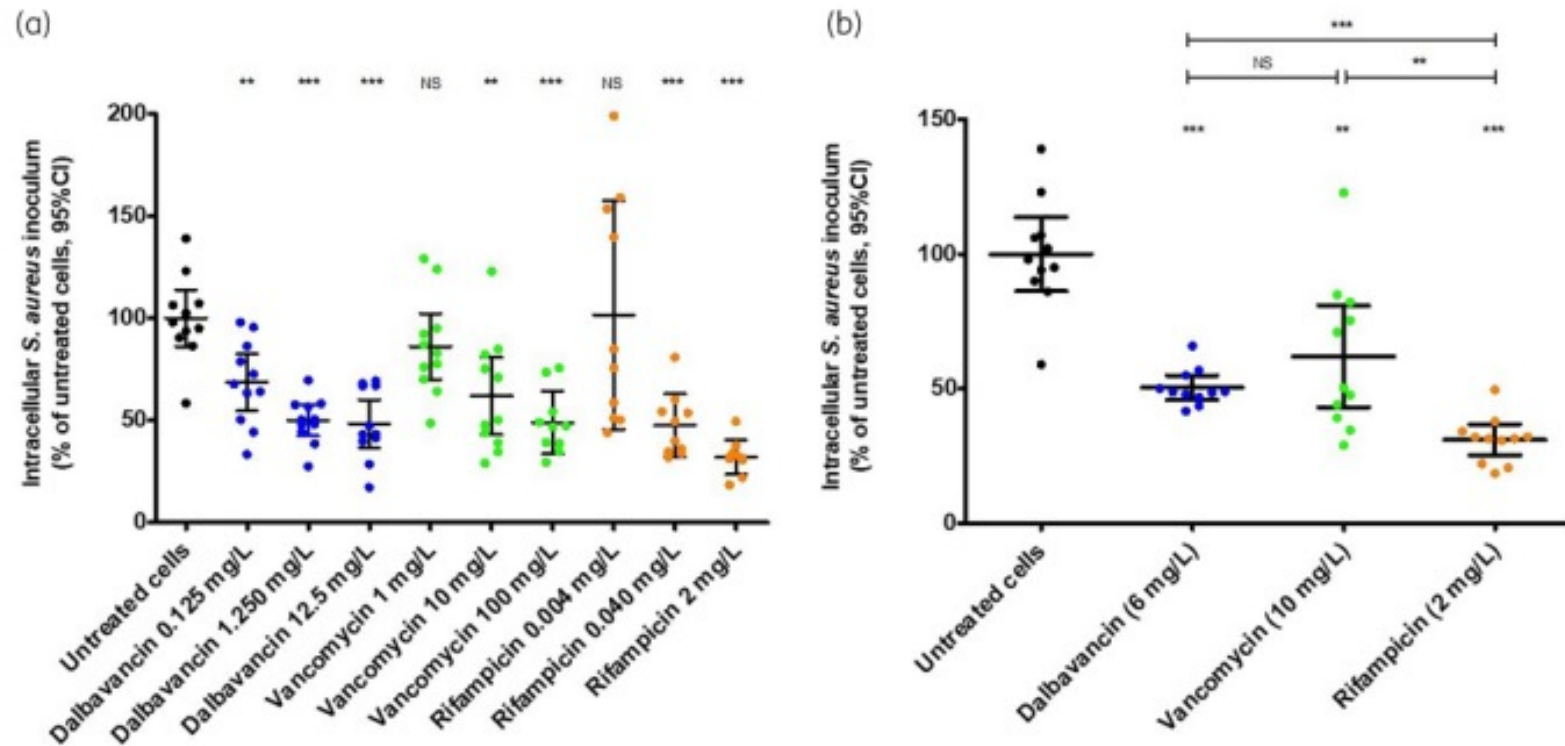
Activité intracellulaire moyenne



1500 mg : 2 330 €
1000 mg : 1550 €
500 mg : 760 €

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Dalbavancine : quelle utilisation dans les IOA ?

A prospective, multicenter cohort study assessing the use, effectiveness and safety of dalbavancin in France

Courjon J, Senneville E, Illes HG, Pavese P, Boutoille D, Daoud F, Dunkel N, Tattevin P

33rd **ECCMID** EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Copenhagen, Denmark
15–18 April 2023

Cohorte prospective observationnelle française (sept 2018 – avr 2020)
151 adultes (62,3% hommes, âge 66 ± 16) ayant reçu au moins 1 dose de dalbavancine



Characteristic at baseline

Age (years)	66 ± 16
Sex, male, n (%)	94 (62.3)
Mean BMI ± SD, kg/m ²	27.6 ± 6.1
Comorbidities	
Charlson comorbidity index ± SD	4 ± 3
Mean number of major comorbidities ± SD	6 ± 5
Renal failure, n (%)	37 (24.5)
Hemodialysis, n (%)	6 (4.0)

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Infection type	N=151 n (%)
Bone and joint infection	83 (55.0)
Multisite infection	24 (15.9)
Vascular infection	22 (14.6)
ABSSSI only	10 (6.6)
Bacteremia only	7 (4.6)
Mediastinitis or pulmonary infection	5 (3.3)
Infection on medical device, n (%)	
None	66 (43.7)
Orthopedic implant (all)	67 (44.4)
PJI	43 (28.4)
Unspecified	8 (5.3)
Vascular access device	7 (4.6)
Aortic or vascular implant	3 (2.0)

Treatment regimen n (%)	N=151
1 injection	26 (17.2)
2 injections	95 (62.9)
3 injections	17 (11.3)
4 injections	5 (3.3)
≥ 5 injections	8 (5.0)
Interval between injections, days (N=125)	
Median (Q1–Q3)	7 (3–20.7)
Cumulative dose administered, mg	
Mean ± SD	3 089 ± 1 461

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	Success	Failure
Indication, n (%)		
ABSSSI only	7 (87.5)	1 (12.5)
Bacteremia only	4 (100.0)	0 (0.0)
Vascular infection	19 (100.0)	0 (0.0)
Mediastinitis or pulmonary infection	4 (80.0)	1 (20.0)
Multisite infection	19 (100.0)	0 (0.0)
Bone and joint infection	66 (89.2)	8 (10.8)
Device-related BJI	46 (87)	7 (13)
Total	119 (92.2)	10 (7.8)

- 67/151 patients (44.4%) reported ≥ 1 adverse event
- 14 AEs were related to Dalbavancin
- 1 patient with serious AE (7,9%) : syncope, hypotension

Dalbavancine : quelle posologie dans les IOA ?

Population Pharmacokinetics of Dalbavancin and Dosing Consideration for Optimal Treatment of Adult Patients with Staphylococcal Osteoarticular Infections

Pier Giorgio Cojutti,^{a,b} Matteo Rinaldi,^{c,d} Eleonora Zamparini,^{c,d} Nicolò Rossi,^{c,d} Sara Tedeschi,^{c,d} Matteo Conti,^c Federico Pea,^{c,e} Pierluigi Viale^{c,d}

n=15 patients traités pour IOA

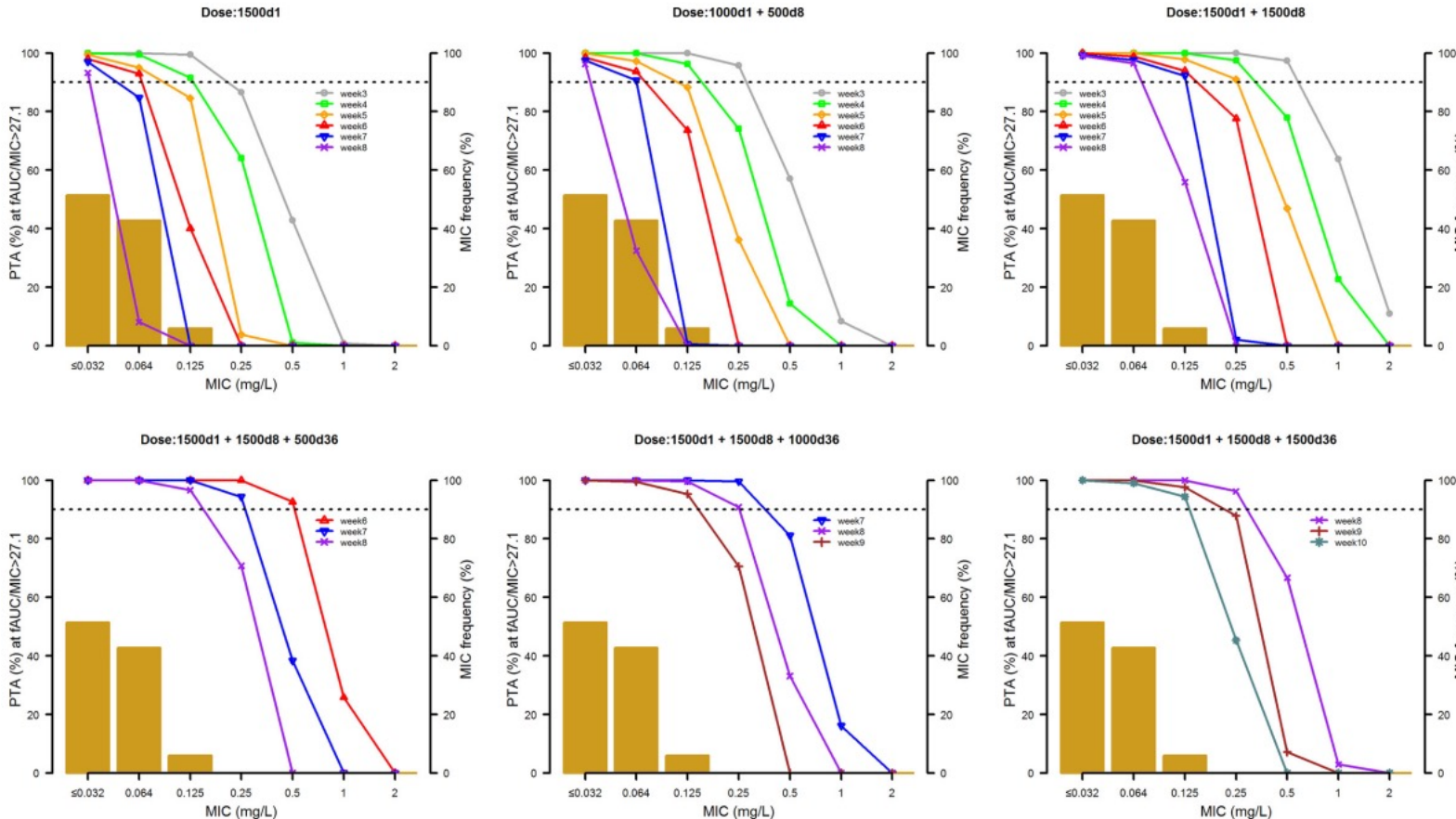






Schéma 1500 mg J1-J8
= exposition bactéricide 4 sem
si *S. aureus* CMI max (0,125 mg/L)

3^e dose 1000 mg à M1
= exposition bactéricide jusqu'à S8

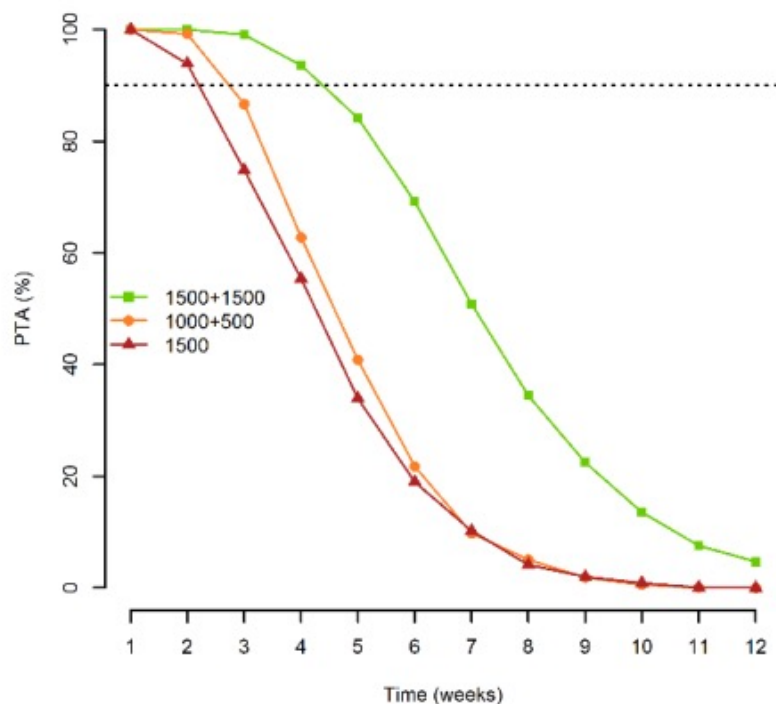
Dalbavancine : quelle posologie dans les IOA ?

Population Pharmacokinetic and Pharmacodynamic Analysis of Dalbavancin for Long-Term Treatment of Subacute and/or Chronic Infectious Diseases: The Major Role of Therapeutic Drug Monitoring

Pier Giorgio Cojutti¹, Sara Tedeschi^{2,3}, Milo Gatti^{1,3} , Eleonora Zamparini², Marianna Meschiari⁴ , Paola Della Siega⁵, Maria Mazzitelli⁶ , Laura Soavi⁷, Raffaella Binazzi⁸, Elke Maria Erne⁸, Marco Rizzi⁷, Anna Maria Cattelan⁶, Carlo Tascini⁵, Cristina Mussini⁴, Pierluigi Viale^{2,3} and Federico Pea^{1,3,*} 

n=66 patients dont 7 EI

CL_{CR}: 90-120 mL/min/1.73 m²



CL_{CR}: 90-120 mL/min/1.73 m²

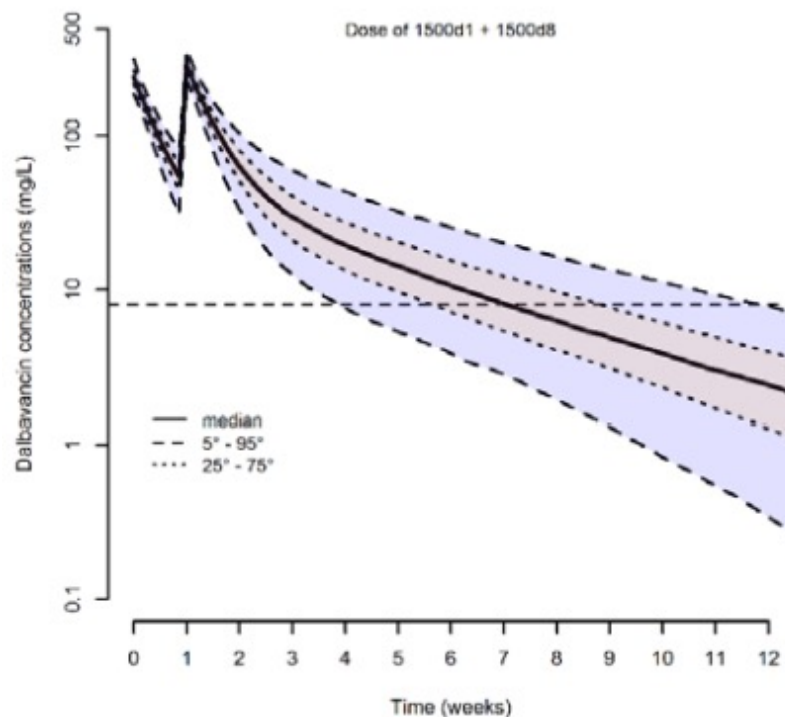


Schéma 1500 mg J1-J8
= exposition bactéricide 4 sem
si *S. aureus* CMI max (0,125 mg/L)

Schéma 1000 mg J1-J8
= idem si DFG < 30 mL/min

Dalbavancine : quelle posologie dans les IOA ?

Avis CAI HCL

- **1500 mg à J1 et J8** (1000 mg si DFG < 30 mL/min)
- si nécessité de traitement \geq 4-6 sem : **nécessité de suivi PK pour modélisation**
 - Résiduel à J8 pour déterminer le timing et la dose de la 3^e injection
 - Résiduel + pic à J8 ou avant 3^e injection pour injections suivantes (cible PK/PD = AUC/CMI)

Dalbavancine : quelle posologie dans les IOA ?

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IOA-12



Quelle posologie de dalbavancine dans les infections ostéo-articulaires ? Apport des dosages et de la modélisation pharmacocinétique

G. Fossas, L. Pagnot, C. Baudart, J. Reverchon, M. Grégoire, L. Bourguignon, T. Ferry, S. Goutelle

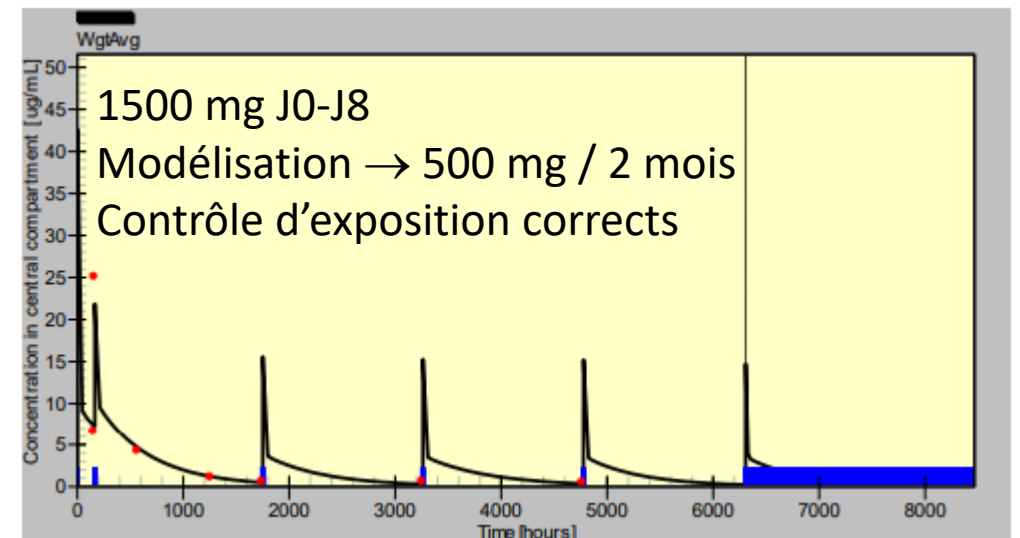


16 patients / IOA

Moyenne $8,6 \pm 10$ doses (max = 37)

Traitements suppressifs

Modélisation \rightarrow Personnalisation des doses / intervalles



Oritavancine : quel rationnel ?



Demi-vie : 245h (10 jours)



Diffusion osseuse

- Concentration constantes J7 (lapin)
- Ration AUC os/plasma $\approx 1,1-3,1$



Activité anti-biofilm

- *in vitro* et *in vivo*
- *S. aureus* et *S. epidermidis*
surtout avec RMP
- *E. faecalis* et *E. faecium*

Yan et al, AAC 2018
Yan et al, IJAA 2018
Yan et al, DMID 2018
Belley et al, AAC 2009
Yan et al, DMID 2018

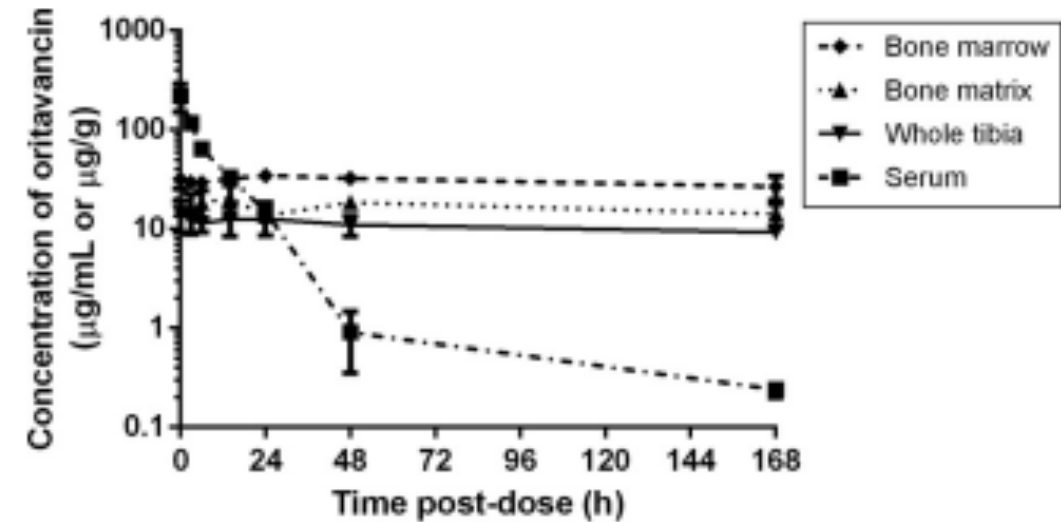
Activité intracellulaire (modèle macrophages)



2 500 €

Oritavancin Pharmacokinetics and Bone Penetration in Rabbits

Dario Lehoux, Valerie Ostiguy, Cordelia Cadieux, Mireille Malouin, Odette Belanger, Adel Rafai Far, Thomas R. Parr, Jr.



Distribution rapide – Concentration stable à J7

Oritavancine : quelles données dans les IOA ?

Review

Role of Oritavancin in the Treatment of Infective Endocarditis, Catheter- or Device-Related Infections, Bloodstream Infections, and Bone and Prosthetic Joint Infections in Humans: Narrative Review and Possible Developments

Tommaso Lupia ^{1,*}, Ilaria De Benedetto ², Roberta Bosio ², Nour Shbaklo ², Francesco Giuseppe De Rosa ^{1,2} and Silvia Corcione ^{2,3}

First Author et al. [Ref]	Type of Study	N. of Patients Treated	Dosing and Interval	Pathogen(s)	Outcome	Adverse Effects
Van Hise et al. (2020) [21]	multicenter, retrospective, descriptive	134 osteomyelitis, of which 24 prosthetic	1200 mg, then 800 mg weekly (4 to 5 doses)	71.9% MRSA	88.1% clinical success at the end of therapy	3 hypoglycemia, 1 tachycardia, 1 tachycardia with chest pain
Redell et al. (2019) [20]	retrospective, observational	438, of which 18 osteomyelitis and 3 prosthetic	1200 mg every 6–14 days (1–10 doses)	74% <i>S. aureus</i> of which 59.3% MRSA	93.8% cure or 30-days improvement	6.6% of patients reported an adverse event
Shulz et al. (2018) [18]	retrospective, observational	17 including osteomyelitis	1200 mg (2–18 doses)	NA	100% clinical success or improvement	24% of patients reported an adverse event
Delaportas et al. (2017) [22]	case report	1 osteomyelitis	1200 mg weekly (6 doses)	MSSA	clinical cure	NA
Chastain et al. (2018) [23]	case series	9 chronic osteomyelitis	1200 mg—variable time between doses (2–6 doses)	5 MRSA	100% clinical cure at 6-months follow up	None
Nguyen et al. (2020) [24]	case report	1 prosthetic joint infection	daptomycin plus ampicillin 10 days, then 1200 mg weekly (6 doses)	vancomycin sensitive <i>E. faecalis</i>	clinical cure	NA
Dahesh et al. (2019) [25]	case report	1 prosthetic vertebral osteomyelitis	1200 mg weekly (2 doses), then 800 mg weekly (8 doses) plus ampicillin	vancomycin-resistant <i>E. faecium</i>	clinical cure	NA

Antibiotiques à longue durée d'action : une place dans les ciments ?

Determination of the Elution Capacity of Dalbavancin in Bone Cements: New Alternative for the Treatment of Biofilm-Related Peri-Prosthetic Joint Infections Based on an *In Vitro* Study

Mar Sánchez-Somolinos¹, Marta Díaz-Navarro^{1,2}, Antonio Benjumea³, Marta Tormo⁴, José Matas³, Javier Vaquero^{2,3,5}, Patricia Muñoz^{2,3,5,6}, Pablo Sanz-Ruiz^{2,3,5} and María Guebbe^{1,2,*}

Ciment Palacos®R + 2,5 ou 5% de VANCO ou DALBA
Incubés en PBS à 37°C

Elution cumulée vancomycine > dalbavancine

- Persistance tissulaire ?
- Ratio [C] / CMI

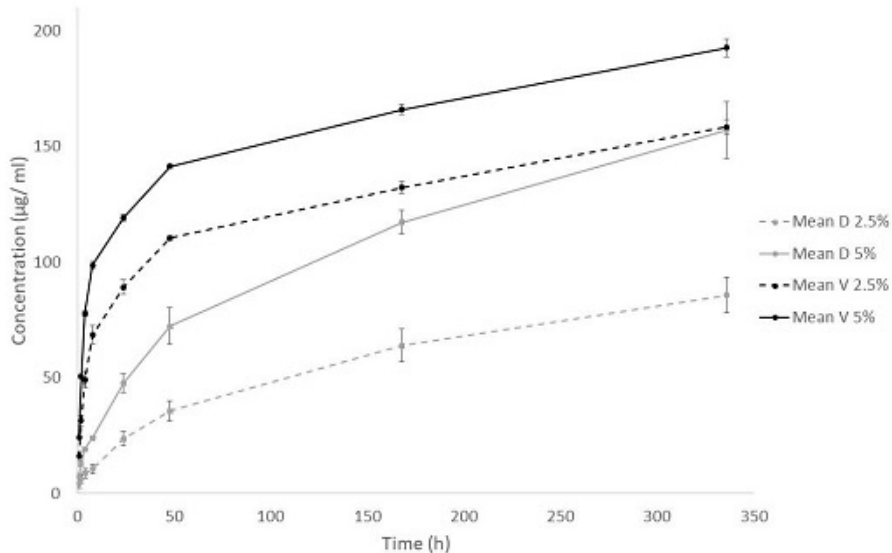


Figure 1. Cumulative antibiotic release over 14-day period for each group of antibiotics. V, vancomycin; D, dalbavancin; h, hours.

Oritavancin polymethylmethacrylate (PMMA)—compressive strength testing and in vitro elution

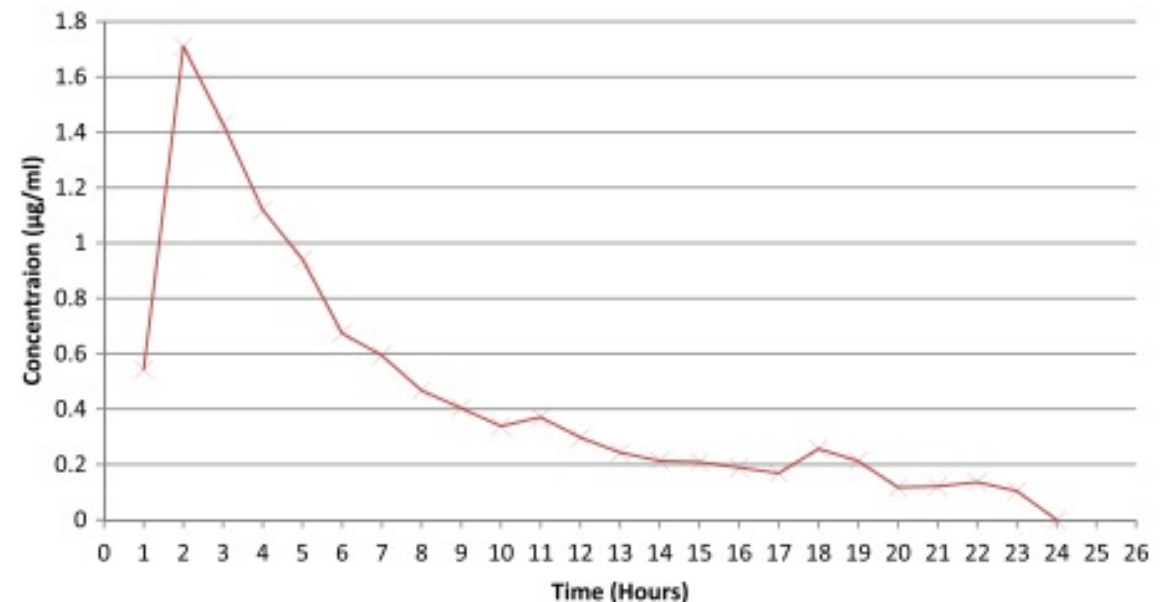


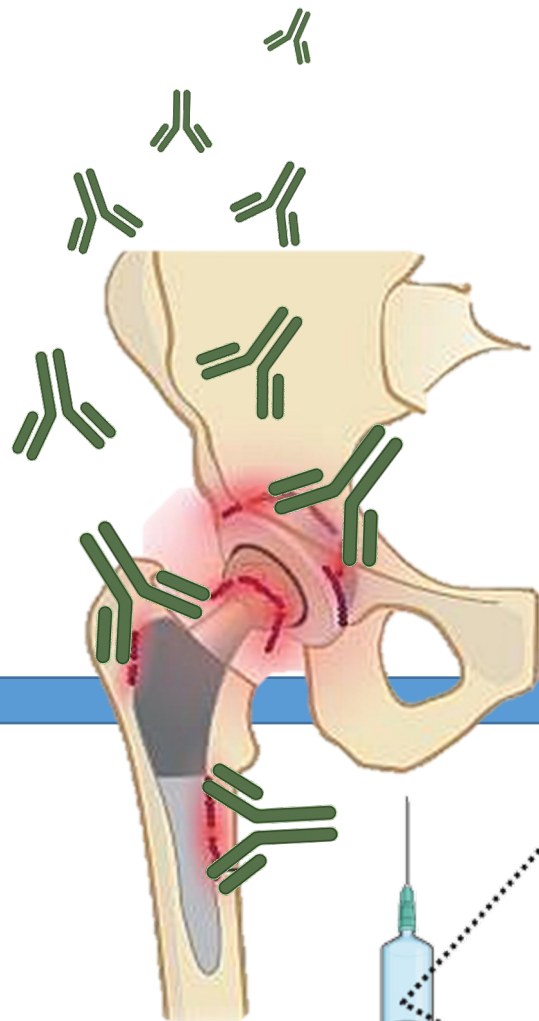
Suzannah M. Schmidt-Malan¹, Kerryl E. Greenwood-Quaintance¹, Lawrence J. Berglund⁴, Jayawant Mandrekar³ and Robin Patel^{1,2*}

PMMA Simplex P® + 7,5% de VANCO ou ORITA

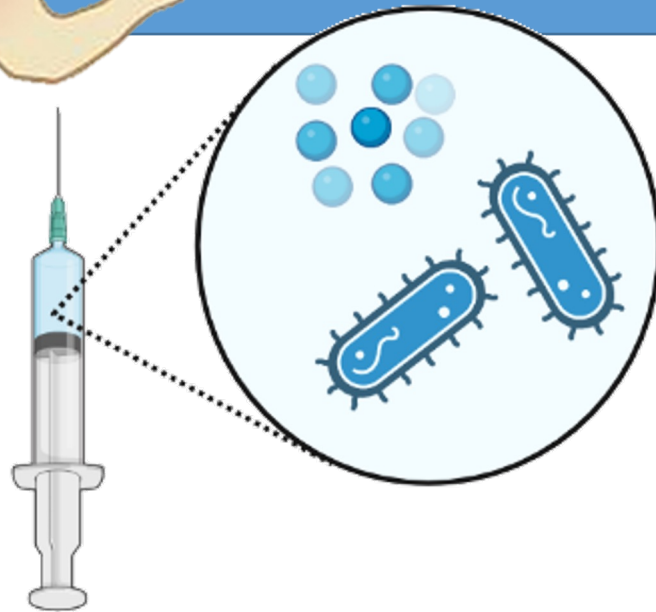
Diminution moindre des capacités mécaniques du ciment vs vanco

Faible niveau d'éluion

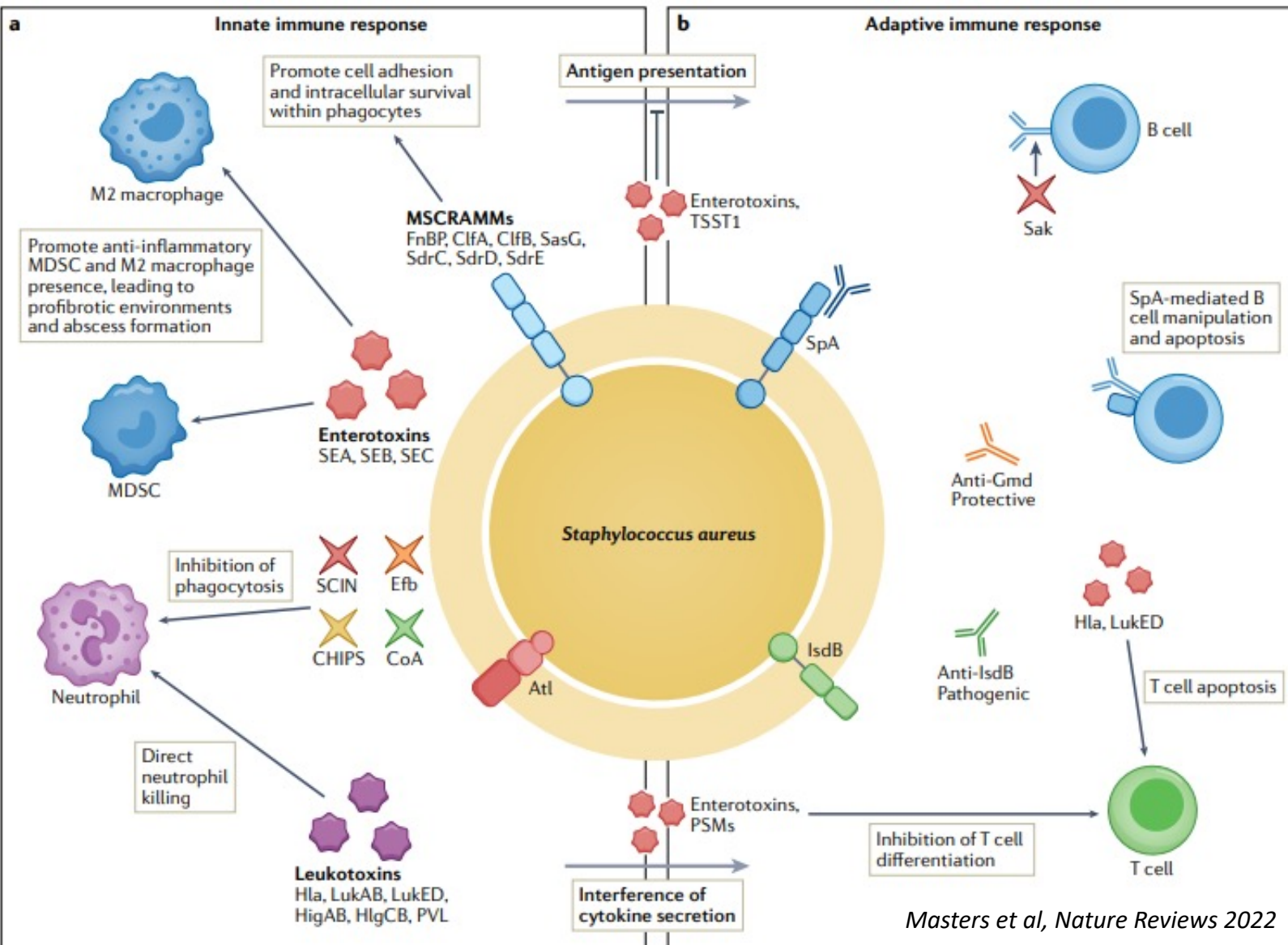




2 – Stratégie non antibiotique : immunothérapie



Immunothérapie : rationnel et problématique



- ① **Echappement à la réponse innée**
 - Survie intracellulaire (MSCRAMMs)
 - Inhibition de la phagocytose (MSCRAMMs, entérotoxines)
 - Leucotoxines
- ② **Action sur la synapse immunitaire**
 - Présentation d'Ag
 - Production de cytokines
- ③ **Echappement à la réponse adaptative**
 - Inhibition T (Hla, LukED, PSMs)
 - Inhibition B (SpA, Sak)
 - Effet superantigénique
- ④ **Effet anticorps ambivalent**
 - Protecteur
 - Facilitants : anti-IsdB

Vaccination et infections sur matériel : où en est-on ?

Inferring reasons for the failure of *Staphylococcus aureus* vaccines in clinical trials

Fabio Bagnoli*, Sylvie Bertholet and Guido Grandi

RAISONS DE L'ECHEC



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Modèles expérimentaux inadaptés

RAISONS DE L'ÉCHEC



Modèles murins +++
Immunité, absence de portage

Models matter: the search for an effective *Staphylococcus aureus* vaccine

Wilmara Salgado-Pabón and Patrick M. Schlievert

Mice are not men

H. Shaw Warren^a, Ronald G. Tompkins^a,
Lyle L. Moldawer^b, Junhee Seok^c,
Weihong Xu^d, Michael N. Mindrinos^d,
Ronald V. Maier^e, Wenzhong Xiao^{a,1}, and
Ronald W. Davis^{d,1}

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Choix des cibles antigéniques

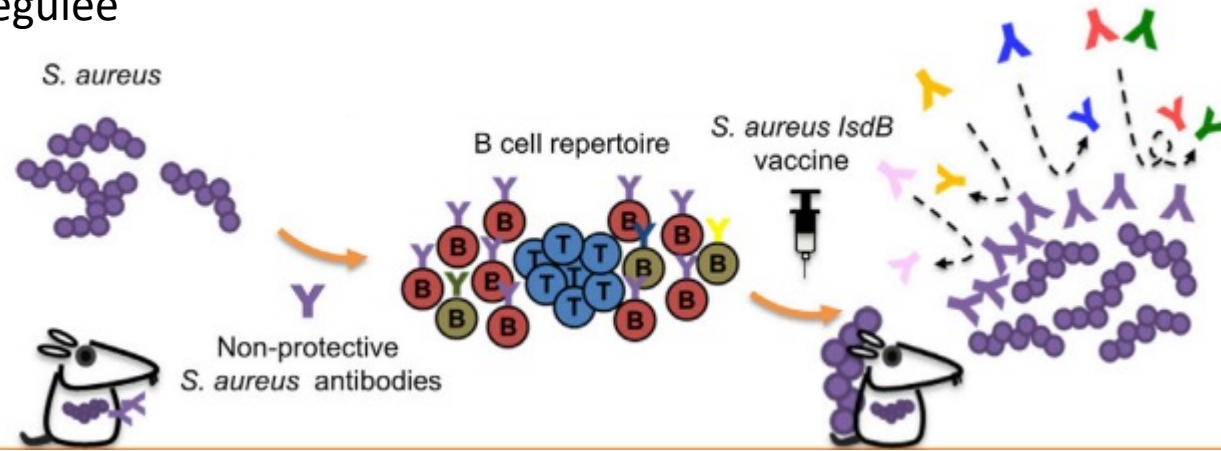
- Ag souvent uniques – Surface
- Redondance / expression régulée
 - Opsonisation inefficace
 - Agrégats
 - Blocage de la réponse spécifique ultérieure

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Ronald V. Maier^e, Wenzhong Xiao^{a,1}, and
Ronald W. Davis^{d,1}

Méconnaissance de la réponse immune

- Échappement immunitaire
- Réponse Ac ≠ corrélat de protection
- Réponse cellulaire ?

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 - Blocage de la réponse spécifique ultérieure

Méconnaissance de la réponse immune

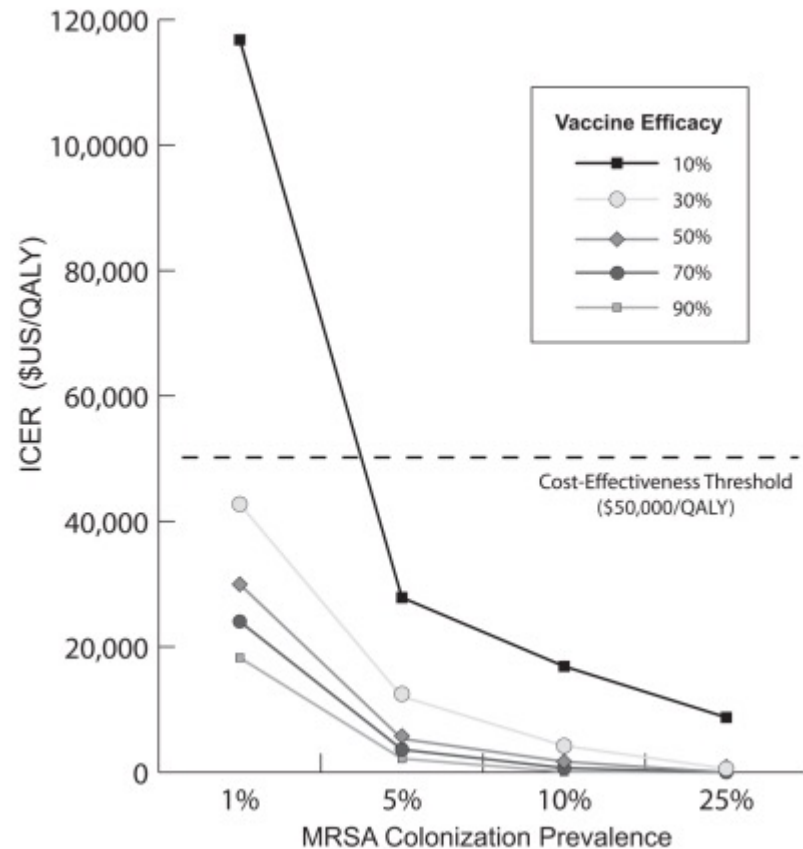
- Échappement immunitaire
- Réponse Ac ≠ corrélat de protection
- Réponse cellulaire ?

Absence de stratégie contre des infections spécifiques

Vaccination et infections sur matériel : où en est-on ?

Staphylococcus aureus Vaccine for Orthopedic Patients: An Economic Model and Analysis

Bruce Y. Lee, MD, MBA^{1,2,3}, Ann E. Wiringa, BS^{1,2,3}, Rachel R. Bailey, MPH^{1,2,3}, G. Jonathan Lewis, DO, MPH^{1,2,3}, Jared Feura^{1,2,3}, and Robert R. Muder, MD⁴



Vaccines for healthcare associated infections without vaccine prevention to date

Gagneux-Brunon Amandine^{a,b,c,*}, Julie Gagnaire^{c,d}, Carole Pelissier^e, Berthelot Philippe^{b,c,d}, Botelho-Nevers Elisabeth^{a,b,c}

Potential Vaccine platforms	Candidates	Company	Phase of clinical development
Recombinant proteins (glycoconjugation)	StaphVax	Nabi pharmaceuticals	Stopped
	V710	Merck	Stopped
	SA4Ag	Pfizer	Stopped in phase IIb
	NDV-3SA5Ag (adjuvanted)	Novadigm therapeutics	Phase II
	STEB-Vax	GSK	Phase I/II
	rFSAV	Integrated Biotherapeutics	Phase I completed
	IBTV02	Olymvax	Phase II
Whole cell vaccines and Live-attenuated vaccination	Lysigin and Startvac (veterinary use)	Integrated Biotherapeutics	Planned
Nucleic acid vaccines	No current candidate		
Extracellular vesicles	No current candidate		

- Cibles multi-antigéniques
- Reverse vaccinologie
- Adjuvants
- Nouvelles vectorisations
- Administration muqueuse
- Vaccins ARN
- « Convergent immunity »
- Populations cibles
- Impact du et sur le portage
- Réponse cellulaire

Staphylococcus aureus vaccine strategy: Promise and challenges

Umesh Chand, Pragnya Priyambada, Pramod Kumar Kushawaha*

Anticorps monoclonaux : une voie à explorer

Anti-Glucosaminidase IgG in Sera as a Biomarker of Host Immunity Against *Staphylococcus aureus* in Orthopaedic Surgery Patients

Nina Gedbjerg, Rachel LaRosa, Joshua G. Hunter, MD, John J. Varrone, MS, Stephen L. Kates, MD, Edward M. Schwarz, PhD, and John L. Daiss, PhD

Evidence of Neutralizing and Non-Neutralizing Anti-Glucosaminidase Antibodies in Patients With *S. Aureus* Osteomyelitis and Their Association With Clinical Outcome Following Surgery in a Clinical Pilot

Shardulendra Prasad Sherchand¹, Rajan P. Adhikari¹, Gowrishankar Muthukrishnan², Tulasikumari Kanipakala¹, John R. Owen³, Chao Xie², M. Javad Aman¹, Richard A. Proctor⁴, Edward M. Schwarz² and Stephen L. Kates^{3*}

Passive Immunization with Anti-Glucosaminidase Monoclonal Antibodies Protects Mice from Implant-Associated Osteomyelitis by Mediating Opsonophagocytosis of *Staphylococcus aureus* Megaclusters

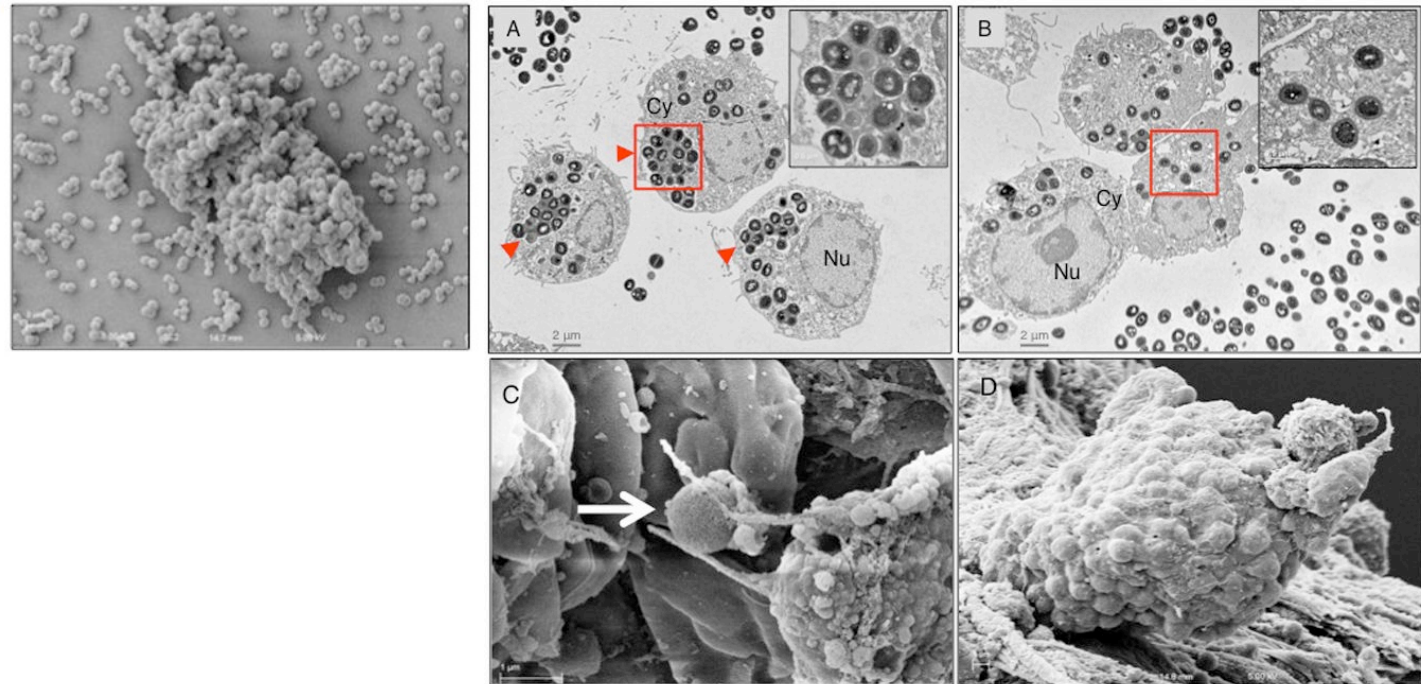
John J. Varrone^{1,2}, Karen L. de Mesy Bentley¹, Sheila N. Bello-Irizarry², Kohei Nishitani², Sarah Mack², Joshua G. Hunter², Stephen L. Kates², John L. Daiss², and Edward M. Schwarz^{1,2}

Ac anti-glucosaminidase (anti-Gmd)

Portion lytique de l'autolysine **AltA** : adhésine, internalisation, échappement immunitaire

Corrélation taux d'Ac anti-Gmd / outcome

- Modèles *in vitro* : mégaclusters, opsonisation
- Patients (≈ 300) : ostéite, PJI, DFI



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Immunotherapy Synergizes with Debridement and Antibiotic Therapy in a Murine 1-Stage Exchange Model of MRSA Implant-Associated Osteomyelitis

Noriaki Yokogawa, MD, PhD^{1,2}, Masahiro Ishikawa, MD, PhD^{1,3}, Kohei Nishitani, MD, PhD^{1,3}, Christopher A. Beck, PhD^{1,4,5}, Hiroyuki Tsuchiya, MD, PhD², Addisu Mesfin, MD^{1,5}, Stephen L. Kates, MD⁶, John L. Daiss, PhD^{1,5}, Chao Xie, MD^{1,5}, and Edward M. Schwarz,

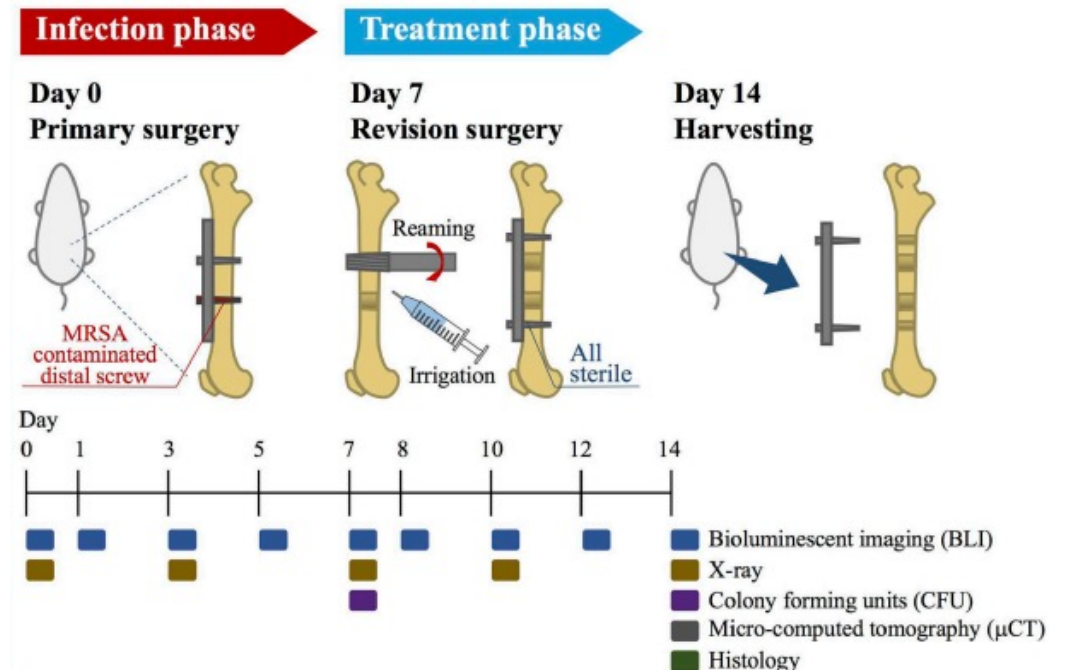
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Immunisation passive : modèles animaux



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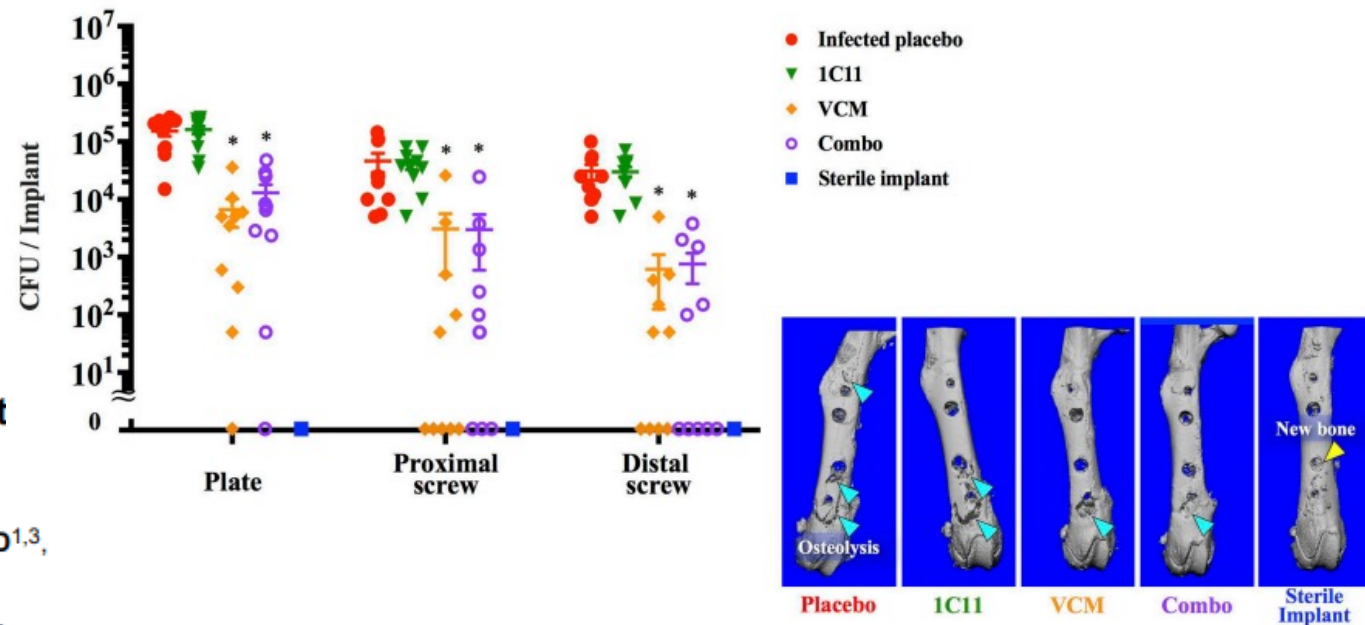
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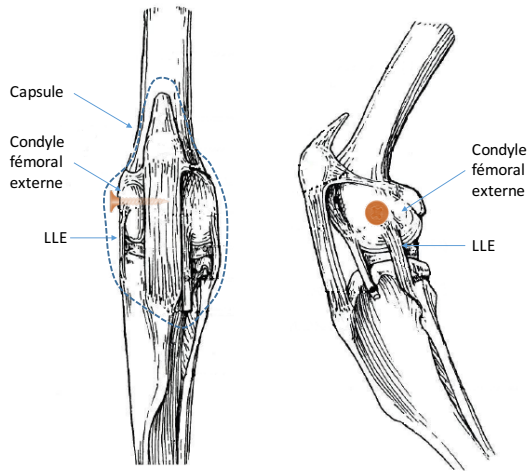
Anticorps monoclonaux : une voie à explorer

Multimechanistic Monoclonal Antibody Combination Targeting Key *Staphylococcus aureus* Virulence Determinants in a Rabbit Model of Prosthetic Joint Infection

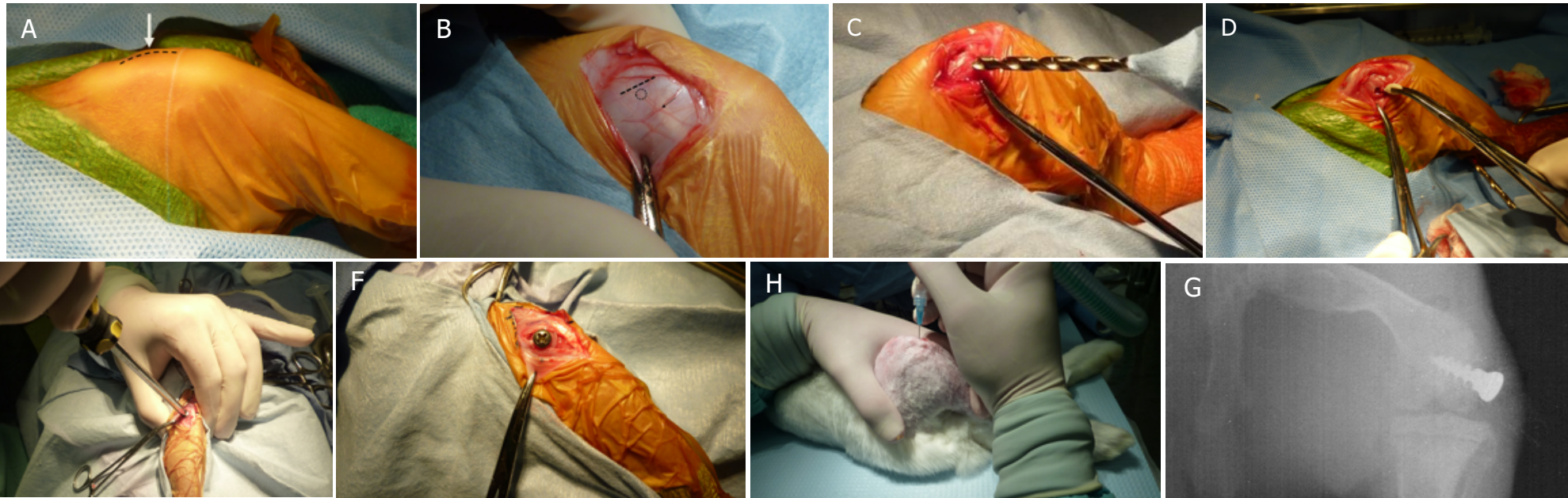
Yanjie Mao,^{a,b*} Florent Valour,^{a,c,d*} Nhu T. Q. Nguyen,^a Thien M. N. Doan,^a Holly Koelkebeck,^e Christopher Richardson,^f Lily I. Cheng,^e Bret R. Sellman,^f Christine Tkaczyk,^f Binh An Diep^a

AZD6389

- **Hla** → réponse inflammatoire et destruction tissulaire
- **ClfA** → adhésine associée aux IOA
- **leukocidins** (LukSF, LukED, HlgAB, and HlgBC) → formes sévères et destructives



Injection d'Ac spécifiques 12h avant la chirurgie
versus IgIV



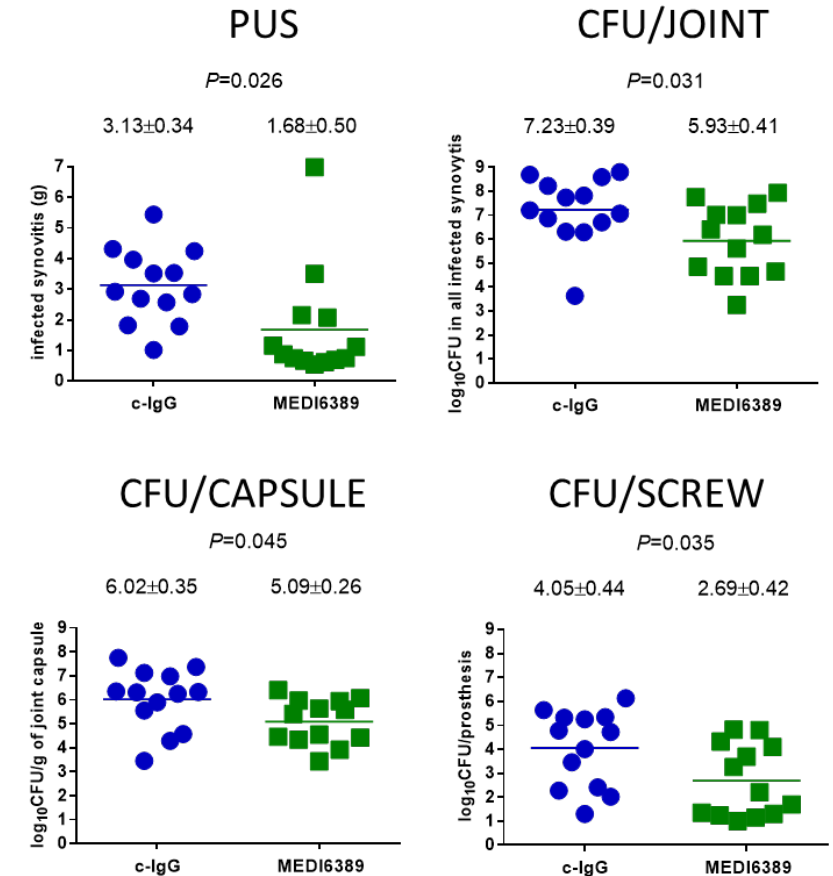
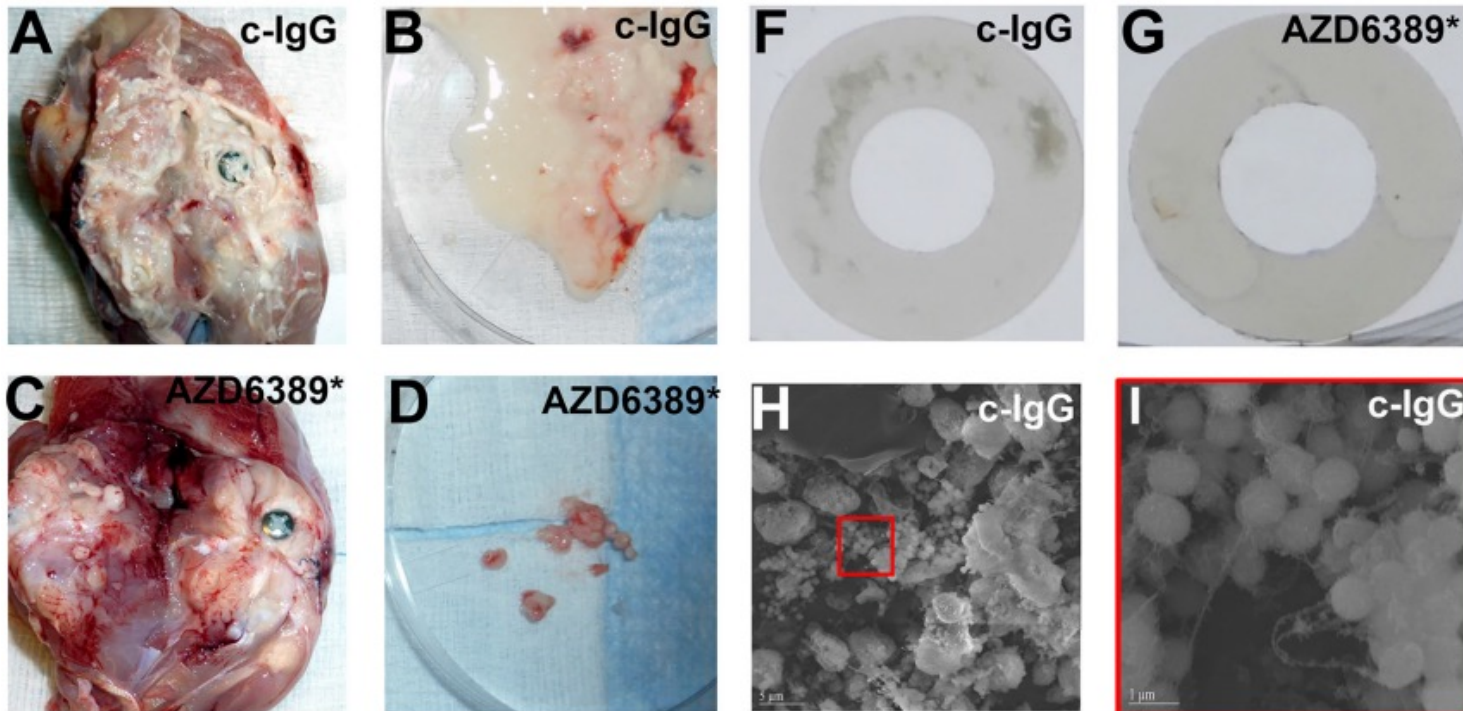
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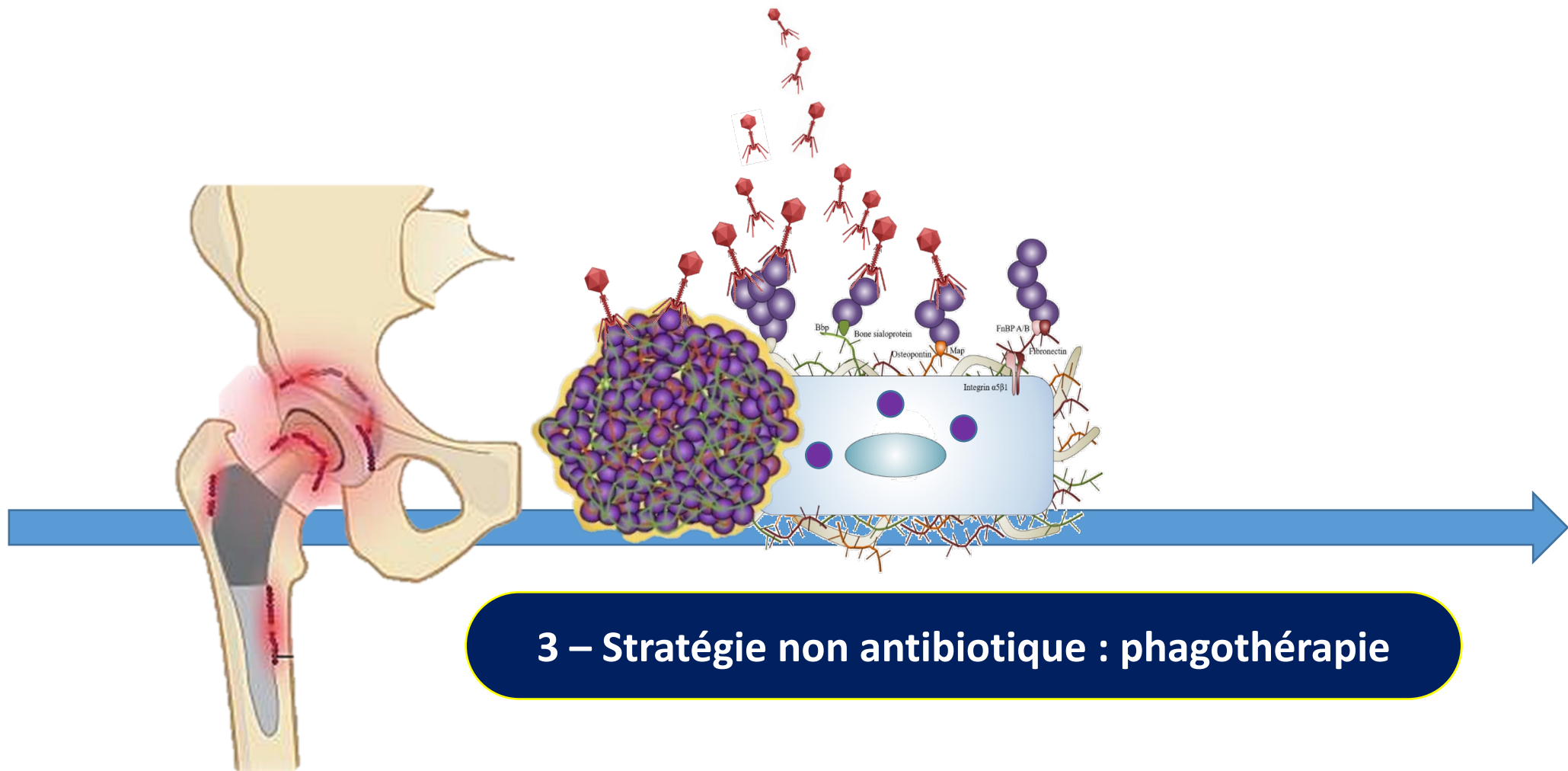
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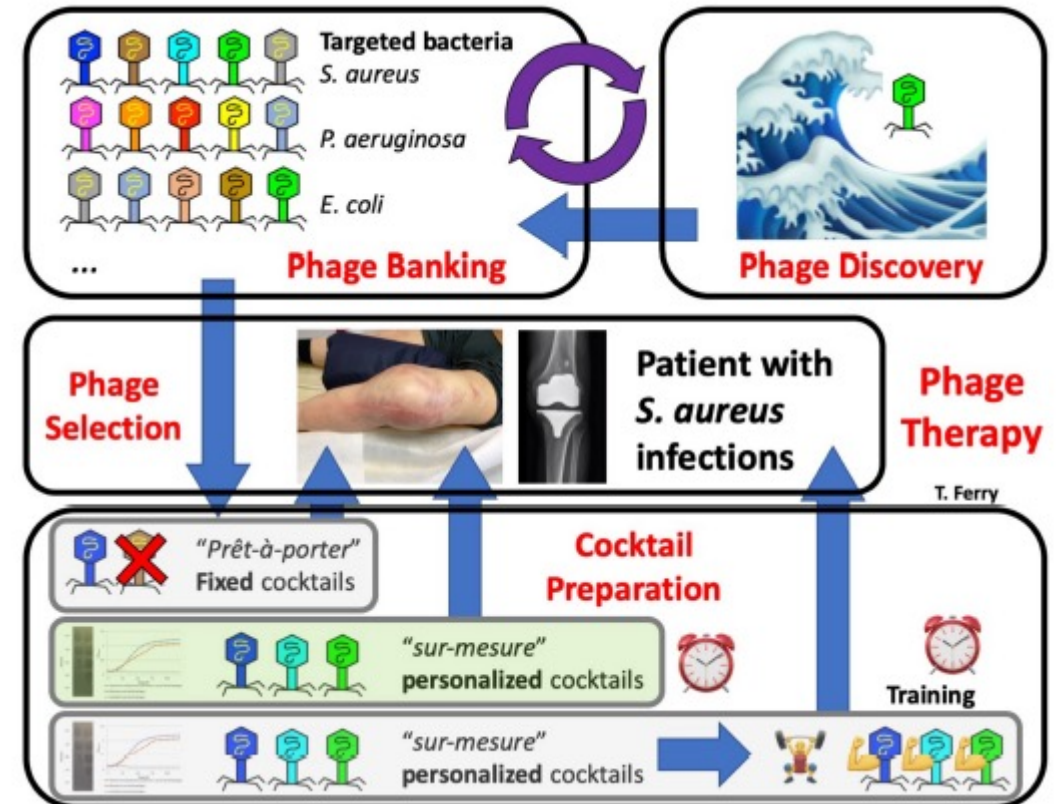
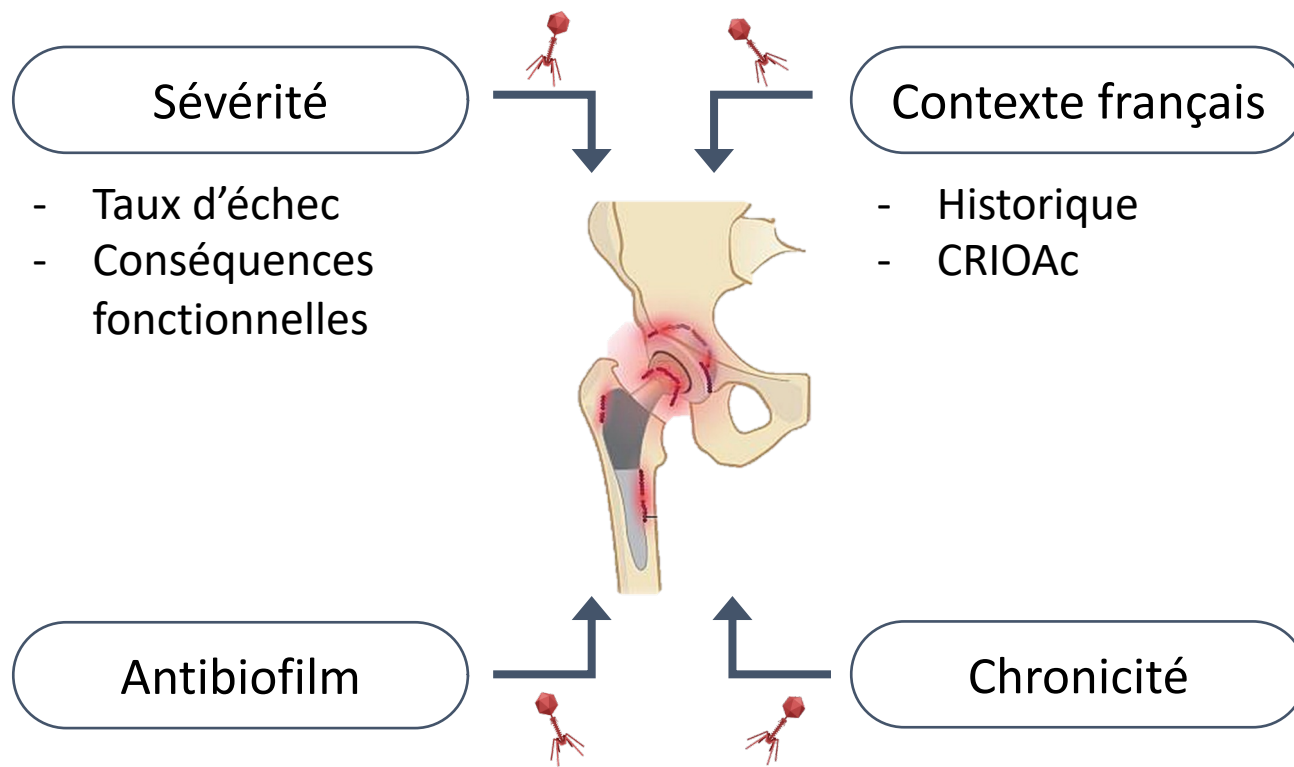




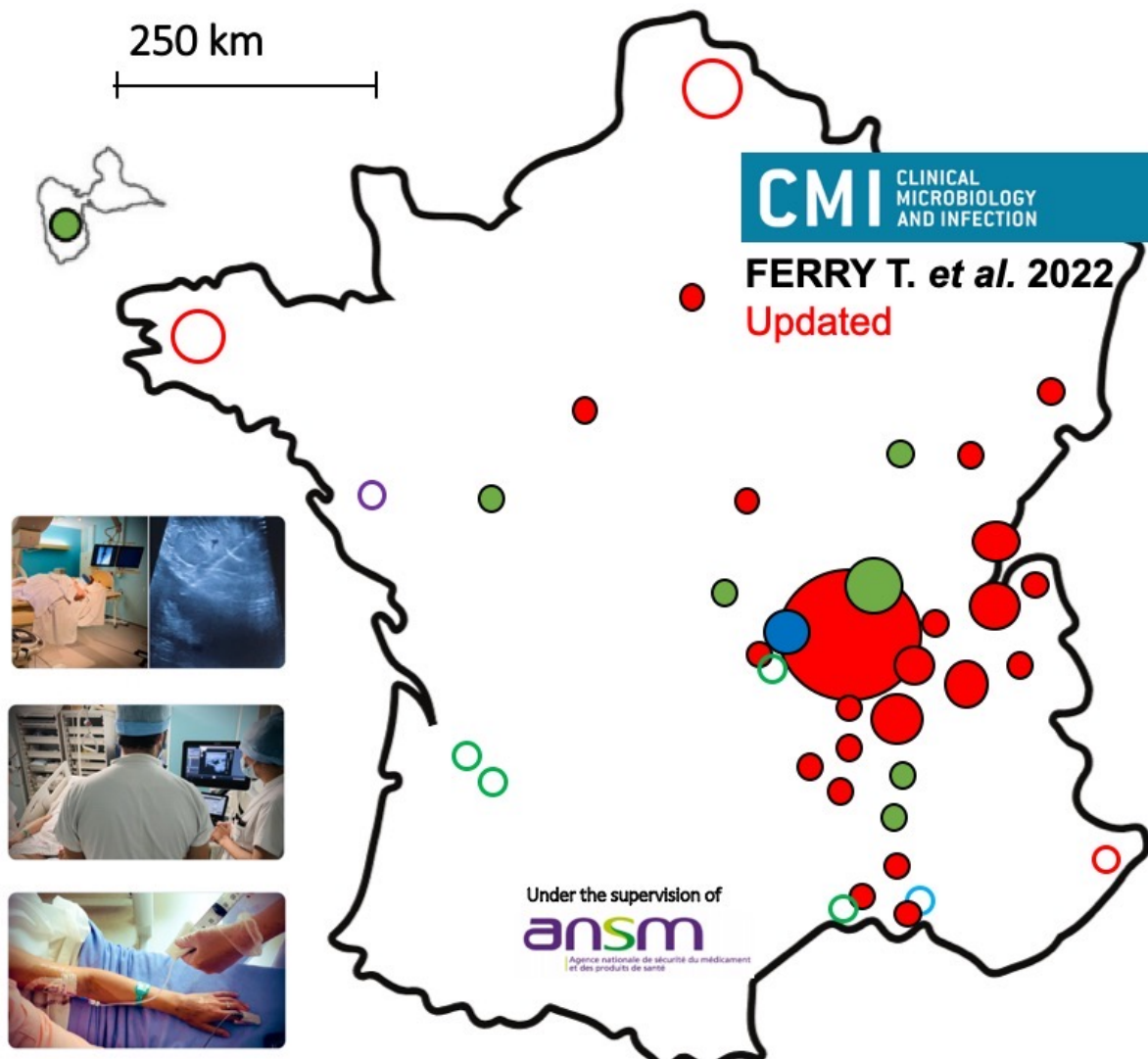
3 – Stratégie non antibiotique : phagothérapie

Past and Future of Phage Therapy and Phage-Derived Proteins in Patients with Bone and Joint Infection

Tristan Ferry ^{1,2,3,4,*}, Camille Kolenda ^{1,2,3,4}, Thomas Briot ¹, Aubin Souche ^{1,2,3,4}, Sébastien Lustig ^{1,2,3}, Jérôme Josse ^{1,2,3,4}, Cécile Batailler ^{1,2,3}, Fabrice Pirot ^{1,2,5}, Mathieu Medina ¹, Gilles Leboucher ¹, Frédéric Laurent ^{1,2,3,4}, on behalf of the Lyon BJI Study Group [†] and on behalf of the PHAGEinLYON Study Group [‡]



Implementation of a Phage Therapy Center in a CRIOAc



55 patients in Lyon since 2017
~80% of the whole patients treated in France



- 51 with phages from PHERECYDES PHARMA
- 4 with phages from MHKA HMRA



- 43 **BJI** (including 35 **PJI**)
- 9 **endocarditis/vascular graft**
- 3 **lung infections** (VAP + bacteremia, pneumonia in lung graft bronchiectasia, cystic fibrosis exacerbation)

+ 13 patients managed outside Lyon ○
including 1 in and 1 in

●○ **BJI** ●○ **Endocarditis** ●○ **Pneumonia**

PhagoDAIR I

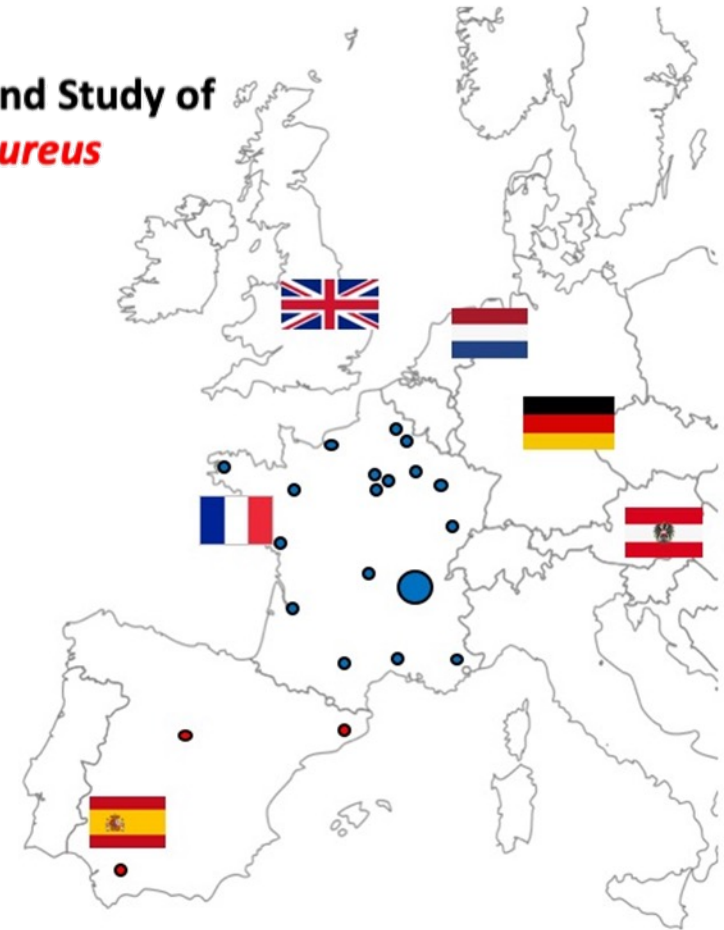
A Pilot, Multicenter, Randomized, Non-Comparative, Double-Blind Study of Phage Therapy in Patients with Hip or Knee PJI due to *S. aureus* Treated with DAIR and Antibiotic Therapy

Inclusion Criteria

1. *S. aureus* monomicrobial knee or hip PJI with clinical signs of infection with indication of DAIR and **Suppressive Antibiotics Therapy (SAT)**.
2. Phagogram displaying the susceptibility of the strain to at least one of the anti-*Staphylococcus aureus* bacteriophages

Primary Objective

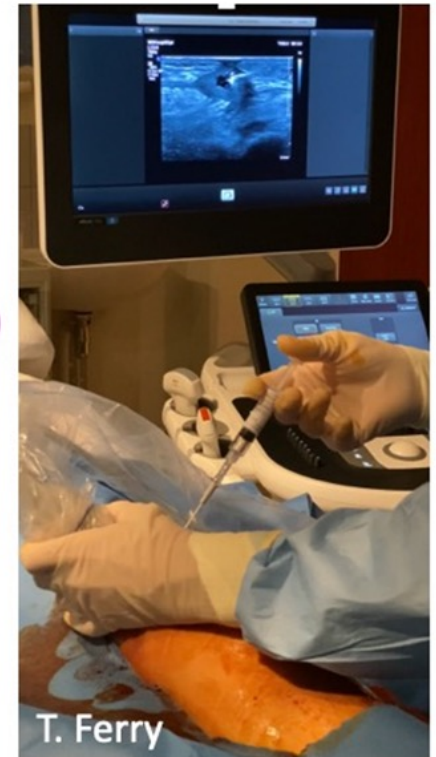
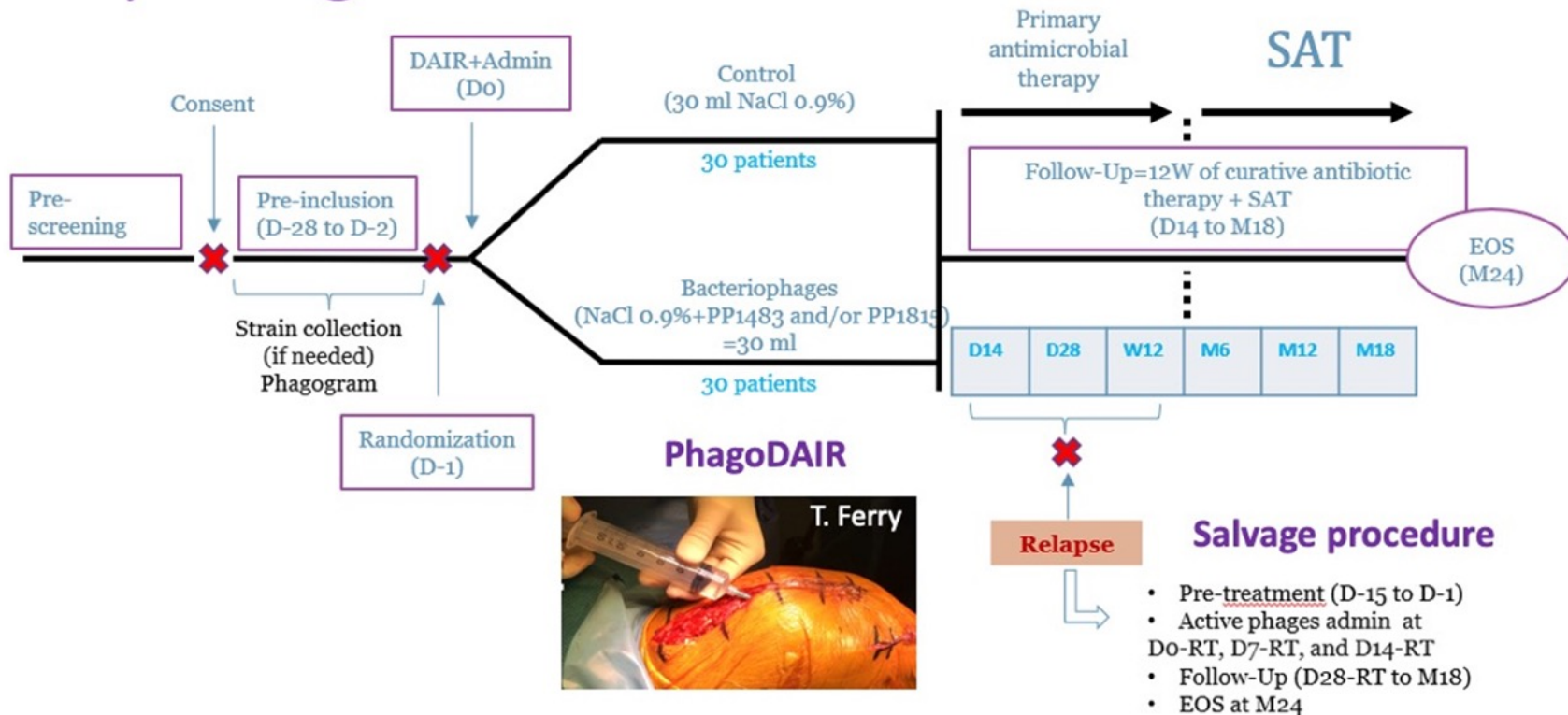
To estimate the **rate of clinical control of infection at Week 12±2** which will allow to calculate the sample size for future comparative studies.



PhagoDAIR I

A Pilot, Multicenter, Randomized, Non-Comparative, Double-Blind Study of Phage Therapy in Patients with Hip or Knee PJI due to *S. aureus* Treated with DAIR and Antibiotic Therapy

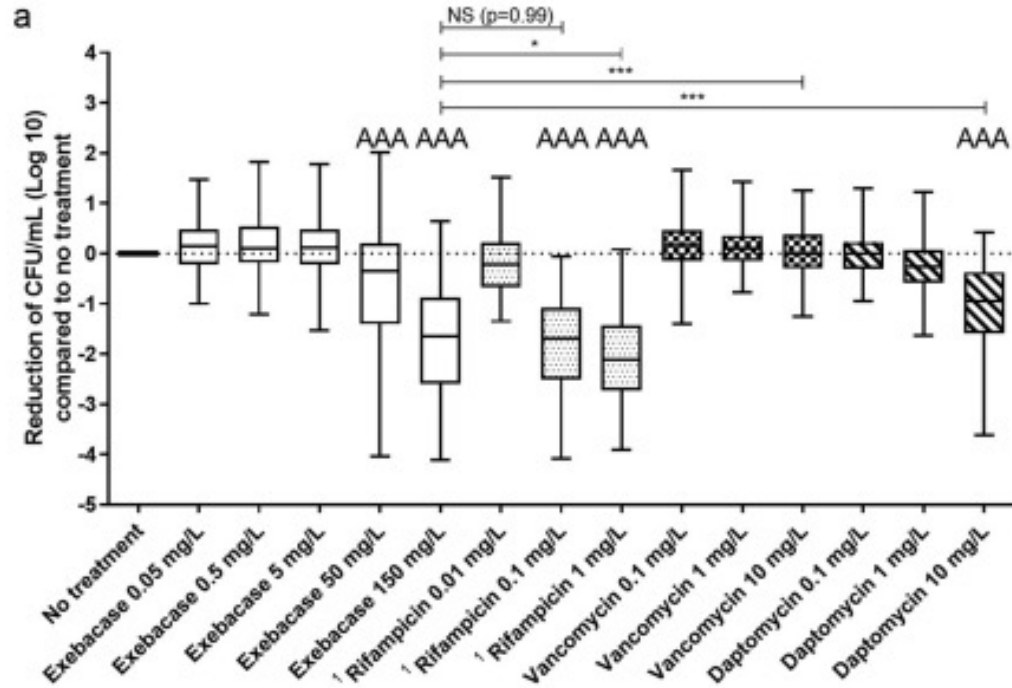
Study design



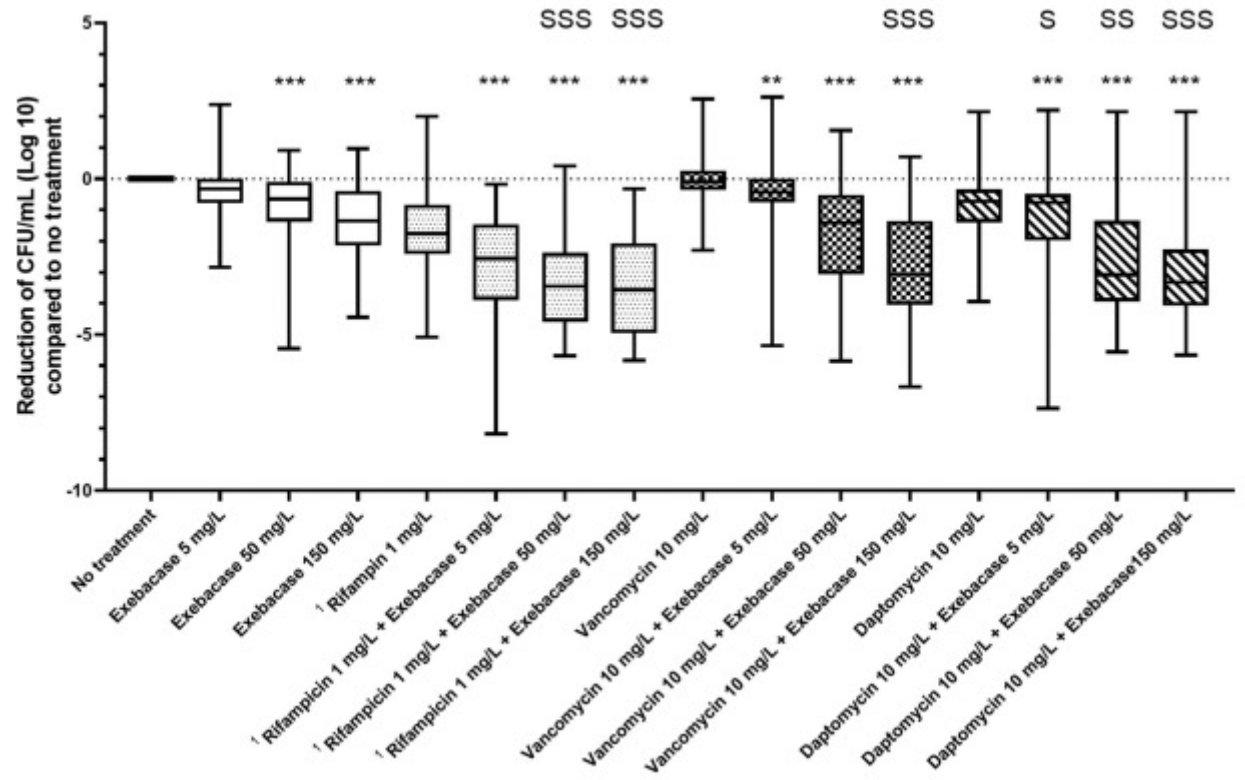
Activity of Exebacase (CF-301) against Biofilms Formed by *Staphylococcus epidermidis* Strains Isolated from Prosthetic Joint Infections

Aubin Souche,^{a,b} Camille Kolenda,^{a,b} Jordan Teoli,^d Raymond Schuch,^c Tristan Ferry,^{a,d,e,f} Frédéric Laurent,^{a,b,d,e} Jérôme Josse^{a,d,e}

19 *S. epidermidis* clinical strains isolated from PJI



Autre thérapie
non conventionnelle
≠ Phagothérapie



Expérience compassionnelle @
15 patients traités



Arthroscopic “Debridement and Implant Retention” With Local Administration of Exebacase (Lysin CF-301) Followed by Suppressive Tedizolid as Salvage Therapy in Elderly Patients for Relapsing Multidrug-Resistant *S. epidermidis* Prosthetic Knee Infection

Tristan Ferry^{1,2,3,4*}, Cécile Batailler^{2,3,5}, Aubin Souche^{2,3,4,6}, Cara Cassino⁷, Christian Chidiac^{1,2,3}, Thomas Perpoint^{1,3}, Claire le Corvaisier⁸, Jérôme Josse^{2,3,4,6}, Romain Gaillard⁵, Julien Roger⁵, Camille Kolenda^{2,3,4,6}, Sébastien Lustig^{2,3,5}, Frédéric Laurent^{2,3,4,6} and the Lyon BJI Study Group

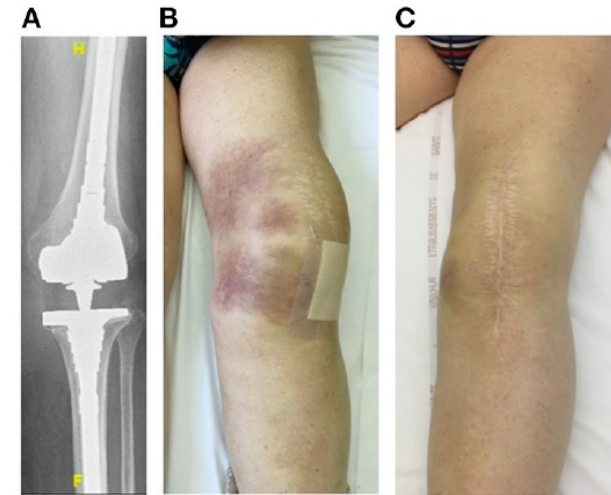


FIGURE 2 | Patient 2 was a 79-year-old man with history of severe ankylosing spondylitis under corticosteroids who presented a chronic left PKI due to *S. hominis* that was treated with a one-stage exchange. A postoperative infection occurred due to MDR *S. epidermidis* (02/12/3013) treated with open DAIR and SAT (minocycline followed by cotrimoxazole due to occurrence of a clinical relapse under minocycline therapy; 10/11/2013). He had a cementless revision prosthesis with long stem with no loosening (A) and clinical signs of septic arthritis (large joint effusion, pain during mobilization, skin inflammation without sinus tract) (B) and *S. epidermidis* grew from joint puncture (9/13/2018). He was treated according to the LysinDAIR procedure (08/11/2018), and a septic collection communicating with the joint was drained. He received daptomycin intravenously and linezolid orally and experienced eosinophilic pneumonia attributed to daptomycin and diarrhea attributed to linezolid. Then, tedizolid was prescribed as SAT, and the outcome was favorable with disappearance of the clinical signs of septic arthritis (C). At 12 months, as a mild joint effusion persisted, a joint puncture was performed, and surprisingly, *S. epidermidis* was still present in culture. At the time of writing (16 months of follow-up after the LysinDAIR procedure), the clinical outcome was still favorable under tedizolid therapy, and the patient was able to resume golf.



Essai thérapeutique monocentrique

Infection PTG à staphylocoques

Traitement par arthroscopie + Lysines de phages

3 mois de traitement antibiotiques

Recrutement régional et extrarégional et
suivi conjoint possible

CF-301-108

Randomised

Clinical Trial

Press release April 2023

**CONTRAFECT ANNOUNCES INITIATION OF A
PHASE 1B/2 STUDY OF EXEBACASE IN
PATIENTS WITH CHRONIC PROSTHETIC JOINT
INFECTIONS OF THE KNEE**



- Mission confiée en février 2023 au CRIOAc Lyon (Pr. T. Ferry) par la DGOS
- RCP en ligne via TEAMS®
- Remplir un fichier powerpoint (à partir d'un template) et convenir d'un RDV de passage
- Supervision ANSM via **RCP Phagothérapie @HCL** pour les indications jugées pertinentes rentrant dans le cadre de traitements compassionnels ou d'essais thérapeutiques



DAIR / 1 temps / 2 temps

Immunothérapie

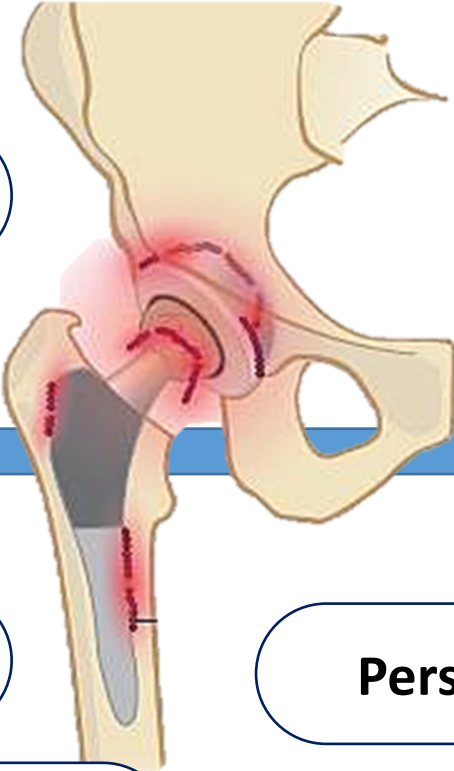
Nouveaux antibiotiques

Protéomique

Biomarqueurs

Phages

Durées de traitement



Prophylaxie

Antibiothérapie locale

Persisters

Substituts osseux

Coating

Biomatériaux

Biologie moléculaire

Laboratoire

**DON'T
MAKE ME
USE MY
ORTHOPEDIC
SURGEON
VOICE**



9^{ème} journée CRIOAc Lyon

Mardi 27 juin 2023



Présentiel (Hôpital de la Croix-Rousse Lyon) / Distanciel
Inscriptions : www.ioa.univ-lyon1.fr

Nouveautés Labellisation DGOS 2023-2028

Nouveautés diagnostiques

Reco « Arthrites septiques »

**Essai thérapeutique
CONVICTION**

Phagothérapie

**IOA chez les patients
traumatisés balistiques**

**Essai thérapeutique
SINBIOSE-H**