

42^e

RÉUNION INTERDISCIPLINAIRE DE
CHIMIOTHÉRAPIE ANTI-INFECTIEUSE

LUNDI 12 & MARDI 13
DÉCEMBRE 2022

PALAIS DES CONGRÈS • PARIS



RICAI

Phagothérapie dans différentes indications cliniques

Tristan Ferry, MD, PhD

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 @FerryLyon 

Infectious and Tropical Diseases Unit, Croix-Rousse Hospital, Hospices Civils de Lyon, Claude Bernard Lyon1 University, Lyon
Centre International de Recherche en Infectiologie, CIRI, Inserm U1111, CNRS UMR5308, ENS de Lyon, UCBL1, Lyon, France
Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

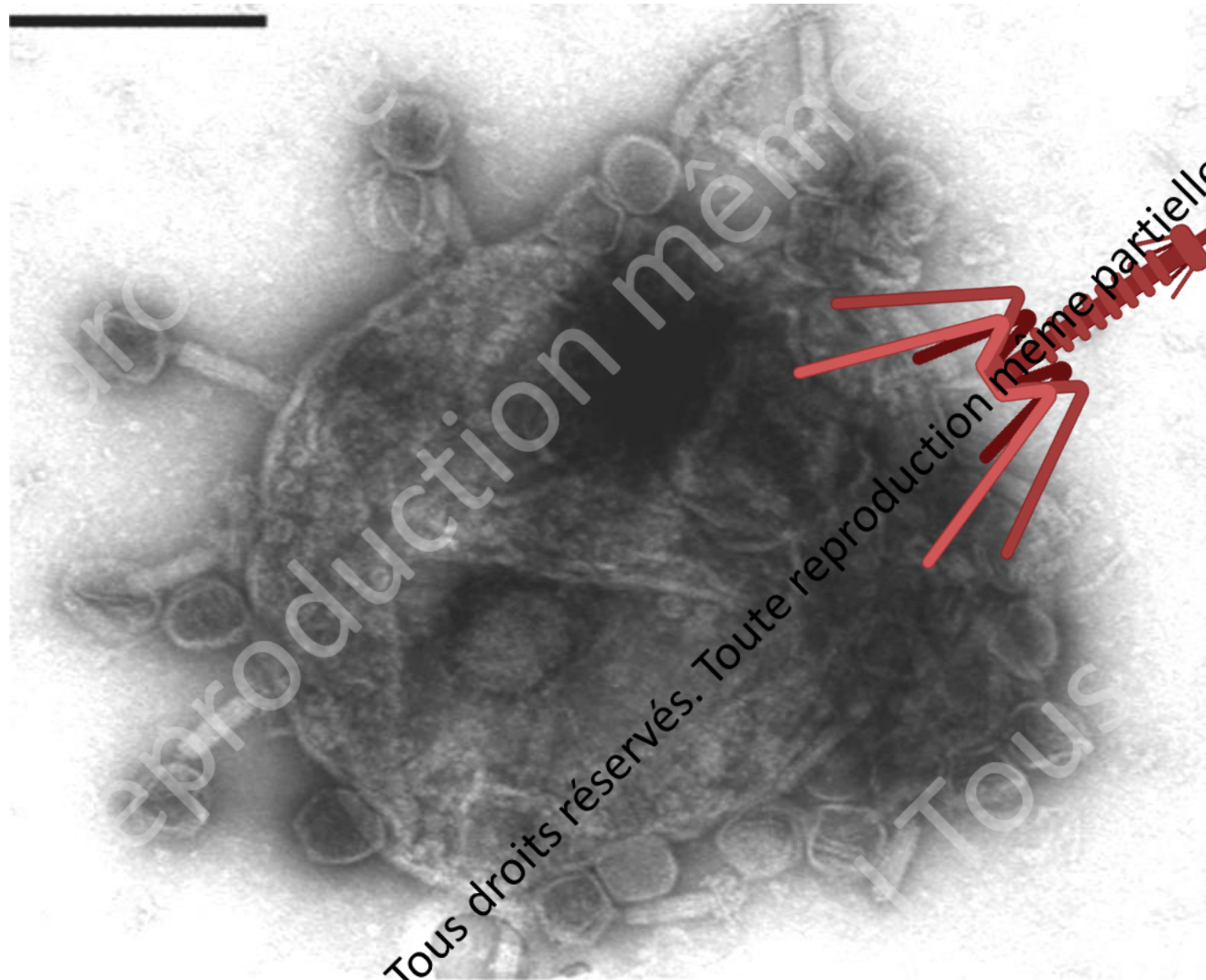
Président du Comité Scientifique des CRIOAc 2017-2022



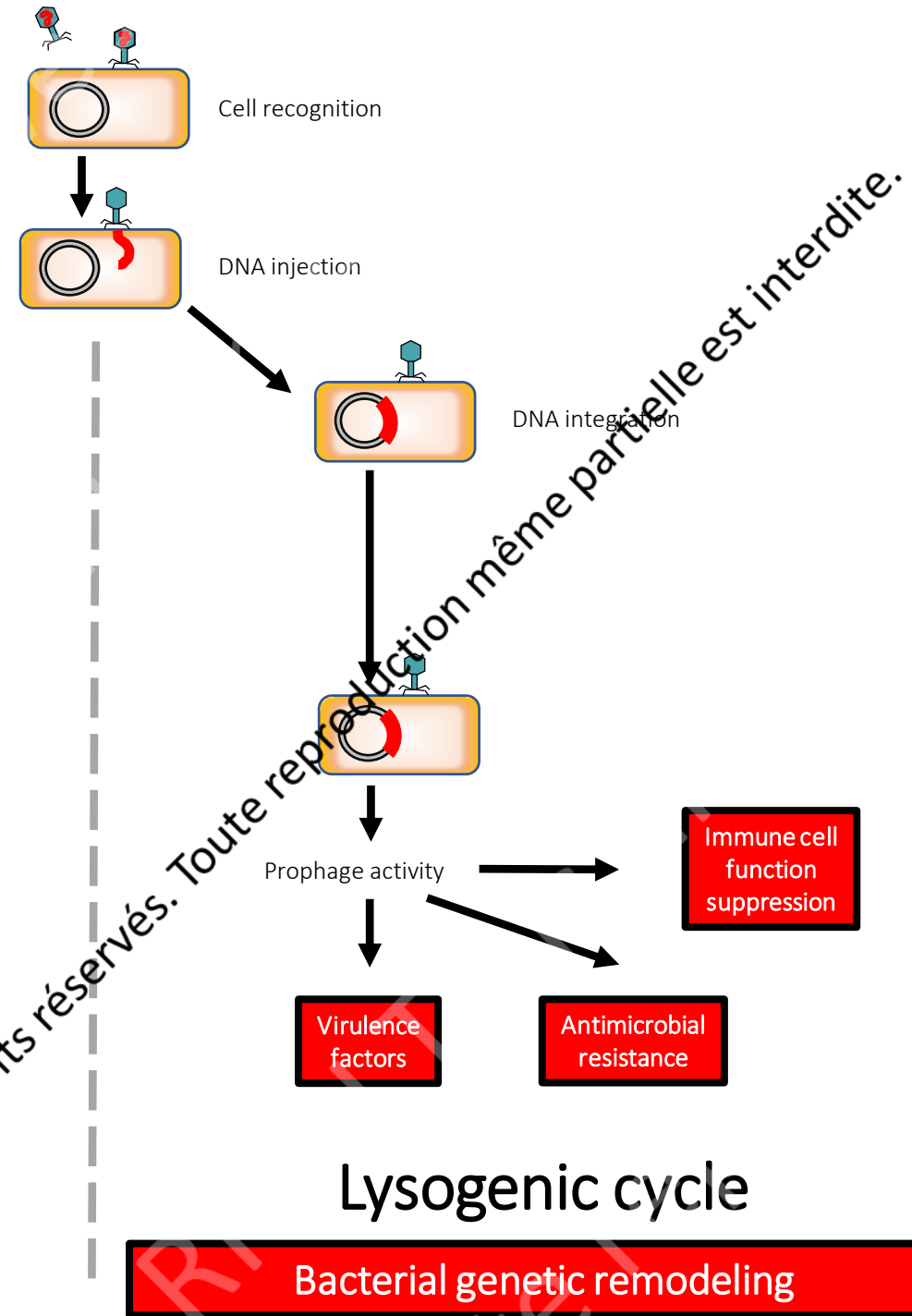
PHAGEⁱⁿLYON

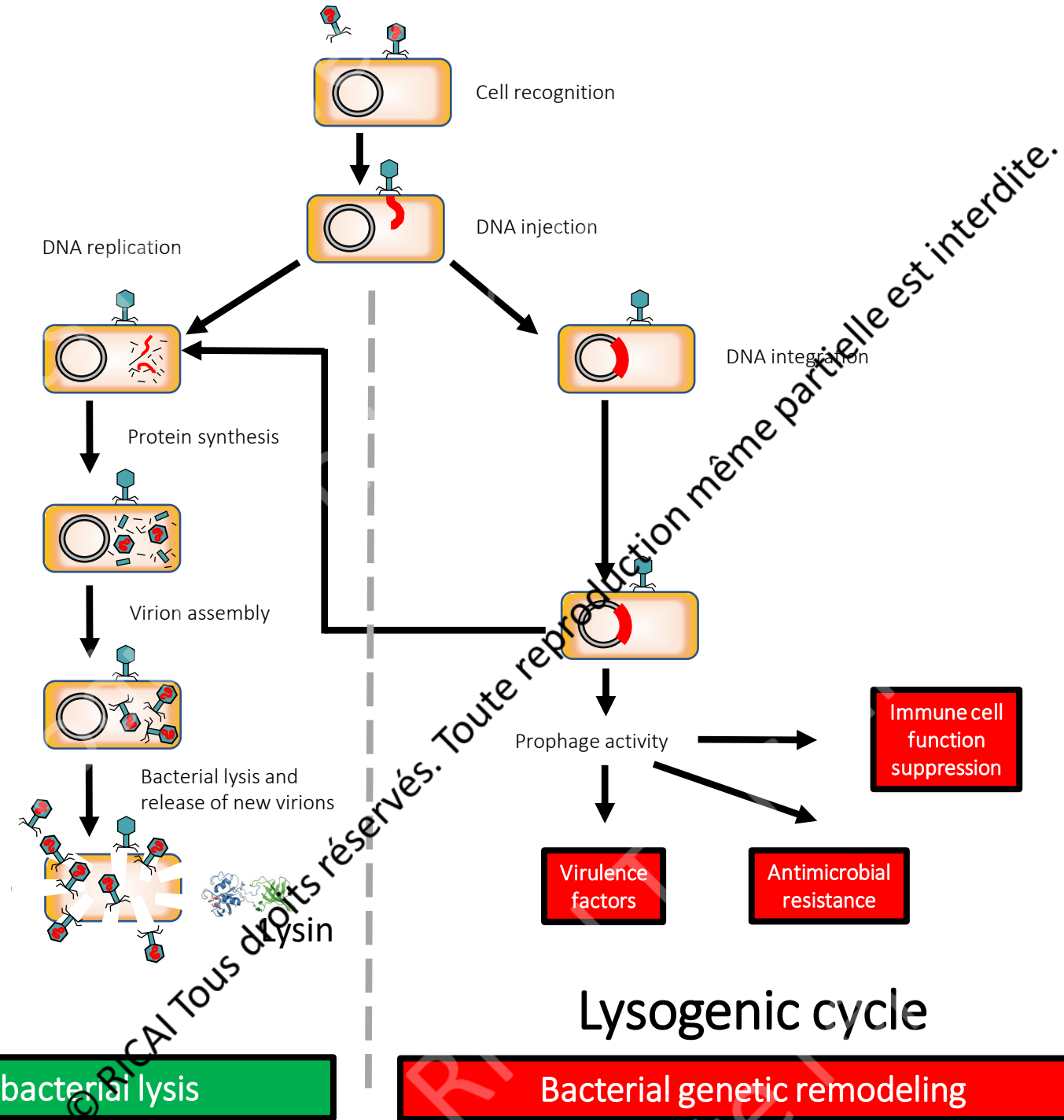


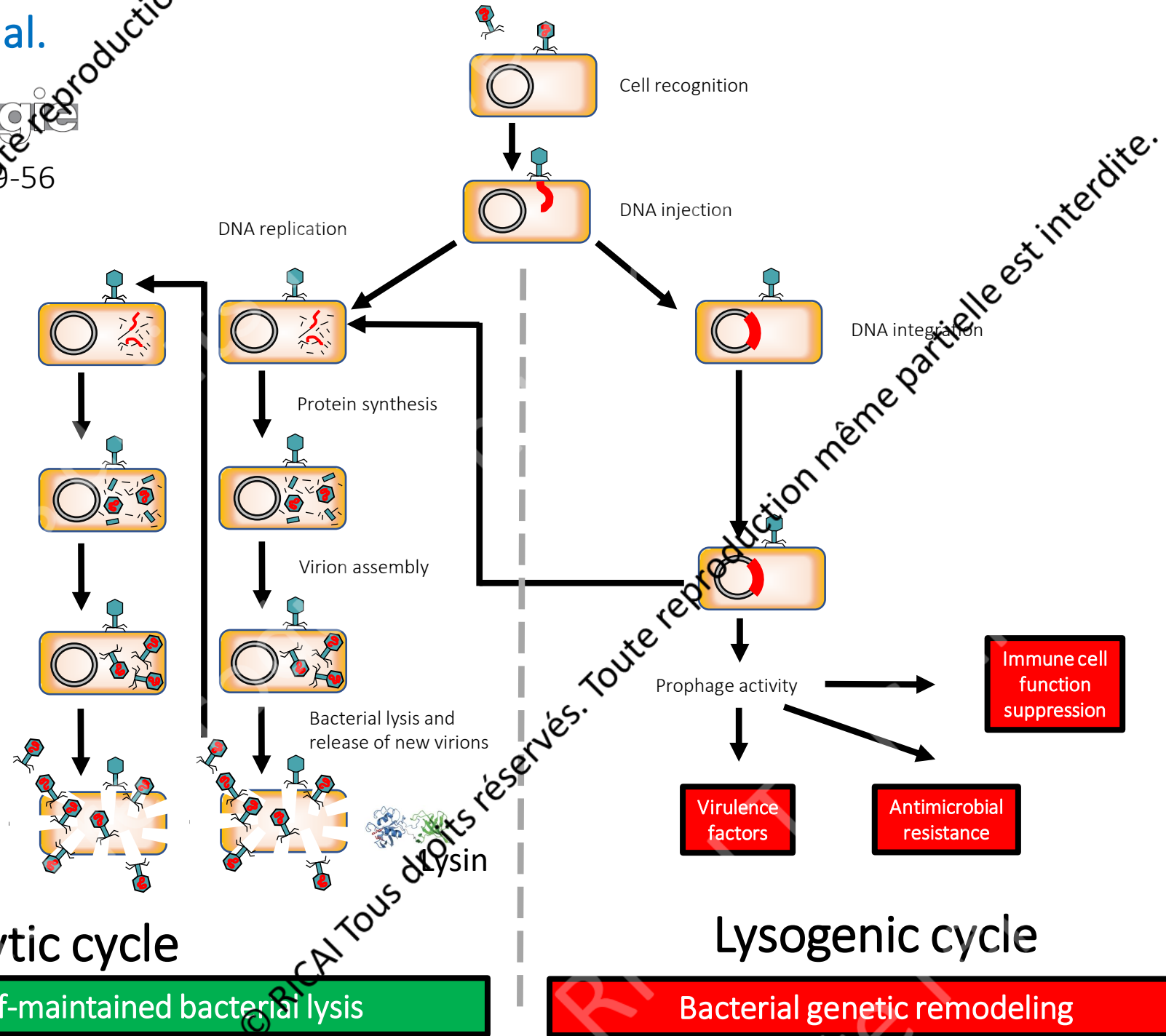
Bacteria have also their pandemics!

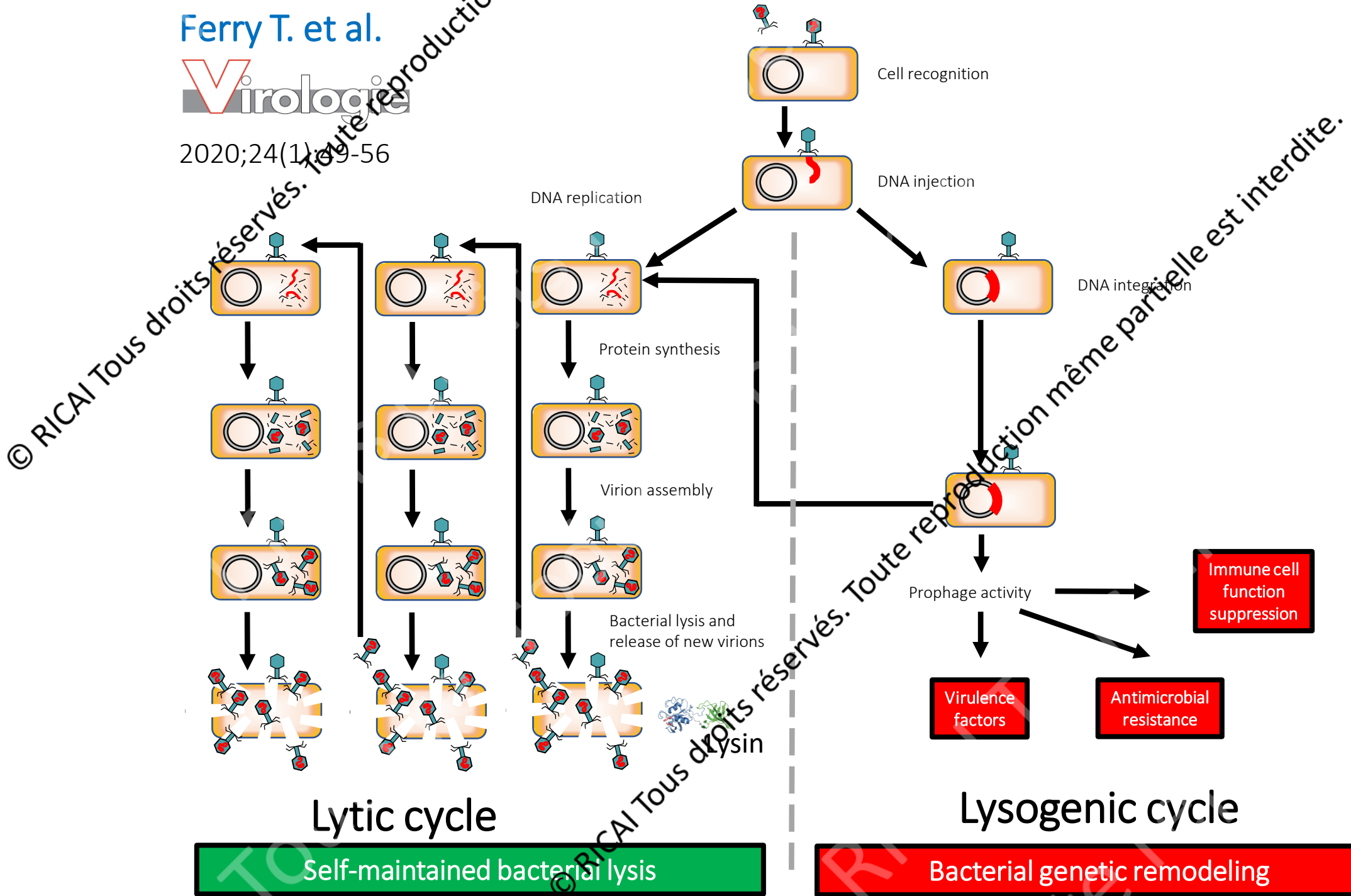


Merrishvili et al. *PLoS ONE* 2009



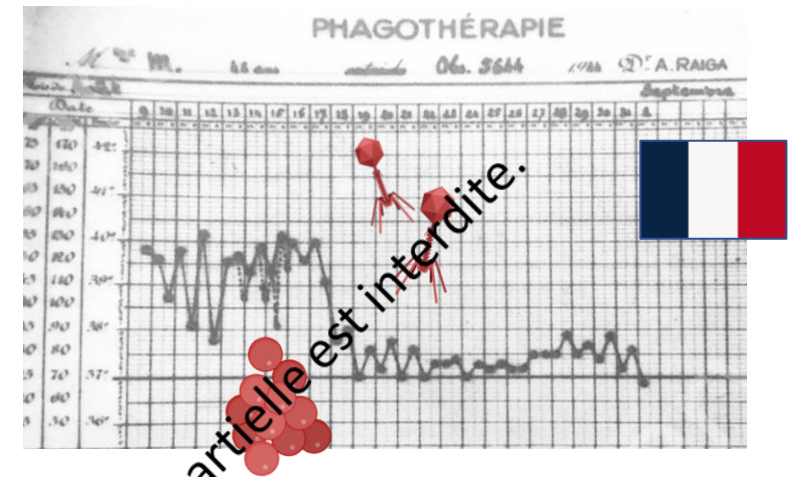






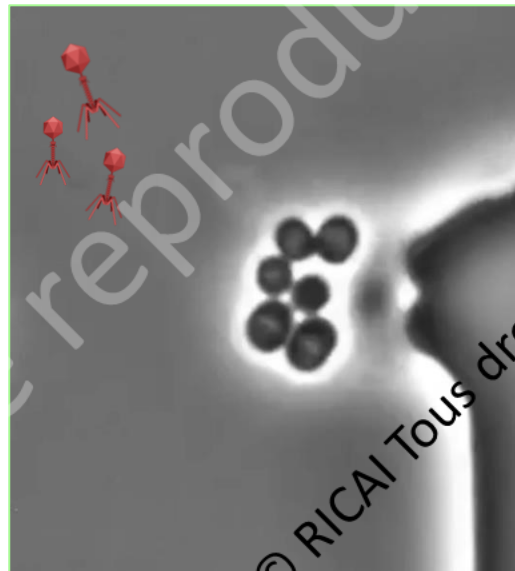
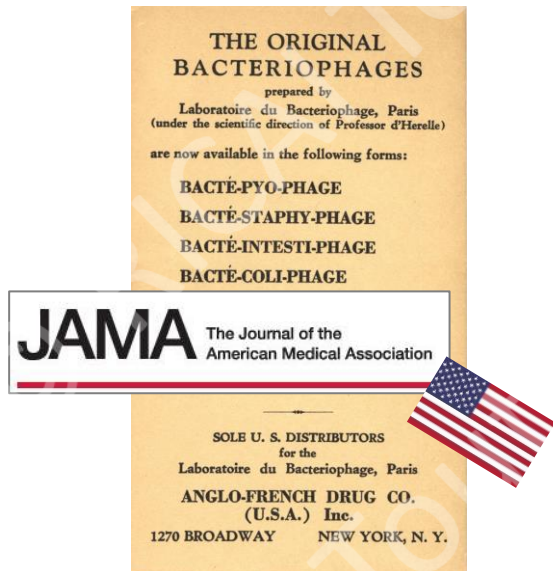
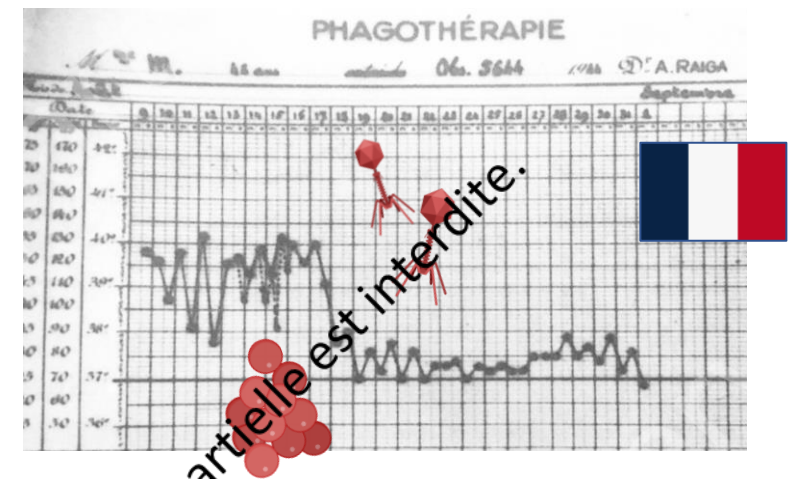
Phage therapy is fascinating

- Viral therapy for bacterial infections
- Story of phage therapy is connected to worldwide geopolitical events



Phage therapy is fascinating

- Viral therapy for bacterial infections
- Story of phage therapy is connected to worldwide geopolitical events
- Potential incredible preclinical efficacy
- Failure to implement phage therapy in the west



S. aureus being lysed
by the Sa2 phage

Bacterial DNA
appeared in green

Courtesy Pascal Maguin
Luciano Marraffini Lab

THE ROCKEFELLER UNIVERSITY



Previous clinical trials have not « failed »

- Most of them were phase I/IIa/IIb and not phase III
- Phages are particular anti-infective agents (≠ antibiotics)
- Need a specific purification process
- Purified phages or phage cocktails are potentially not stable during time
- High specificity of phages
- Potential need for a phagogram (like antibiogram) before treatment



Contemporary

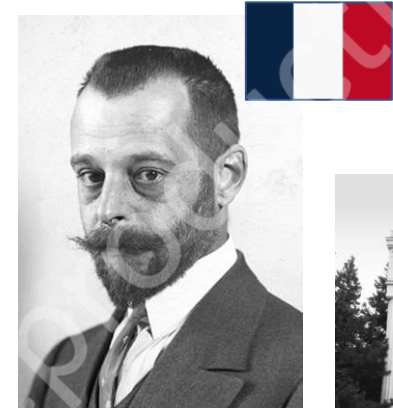
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Don't forget the lessons of the past

Respect the experience of the East



T. FERRY



KEEP
CALM
AND USE

PHARMACEUTICAL
GRADE
PHAGES

PHAGE
20
THERAPY



ESCMID MANAGING INFECTIONS
PROMOTING SCIENCE



ESGNTA
ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY
European Society of Clinical Microbiology and Infectious Diseases

Elected Executive Committee:

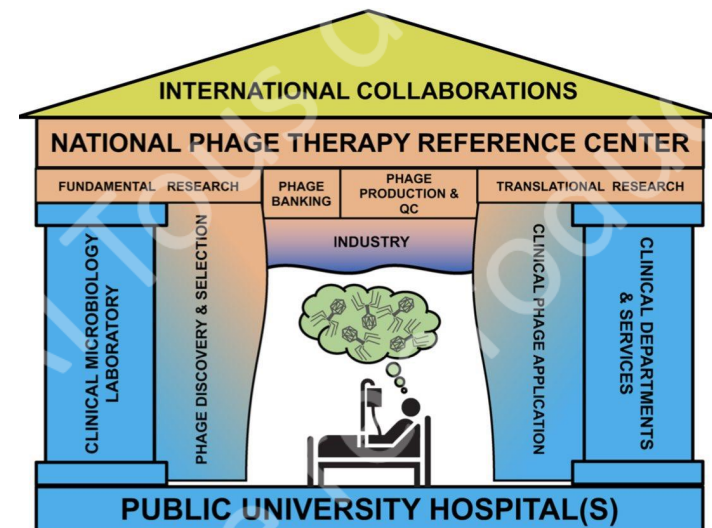
Ran Nir-Paz, Israël

Jean-Paul Pirnay, Belgium

Clinical officer: Tristan Ferry, France

Shawna Mc Callin, Switzerland

Zuzanna Drulis-kawa, Poland

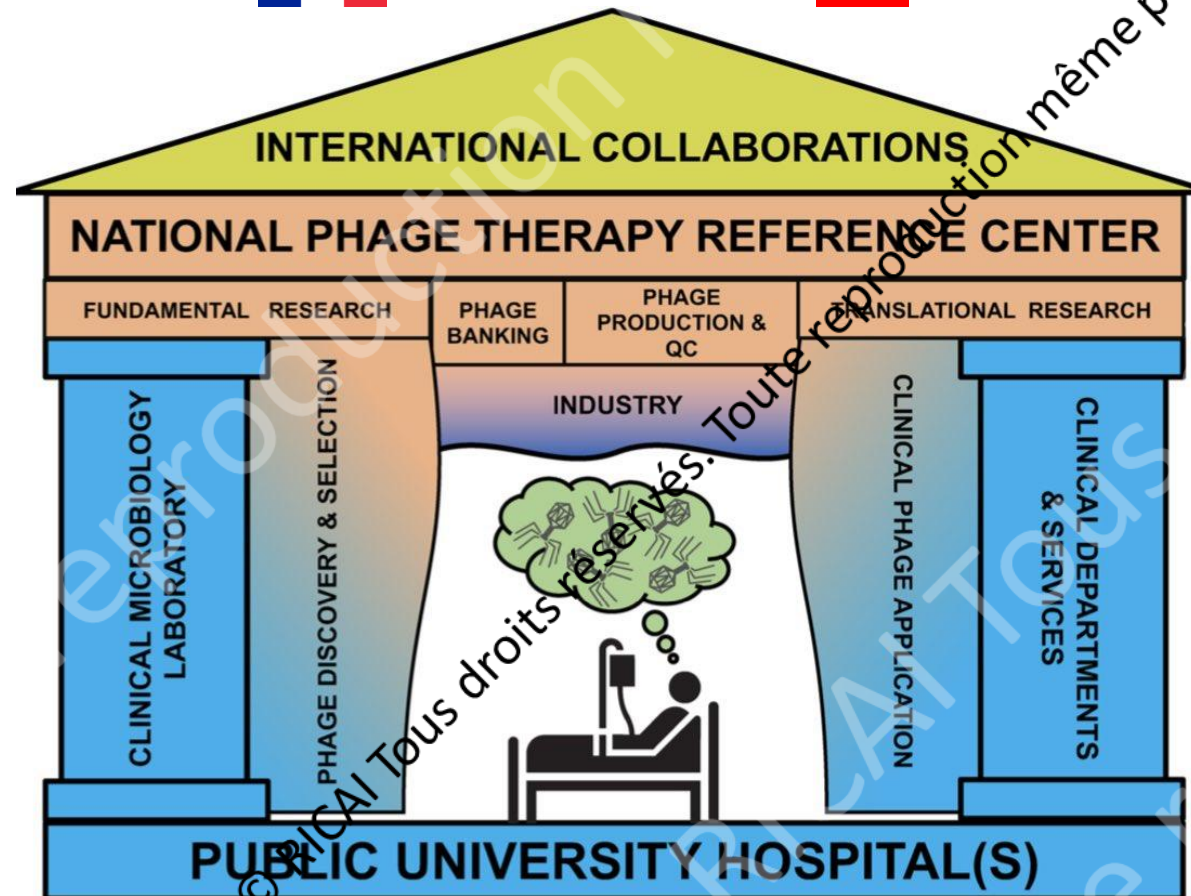
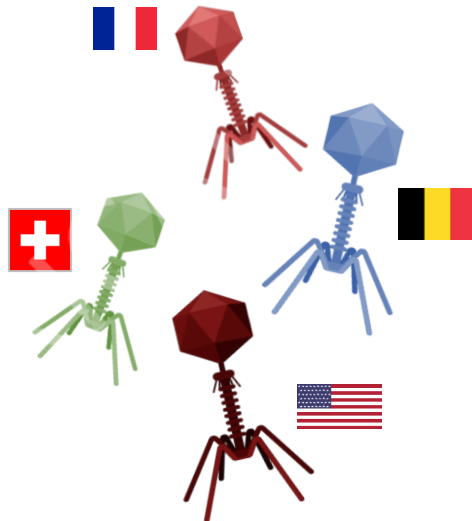


Recent progress toward the implementation of phage therapy in Western medicine

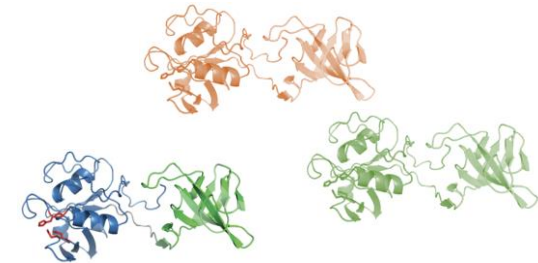
Jean-Paul Pirnay^{1,†}, Tristan Ferry^{2,3,†} and Grégory Resch^{4,*,†}



Phages



Lysins



THE MYTHOLOGY
OF IMAGE THERAPY



T. FERRY

VS.

EBM
Clinical
Trials

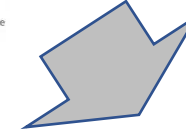
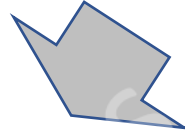


T. FERRY

Développement de la phagothérapie à Lyon



PHAGEinLYON



PHAGEinLYON *Lab*



F. Laurent

PHAG-ONE



Recherche et développement
Production de phages publiques
Développement du phagogramme

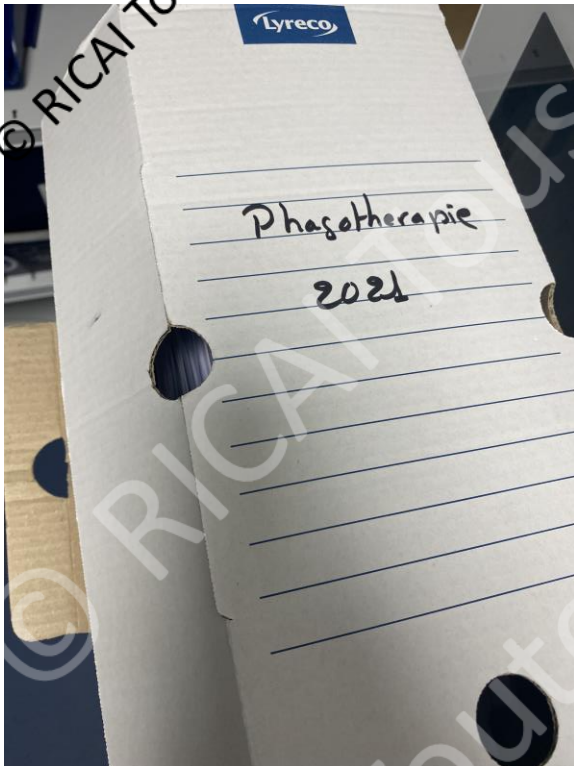
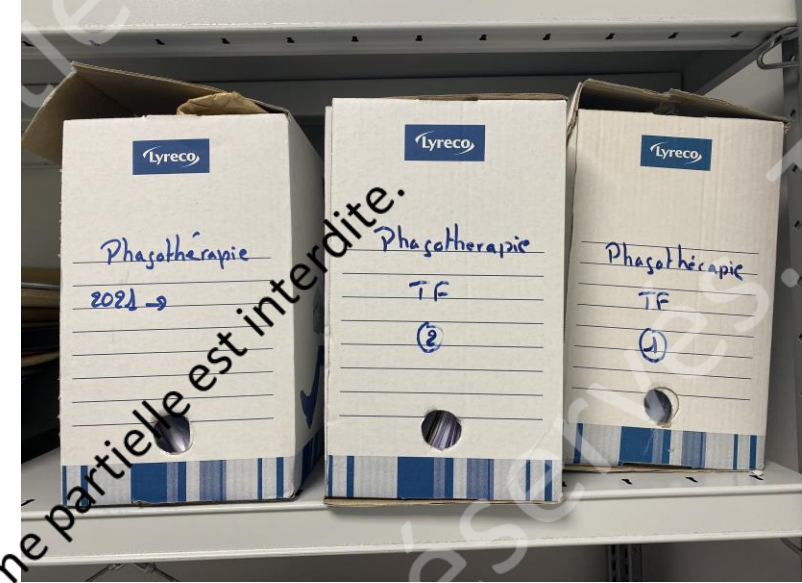
PHAGEinLYON *Clinic*



T. Ferry

Développement clinique
RCP CRIOAc Thérapies innovantes
RCP Phagothérapie
Validation des indications
Prise en charge des patients
Etudes de cohortes
Essais thérapeutiques

PHAGEⁱⁿLYON Clinic



Infections ostéoarticulaires ?

Autres indications ?

Infections en réanimation ?

Infections pulmonaires ?

Infections cardiovasculaires ?

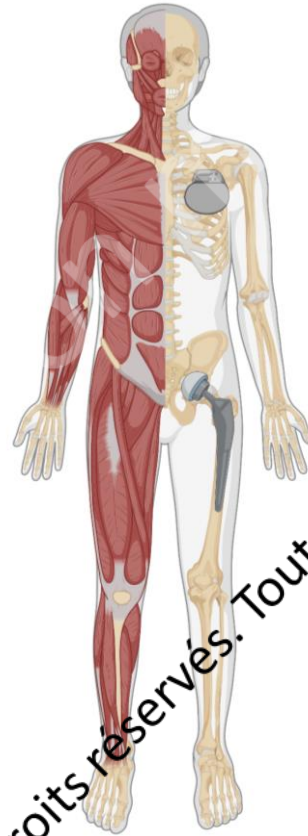
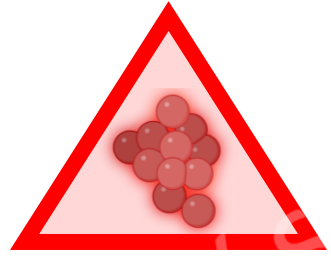
Infections en réanimation ?

Pédiatrie ?

Indications pertinentes vs. non pertinentes

Se limiter aux infections à BMR ?

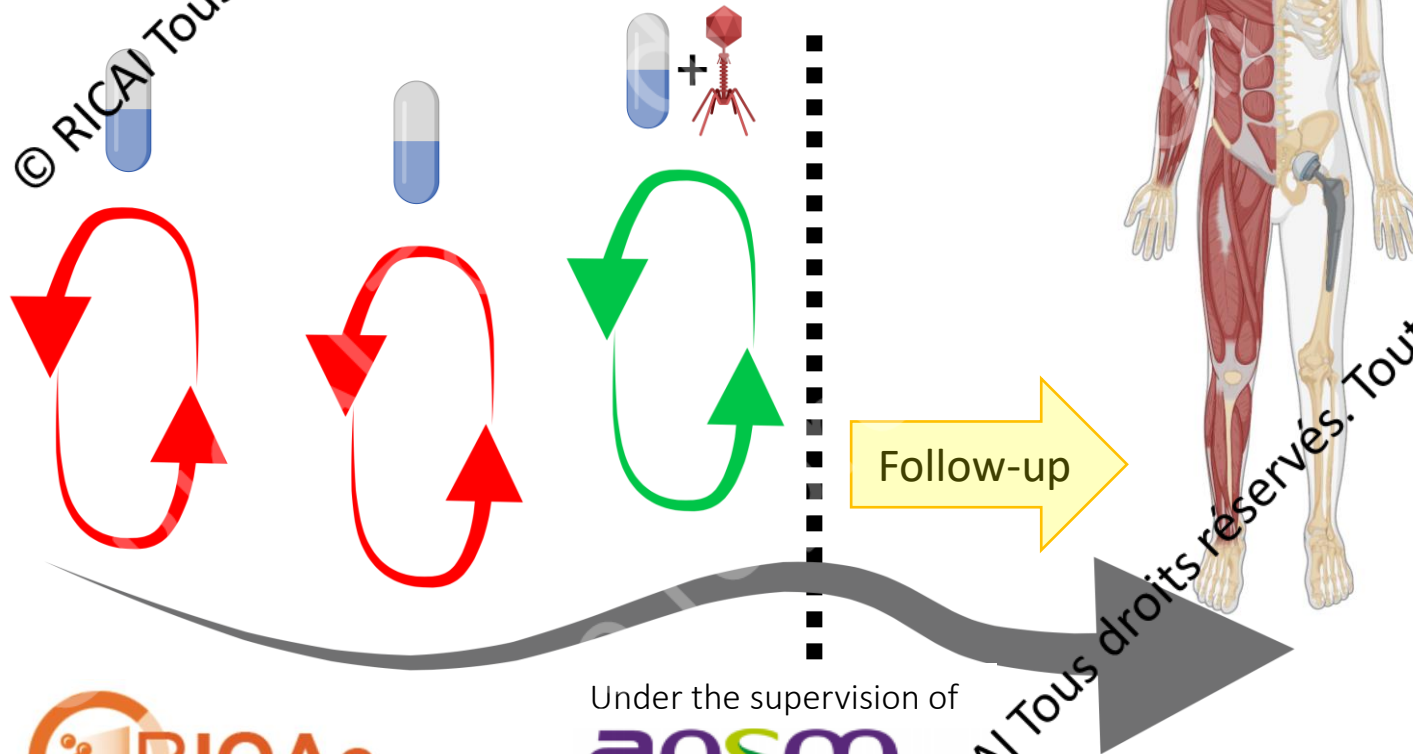
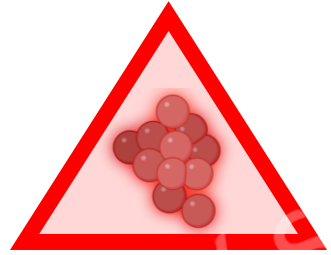
A large panel of severe bacterial infections



A large panel of severe bacterial infections

Some positive signals
in these infections

The patient is his “own control”



Under the supervision of

ansm

Agence nationale de sécurité du médicament
et des produits de santé

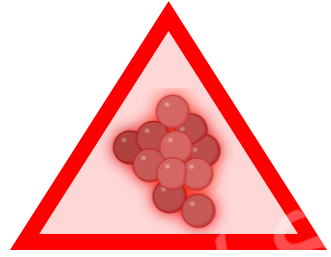
French Health Authority



PHAGE*in***LYON**
Clinic



A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

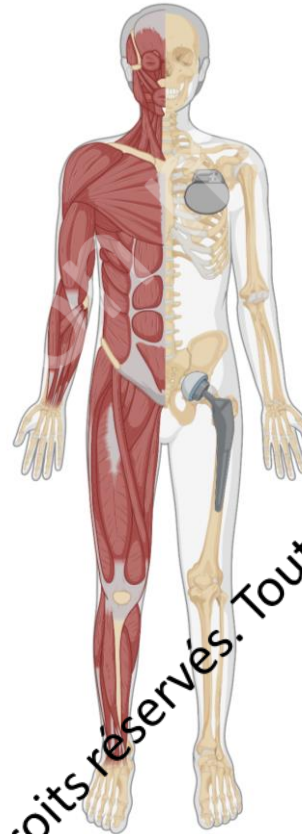
Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection

Digestive-tract infections

Typhoid fever, shigellosis
Cholera



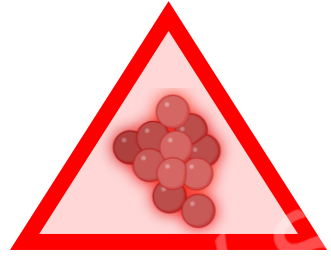
Cardiovascular infections

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Vascular graft infection

Muskuloskeletal infections

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Implant-associated bone and joint infection
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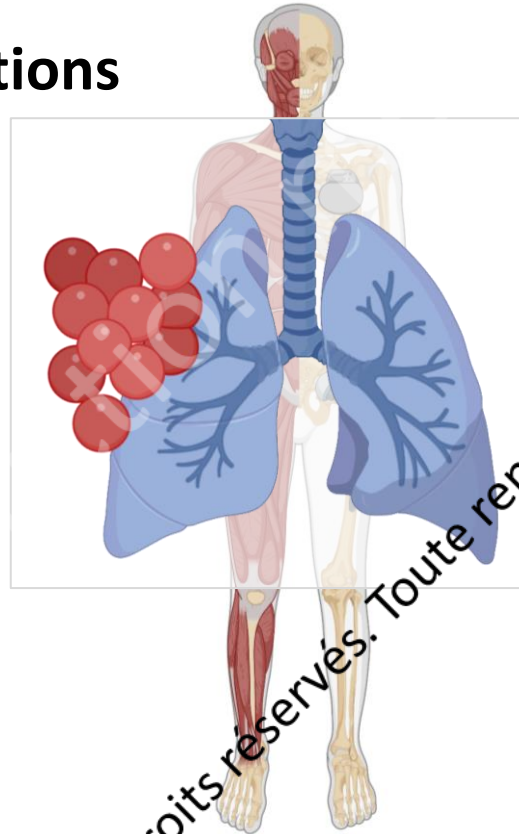
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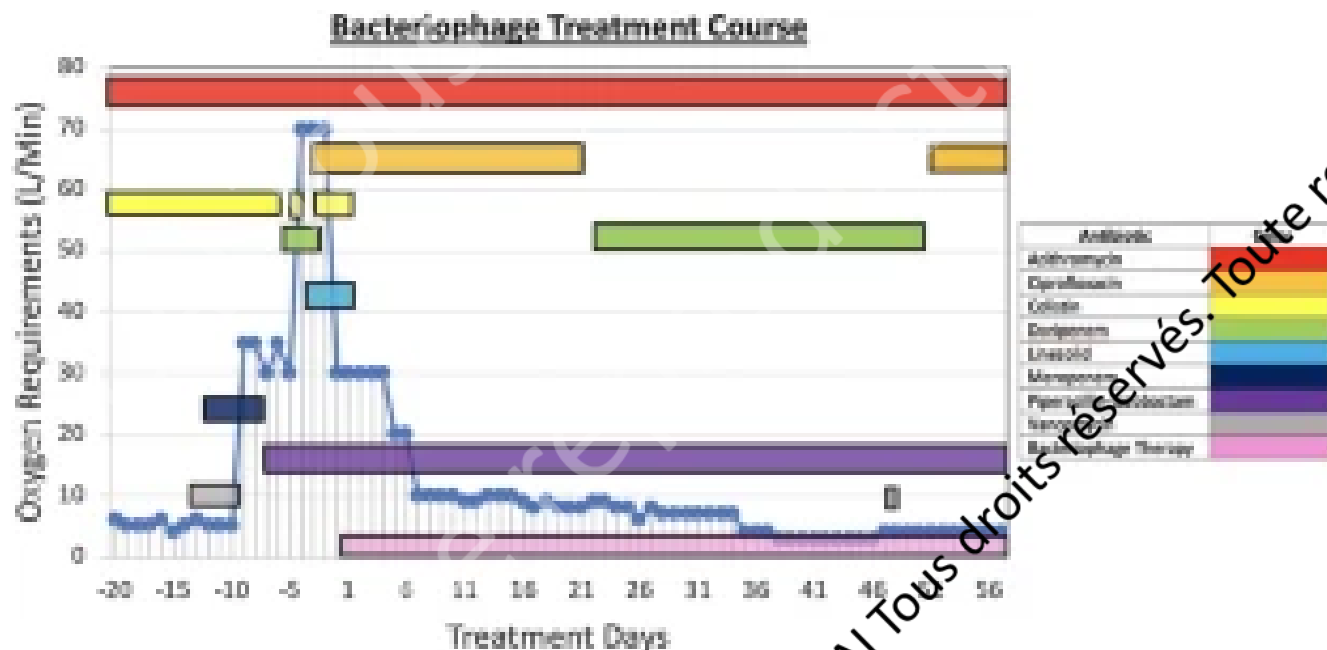
Implant-associated bone and joint infection

Prosthetic joint infection

Successful adjunctive use of bacteriophage therapy for treatment of multidrug-resistant *Pseudomonas aeruginosa* infection in a cystic fibrosis patient

Nancy Law, Cathy Logan, Gordon Yung, Carrie-Lynn Langlais Furr, Susan M. Lehman, Sandra Morales, Francisco Rosas, Alexander Gaidamaka, Igor Bilinsky, Paul Grint, Robert T. Schooley & Saima Aslam

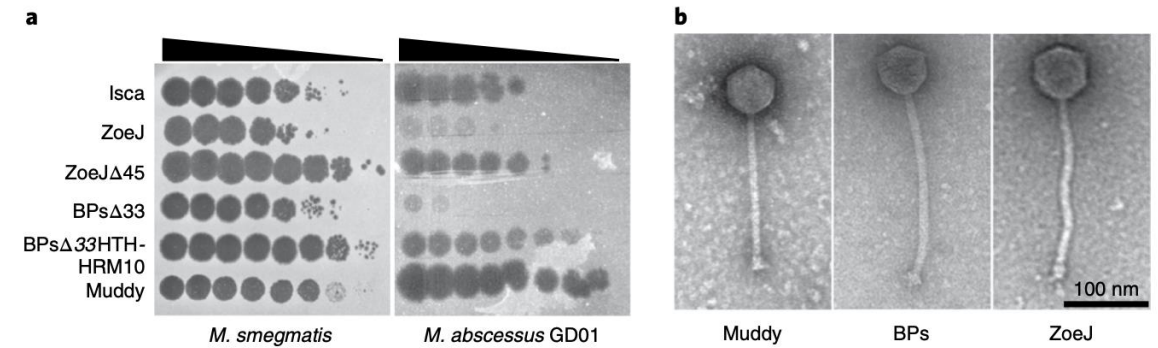
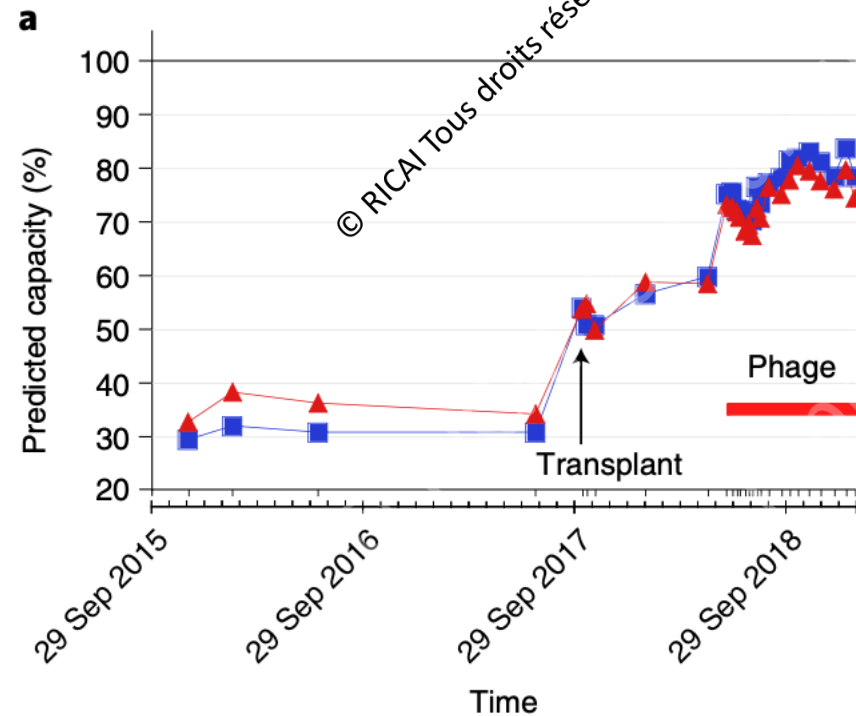
Infection 47, 665–668 (2019) | [Cite this article](#)



Eight weeks of INTRAVENOUS phages (1 injection each 6 hours)

Engineered bacteriophages for treatment of a patient with a disseminated drug-resistant *Mycobacterium abscessus*

Rebekah M. Dedrick^{1,4}, Carlos A. Guerrero-Bustamante^{1,4}, Rebecca A. Garlena¹, Daniel A. Russell¹, Katrina Ford², Kathryn Harris², Kimberly C. Gilmour², James Southill², Deborah Jacobs-Sera¹, Robert T. Schooley³, Graham F. Hatfull^{1*} and Helen Spencer^{1,2*}



Eight weeks of INTRAVENOUS phages (1 injection each 12 hours)

Clinical case (not published; 31th treated patient)

52-year-old man

Burn (81% of the body surface)

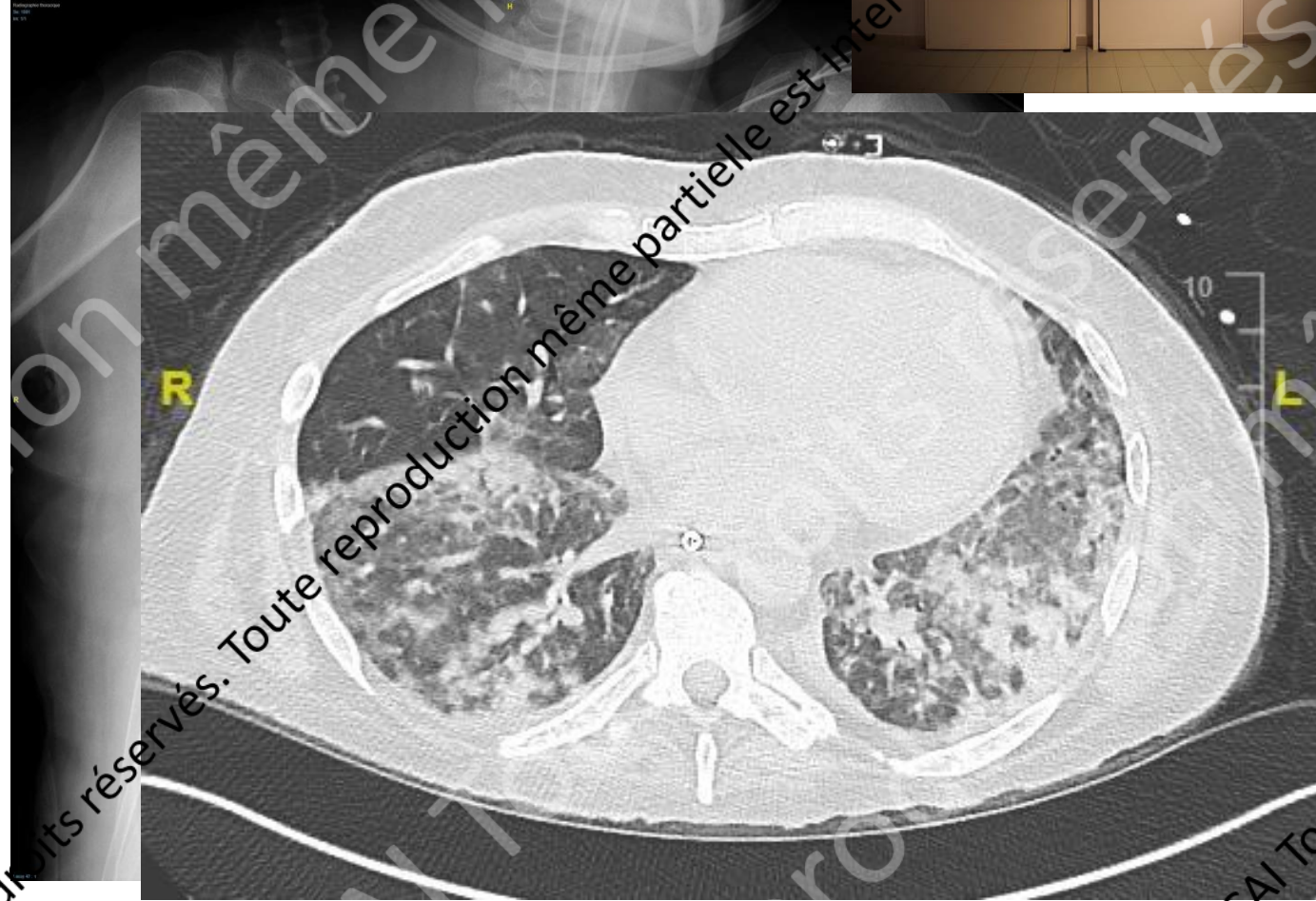
In ICU

Ventilator-associated pneumonia

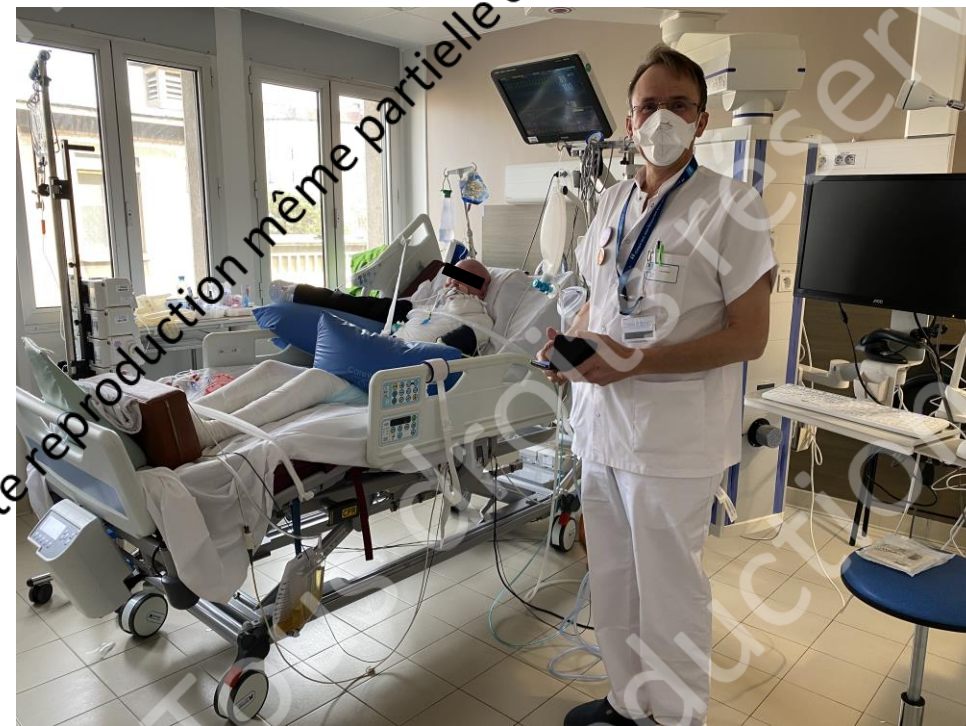
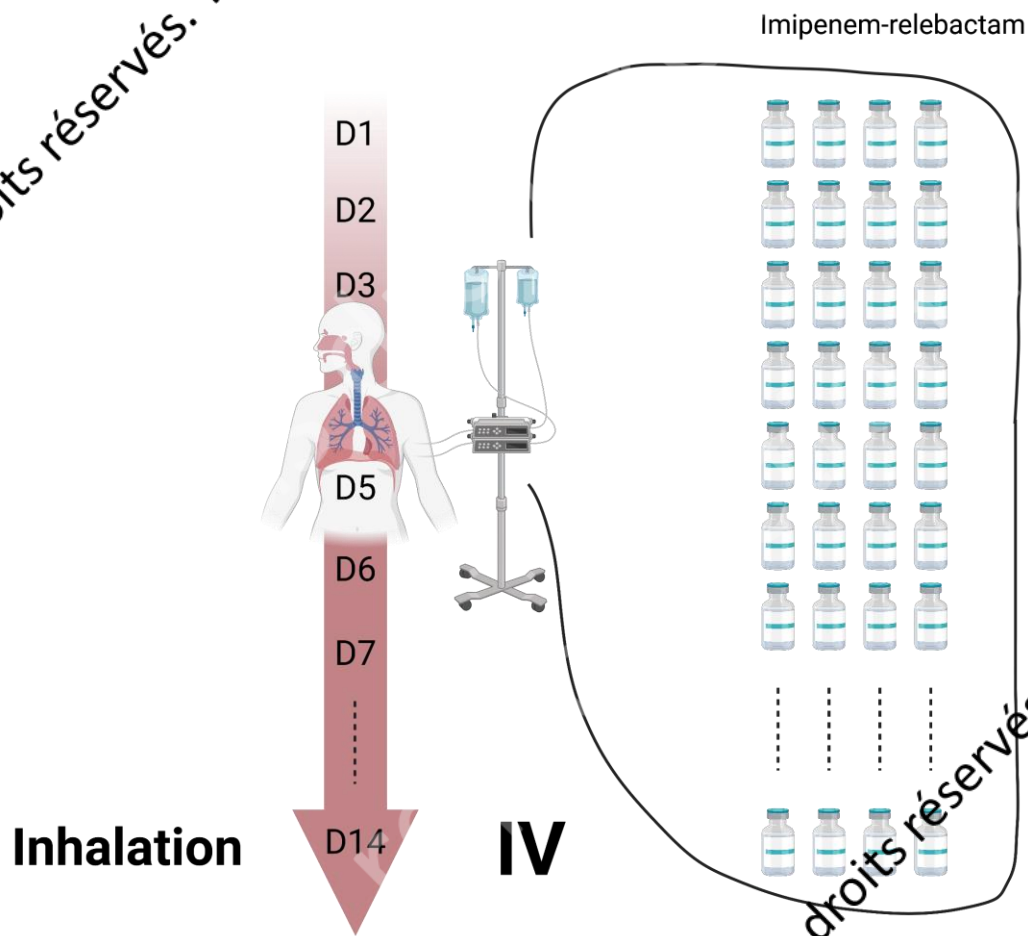
Pandrug-resistant *P. aeruginosa*

Treated with imipenem-relebactam

Relapsing VAP with bacteremia



Clinical case (not published; 31th treated patient)



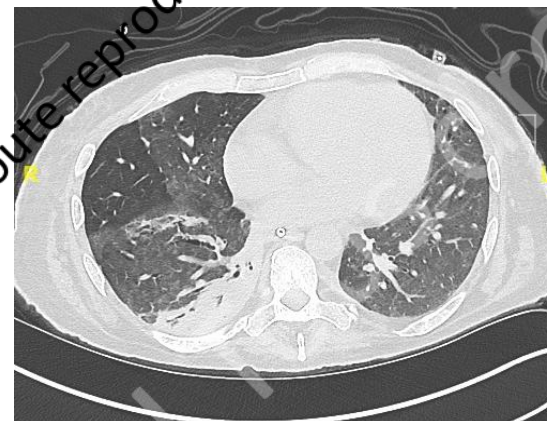
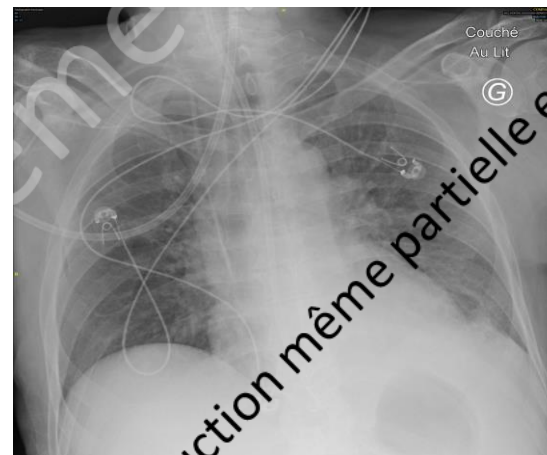
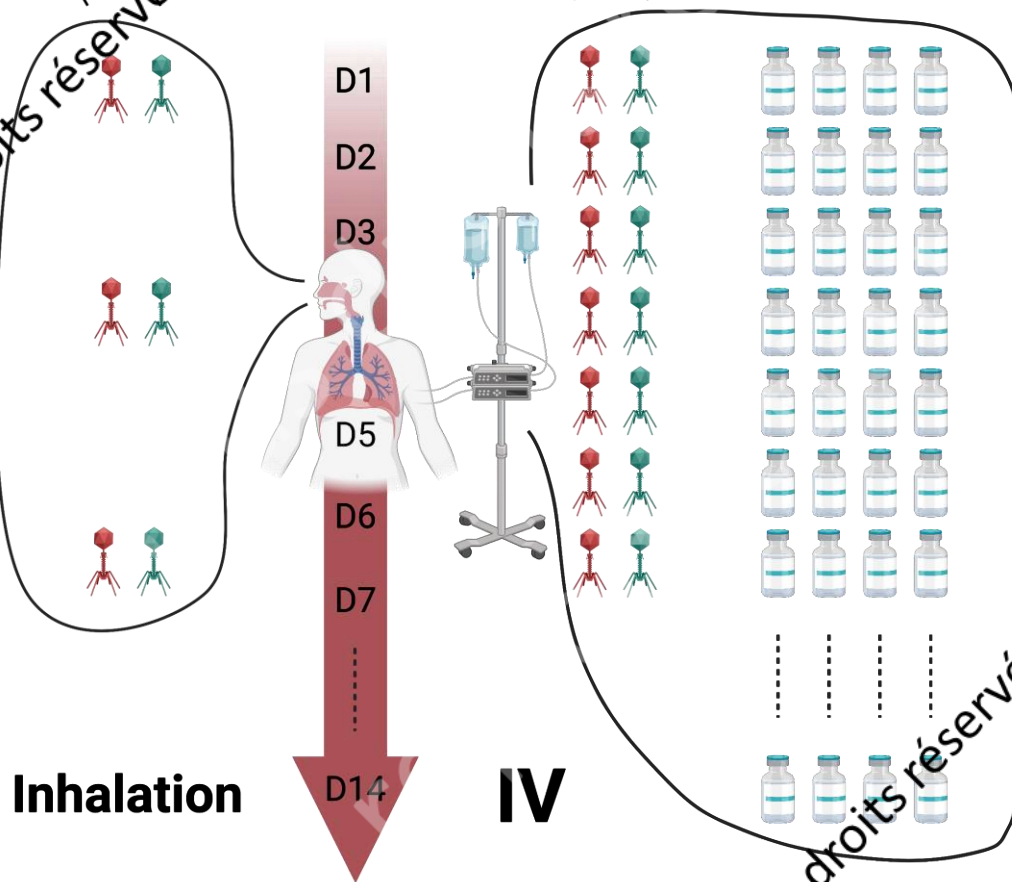
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PHERECYDES
PHARMA

PP1797
PP1792

PP1797
PP1792

Imipenem-relebactam



Courtesy G. Martin

Clinical case (not published; 34th treated patient)

54-year-old woman

Lung transplantation for end-stage COPD

Bronchiectasis

Iterative ***P. aeruginosa*** exacerbations

Requiring oxygen

Clinical case (not published; 34th treated patient)

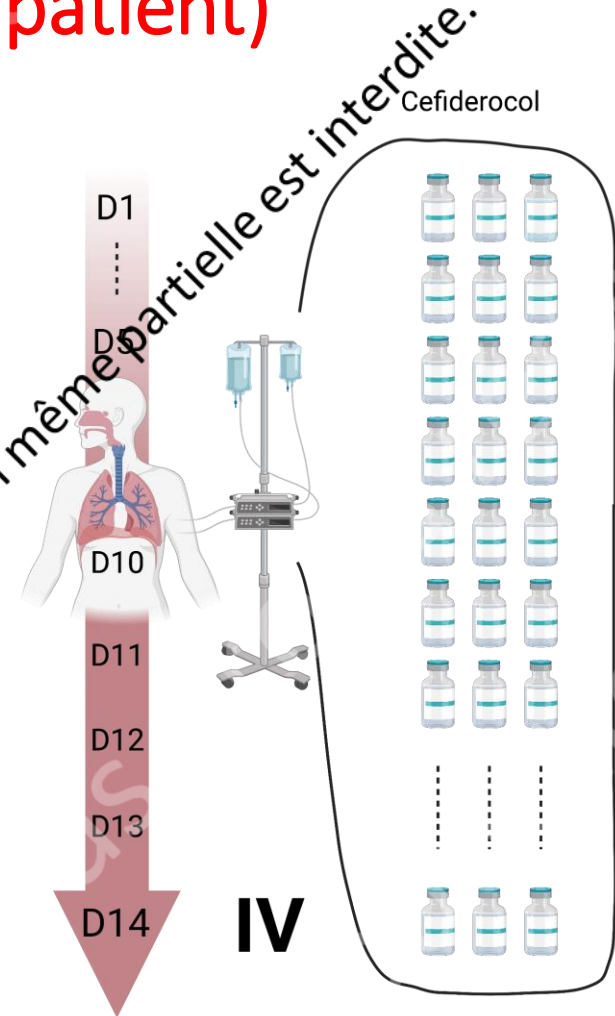
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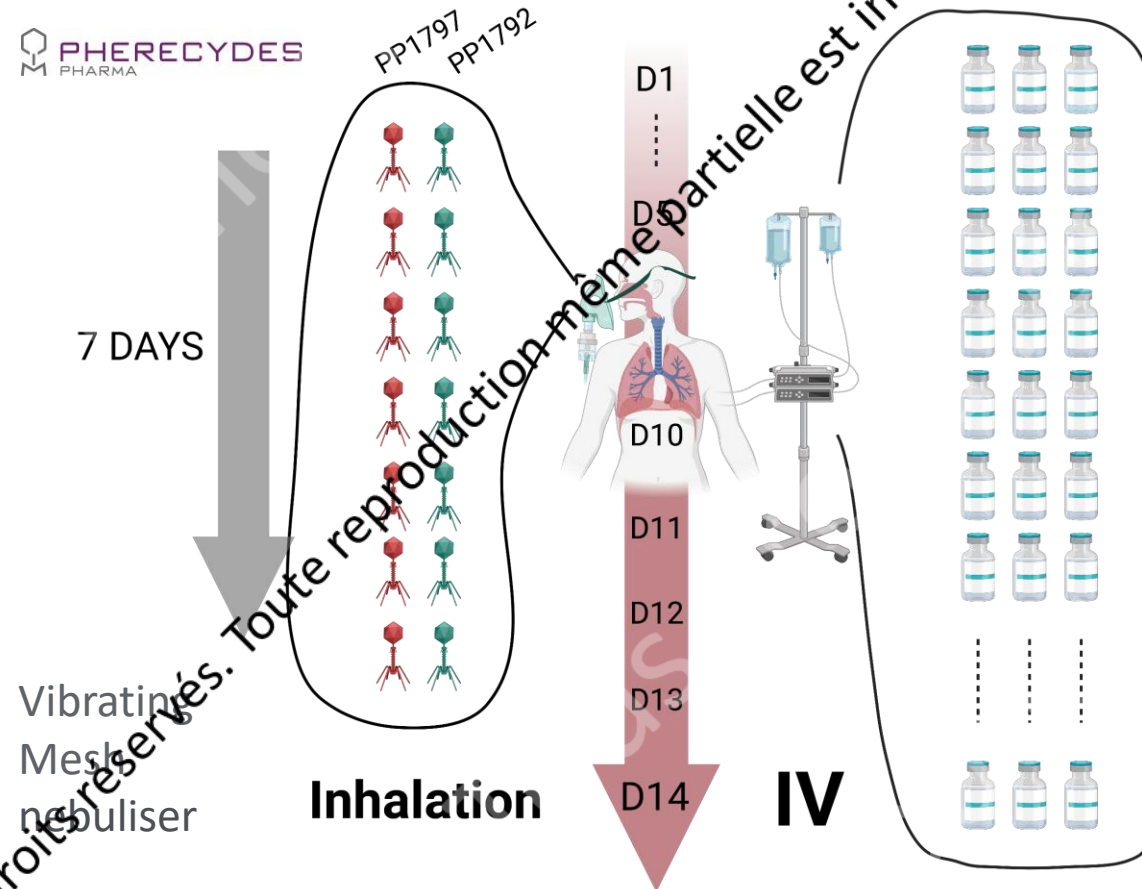
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Clinical case (not published; 34th treated patient)

Requiring oxygen



Clinical case (not published; 34th treated patient)



10,1k
views

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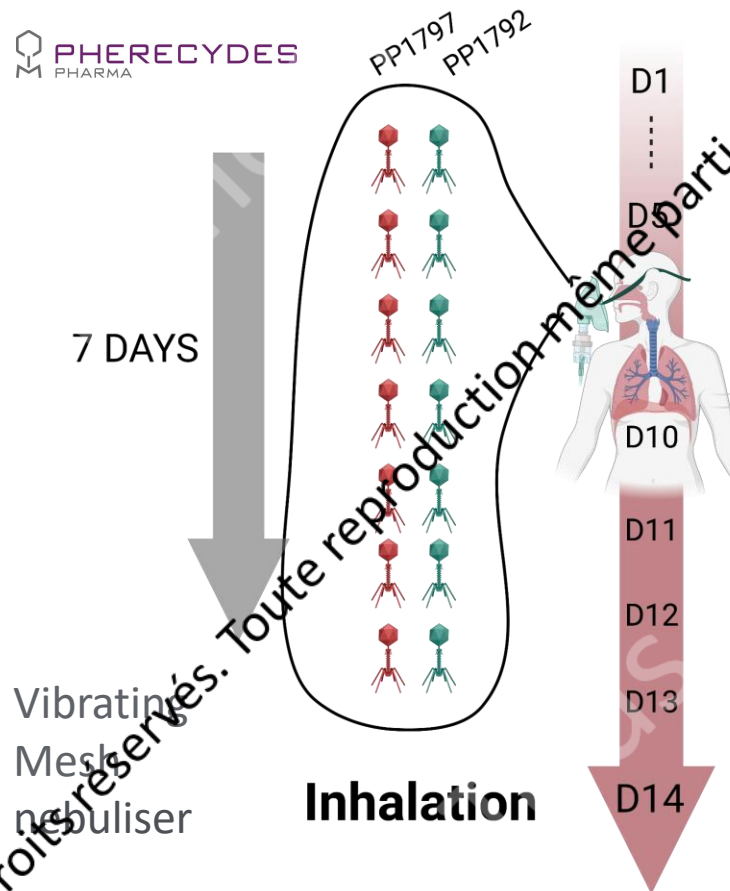
Bronchiectasis

Iterative ***P. aeruginosa*** exacerbations

Requiring oxygen

Local?
IV?

Local + IV?





U.S. National Library of Medicine

ClinicalTrials.gov

Cystic Fibrosis bacteriophage Study at Yale (CYPHY)

Yale

Ph 1/2 Study Evaluating Safety and Tolerability of Inhaled AP-PA02 in Subjects With Chronic Pseudomonas Aeruginosa Lung Infections and Cystic Fibrosis (SWARM-Pa)

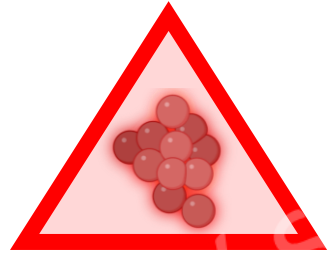


Personalized Phage Treatment in Covid-19 Patients With Bacterial Co-Infections Microbials for Pneumonia or Bacteremia/Septicemia



Etc.

A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

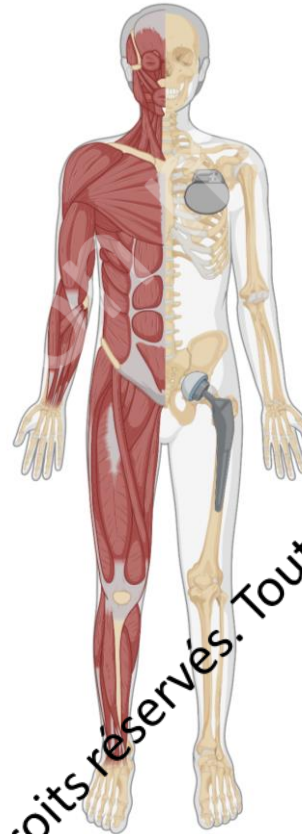
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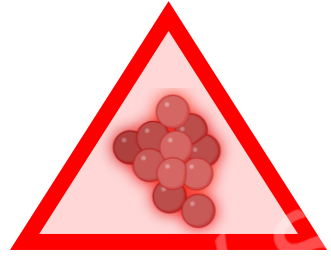
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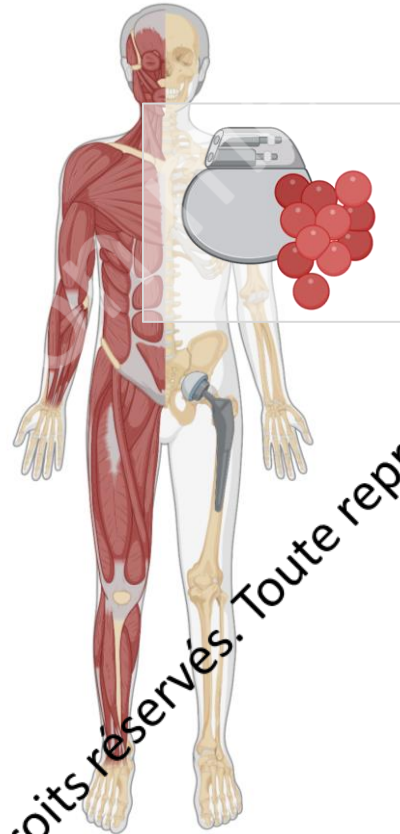
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Novel bacteriophage therapy for treatment of left ventricular assist device infection

Saima Aslam, MD,^a Victor Pretorius, MD,^b Susan M. Lehman, PhD,^c Sandra Morales, PhD,^c and Robert T. Schooley, MD^a

The Journal of
Heart and Lung Transplantation

The Official Publication of the International Society for Heart and Lung Transplantation



UC San Diego
School of Medicine

Center for Innovative Phage
Applications and Therapeutics

In the Division of Infectious Diseases & Global Public Health



Open Forum Infectious Diseases

MAJOR ARTICLE



Infectious Diseases Society of America



hiv medicine association



OXFORD

Lessons Learned From the First 10 Consecutive Cases of Intravenous Bacteriophage Therapy to Treat Multidrug-Resistant Bacterial Infections at a Single Center in the United States

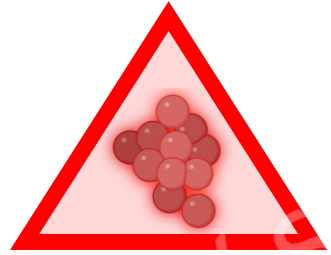
Saima Aslam,^{1,2} Elizabeth Lampley,² Darby Wooten,¹ Maile Karris,¹ Constance Benson,^{1,2} Steffanie Strathdee,^{1,2} and Robert T. Schooley^{1,2}

¹Division of Infectious Diseases and Global Public Health, University of California, San Diego, La Jolla, California, USA, and ²Center for Innovative Phage Applications and Therapeutics, University of California, San Diego, La Jolla, California, USA



figure 1 Sternal wound at baseline (A) and at end of bacteriophage therapy (B) with visible ventricular assist device. (A) Wound with urulence and poorly granulating tissue. (B) Healthy red granulation tissue and reduced purulence.

A large panel of severe bacterial infections



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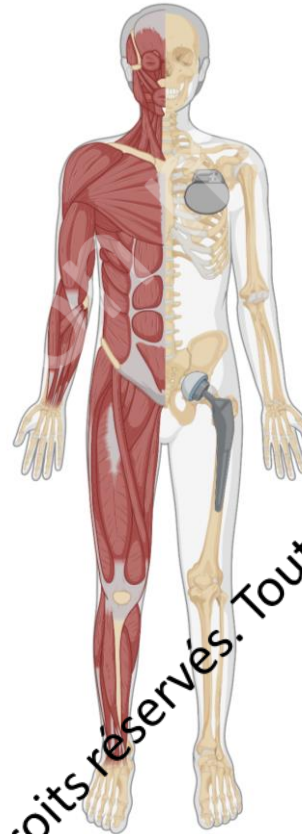
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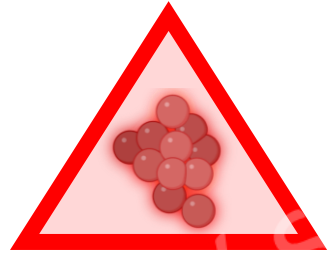
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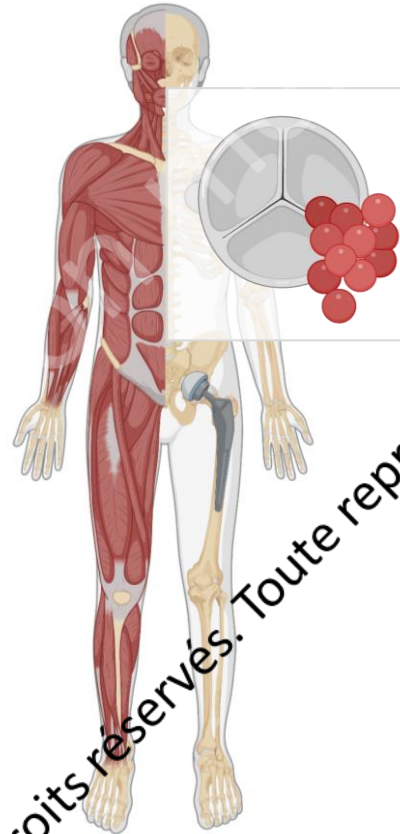
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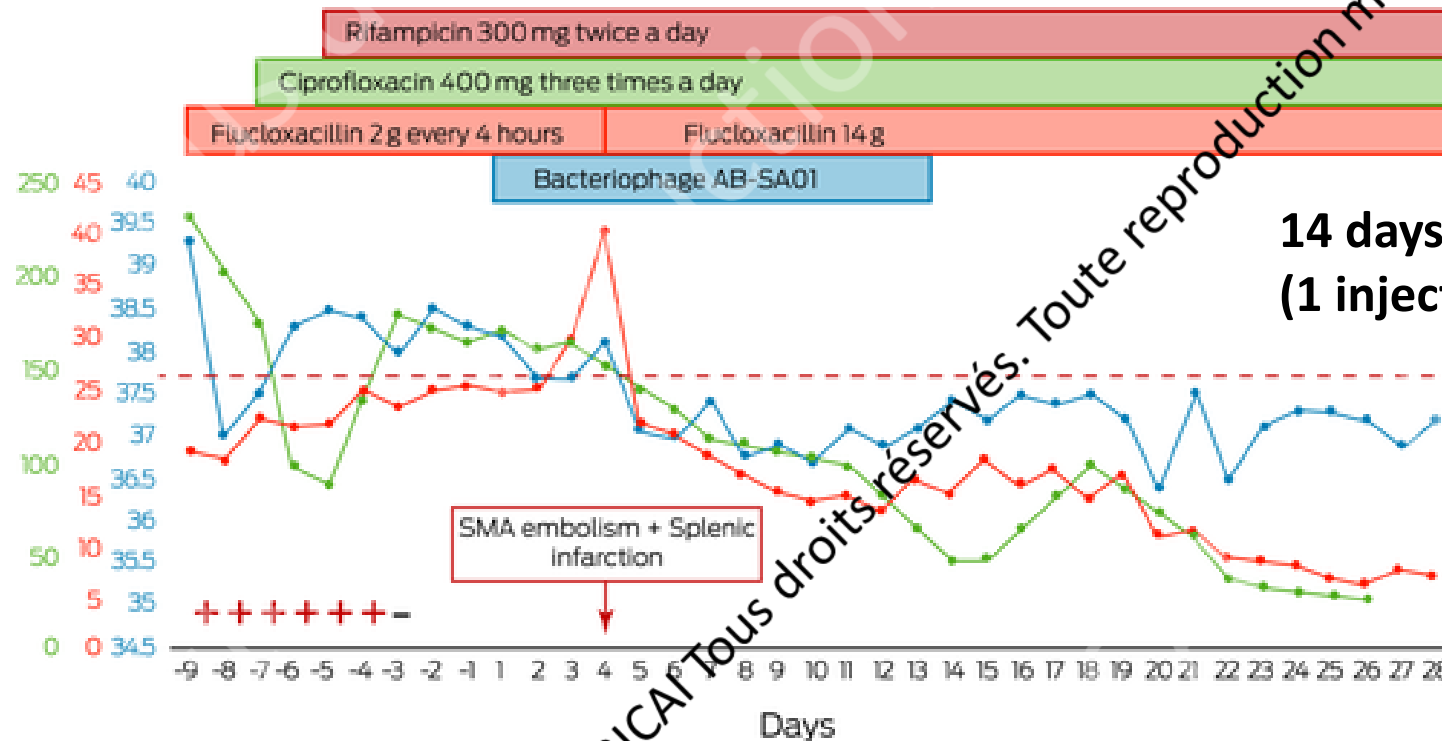
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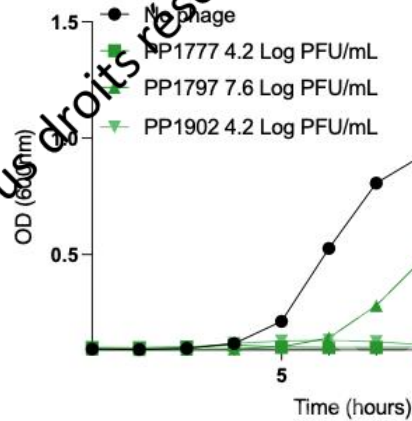
Adjunctive bacteriophage therapy for prosthetic valve endocarditis due to *Staphylococcus aureus*

Timothy Gilbey, Josephine Ho, Louise A Cooley, Aleksandra Petrovic Fabijan, Jonathan R Iredell

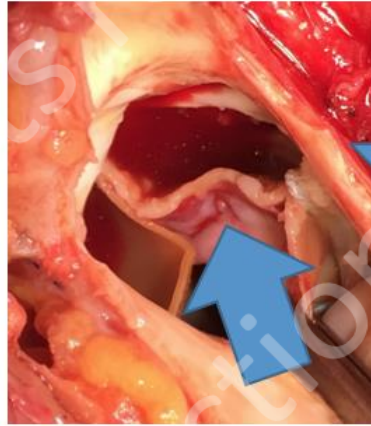


Clinical cases (not published; 7th and 10th treated patients)

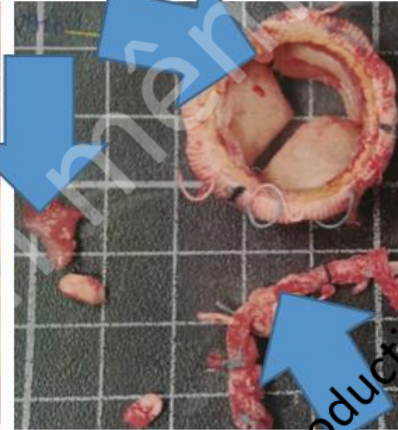
A



B



C



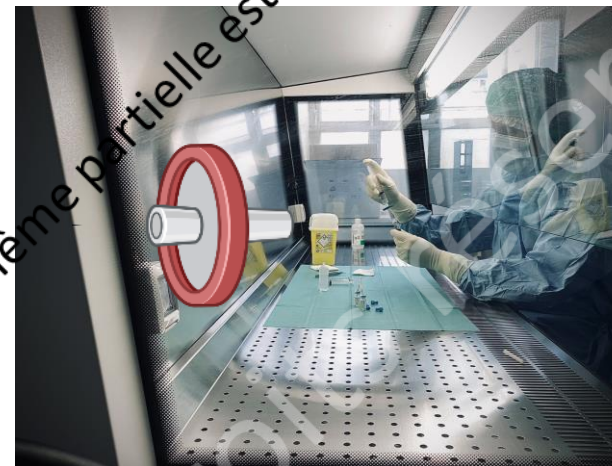
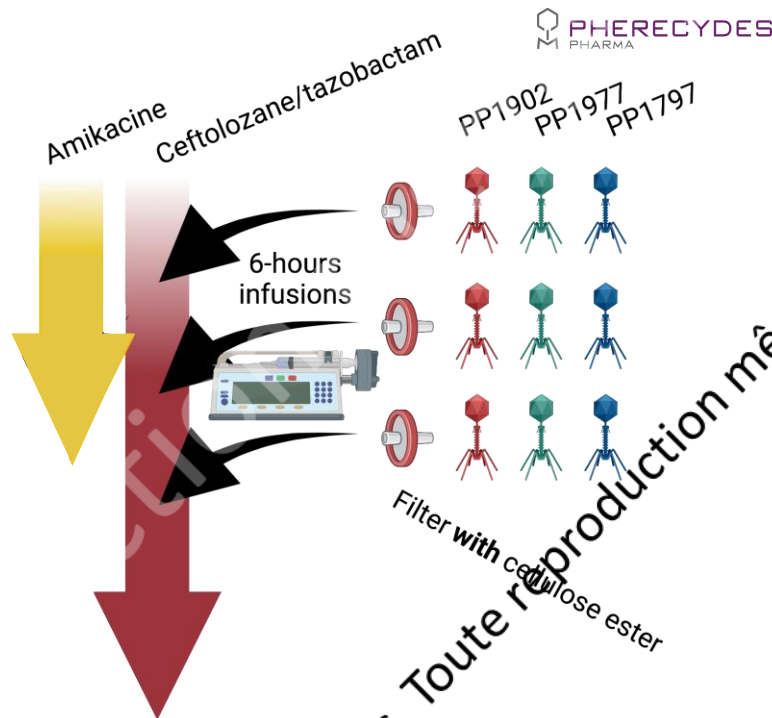
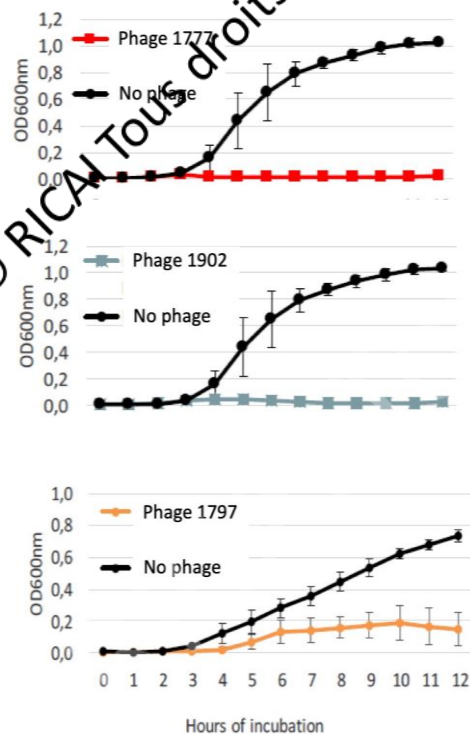
64-year-old man

Bioprosthetic valve endocarditis
due to *P. aeruginosa*

Iterative relapses

Clinical cases (not published; 7th and 10th treated patients)

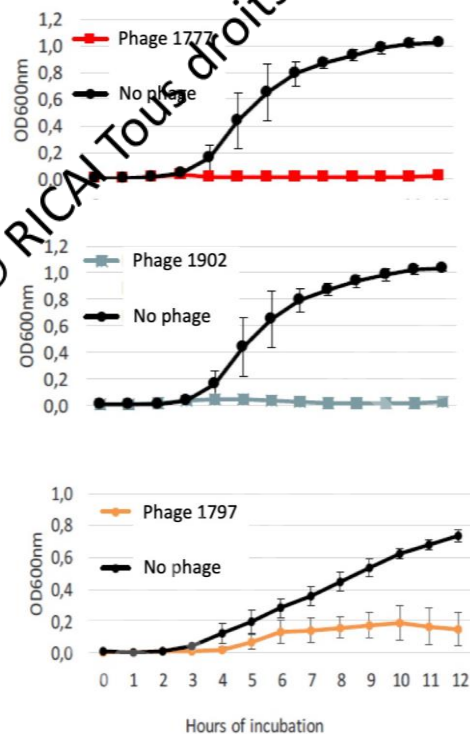
Sequence n°1



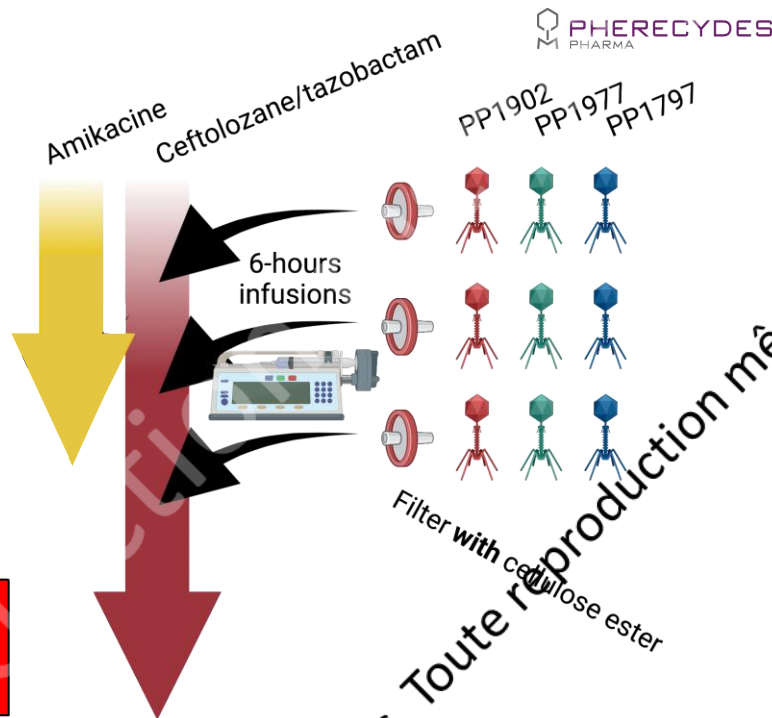
PHAGEinLYON

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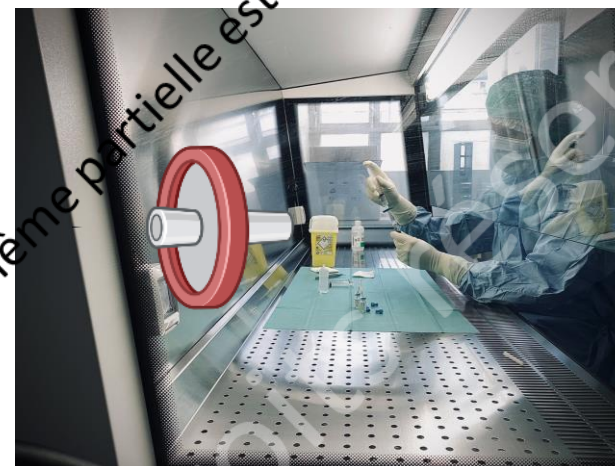
Sequence n°1



FAILURE



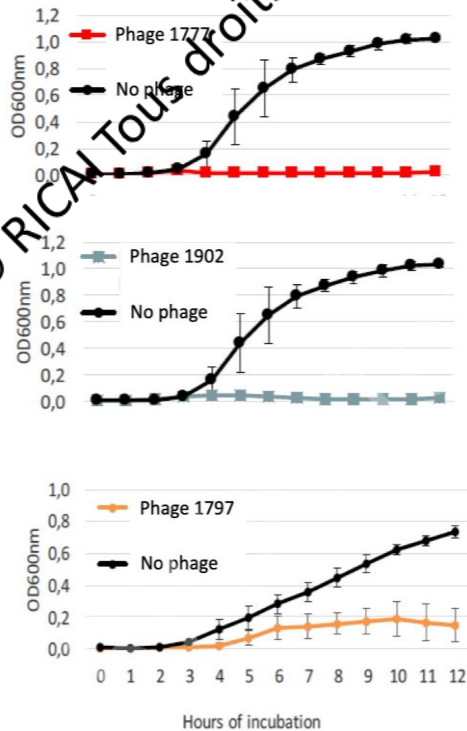
PHERE CYDES
PHARMA



@FerryLyon

Clinical cases (not published; 7th and 10th treated patients)

Sequence n°1



No phage detection in the patient's blood

FAILURE

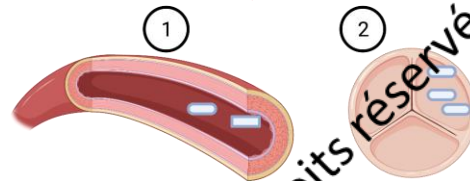
Amikacine
Ceftolozane/tazobactam

PHERE CYDES
PHARMA

PP1902
PP1977
PP1797

6-hours infusions

Filter with cellulose ester



- 1 *P. aeruginosa* detected in blood culture
- 2 Surgery (valve exchange) with *P. aeruginosa* in culture



Antibacterial filter
without
cellulose ester

PHAGEinLYON

Clinical cases (not published; 7th and 10th treated patients)

Sequence n°2

Clinical cases (not published; 7th and 10th treated patients)

Sequence n°2



Phages detected in the patient's blood

FAILURE

Colistine
Ceftolozane/tazobactam

Direct infusion



PHERE CYDES
PHARMA

PP1977
PP1797



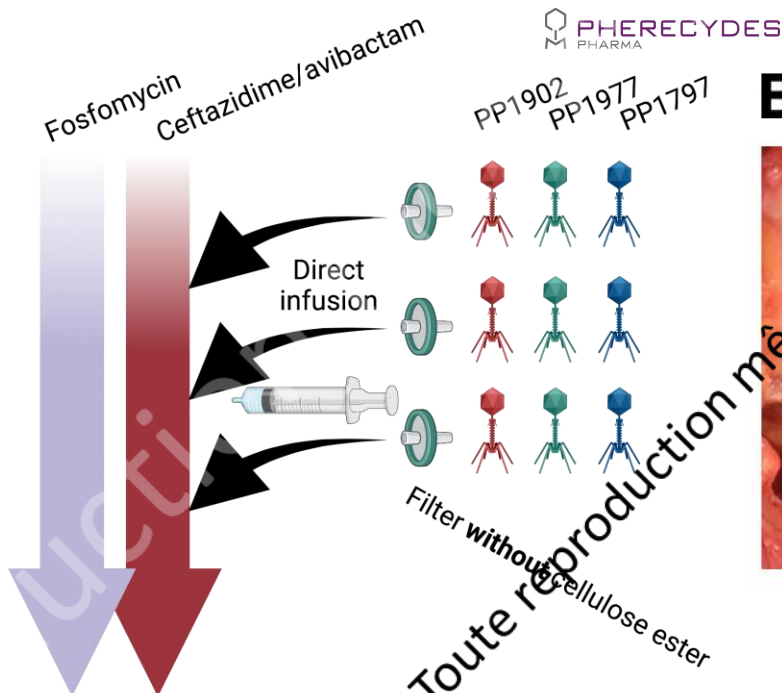
PHAGEinLYON

Clinical cases (not published; 7th and 10th treated patients)

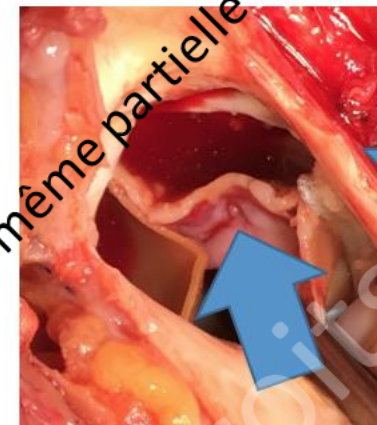
Sequence n°3

Clinical cases (not published; 7th and 10th treated patients)

Sequence n°3



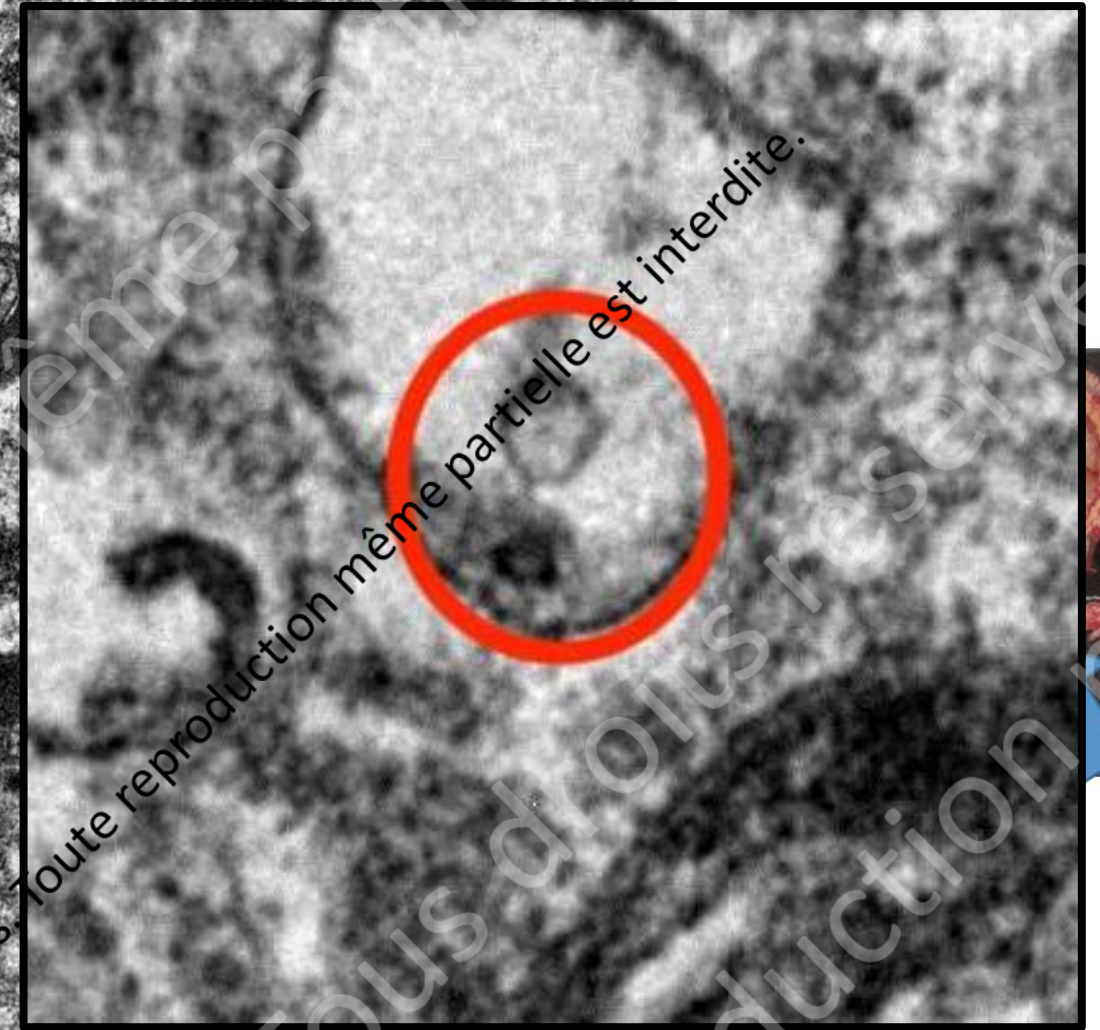
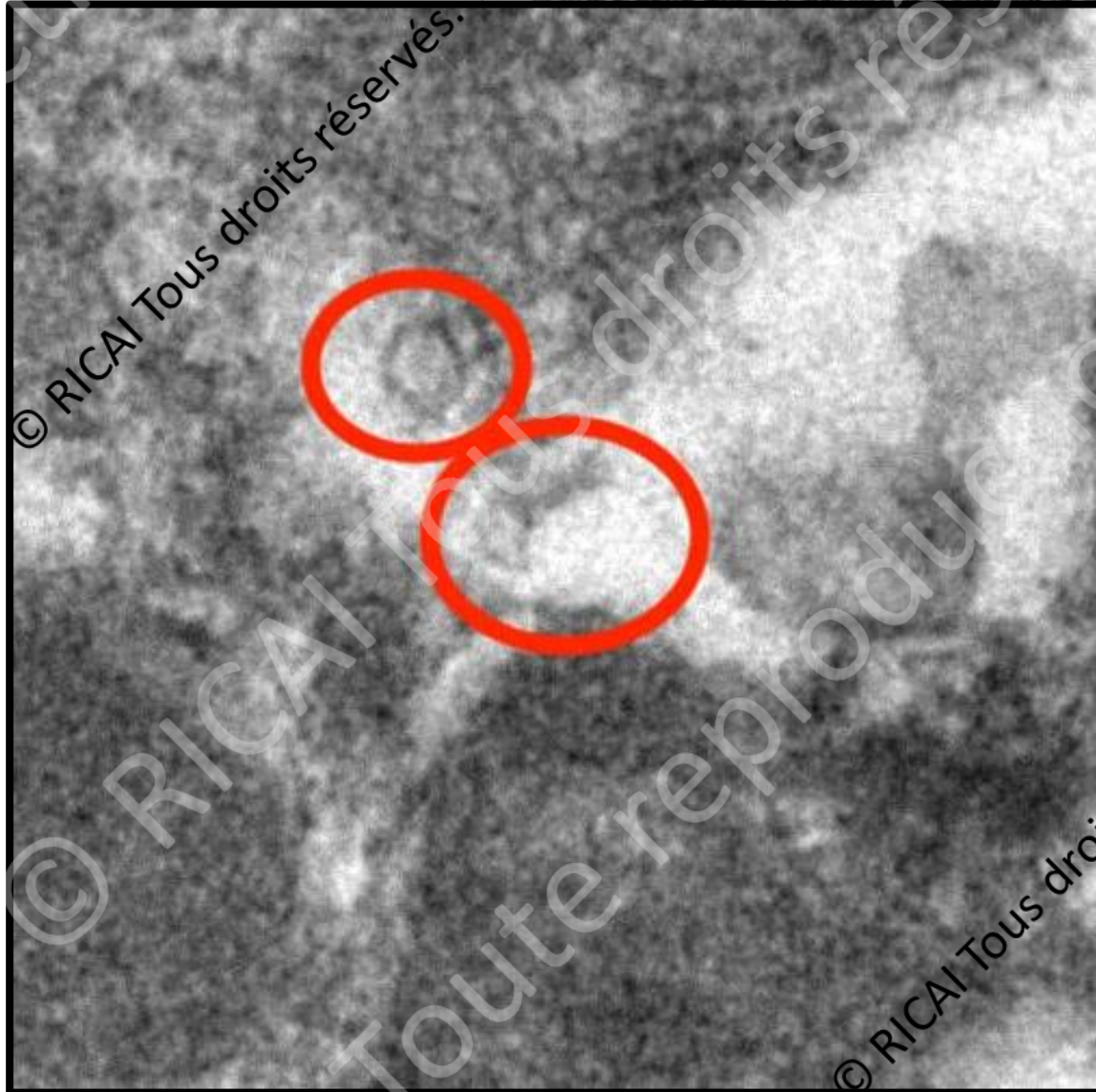
B



C

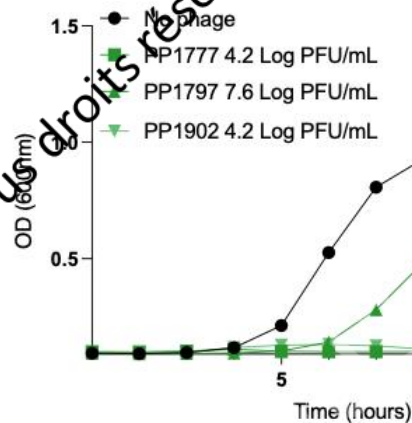


Clinical c

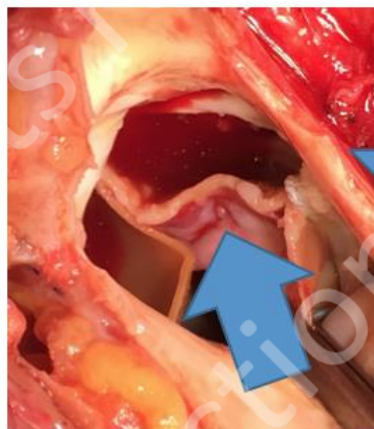


Clinical cases (not published; 7th and 10th treated patients)

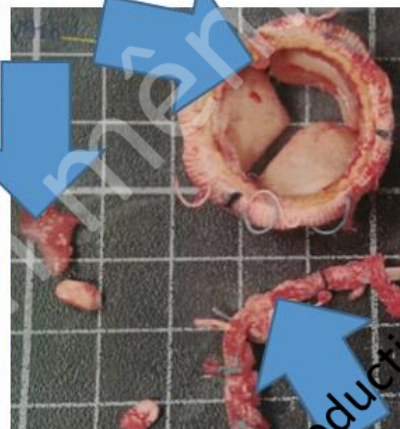
A



B



C

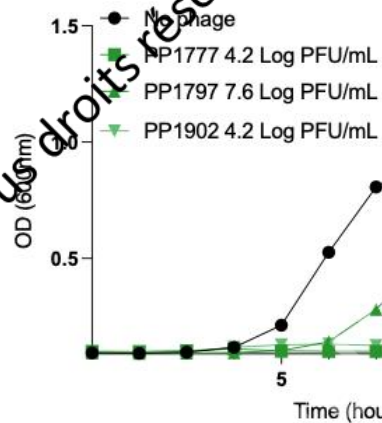


D

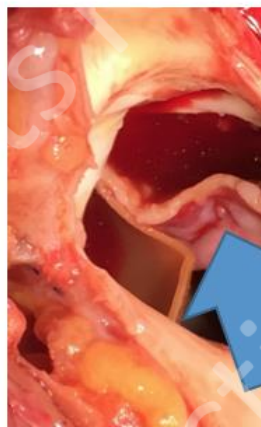


Clinical cases (not published)

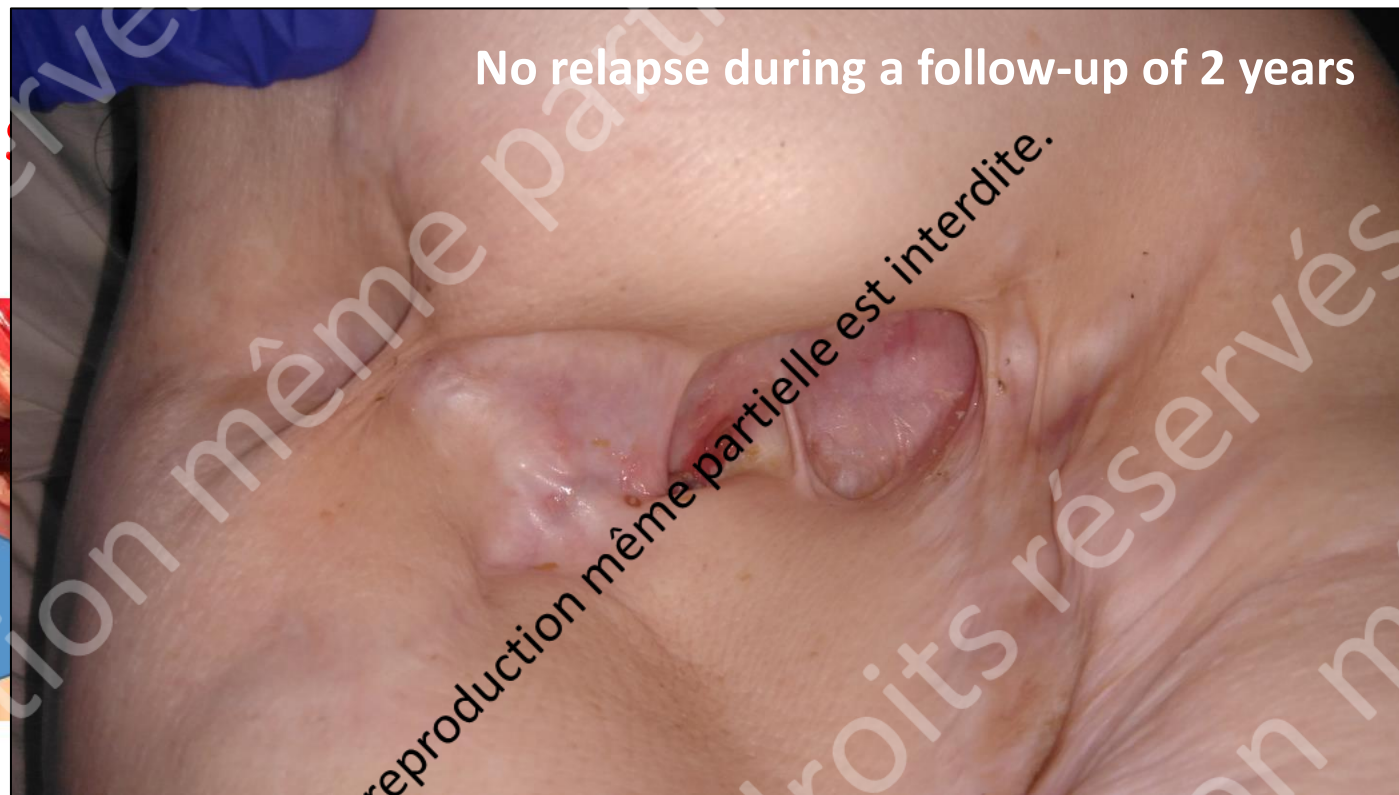
A



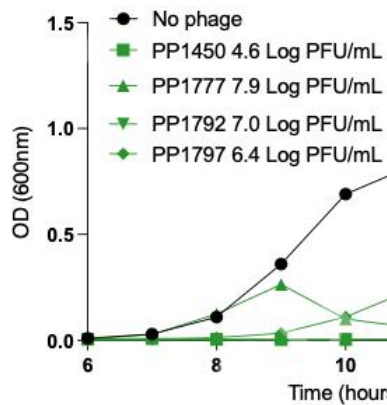
B



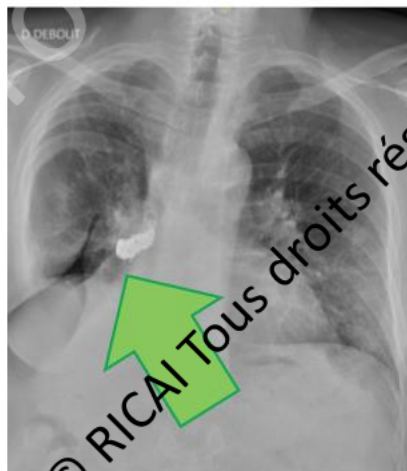
No relapse during a follow-up of 2 years



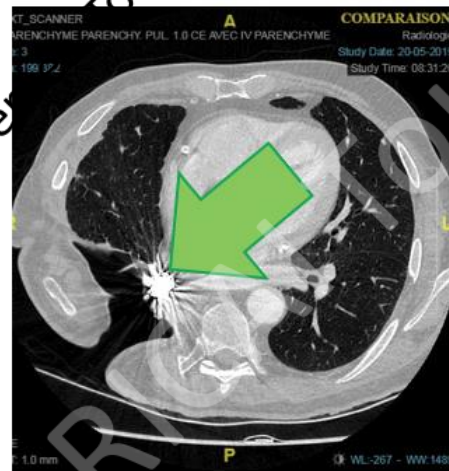
F



G



H



I





U.S. National Library of Medicine

ClinicalTrials.gov

No Studies found for: **phage | Endocarditis, Bacterial**

nature
microbiology

ARTICLES

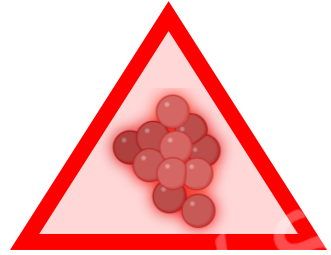
<https://doi.org/10.1038/s41564-019-0634-z>

Safety of bacteriophage therapy in severe *Staphylococcus aureus* infection

Aleksandra Petrovic Fabijan ^{1,2,6}, Ruby C. Y. Lin ^{1,2,3,4,6}, Josephine Ho^{1,2}, Susan Maddocks^{1,2,3},
Nouri L. Ben Zakour^{1,3}, Jonathan R. Iredell ^{1,2,3} * and Westmead Bacteriophage Therapy Team⁵

A lot of things are learned from compassionate cases

A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

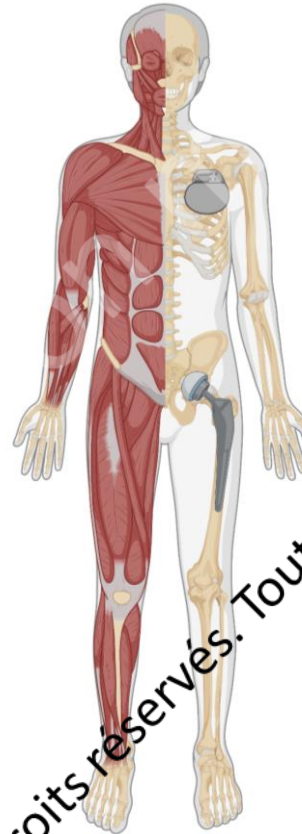
Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection

Digestive-tract infection

Typhoid fever, shigellosis
Cholera



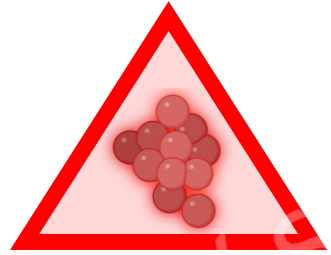
Cardiovascular infections

Endocarditis
Cardiac electronic device infection
Prosthetic valve endocarditis
Vascular graft infection

Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection

A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection

Digestive-tract infection

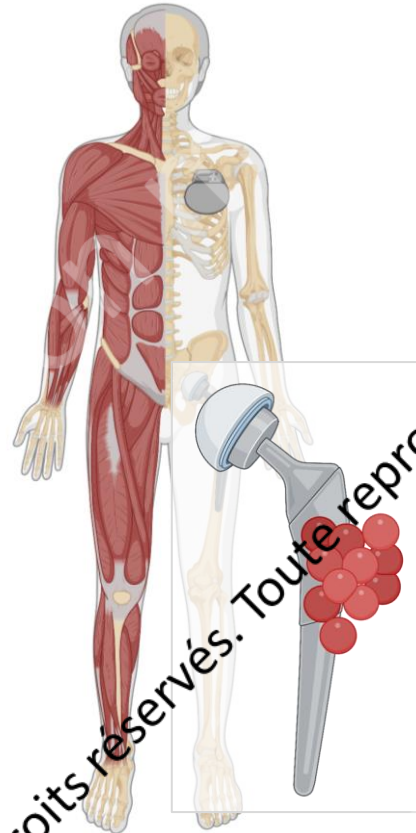
Typhoid fever, shigellosis
Cholera

Cardiovascular infections

Endocarditis
Cardiac electronic device infection
Prosthetic valve endocarditis
Vascular graft infection

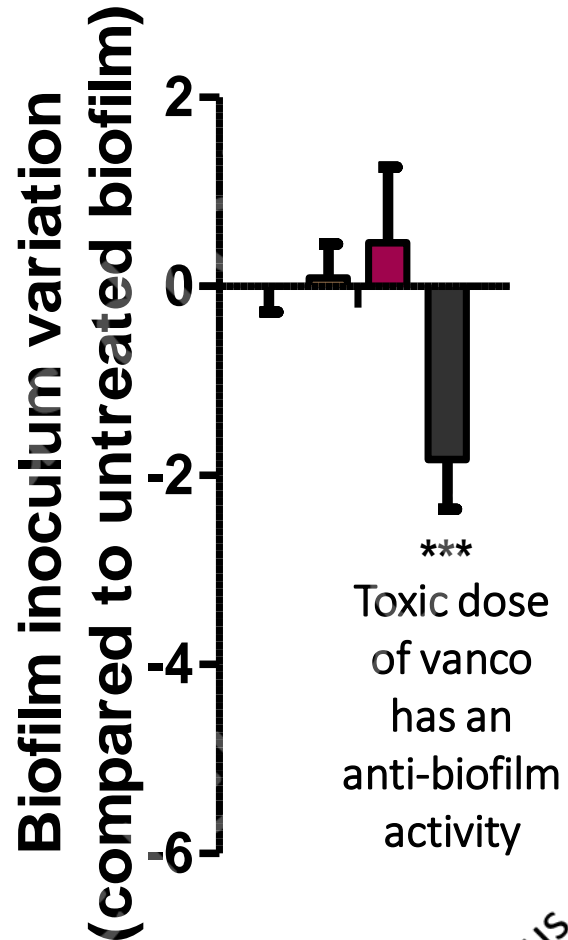
Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection



Phages have antibiofilm activity

vancomycin

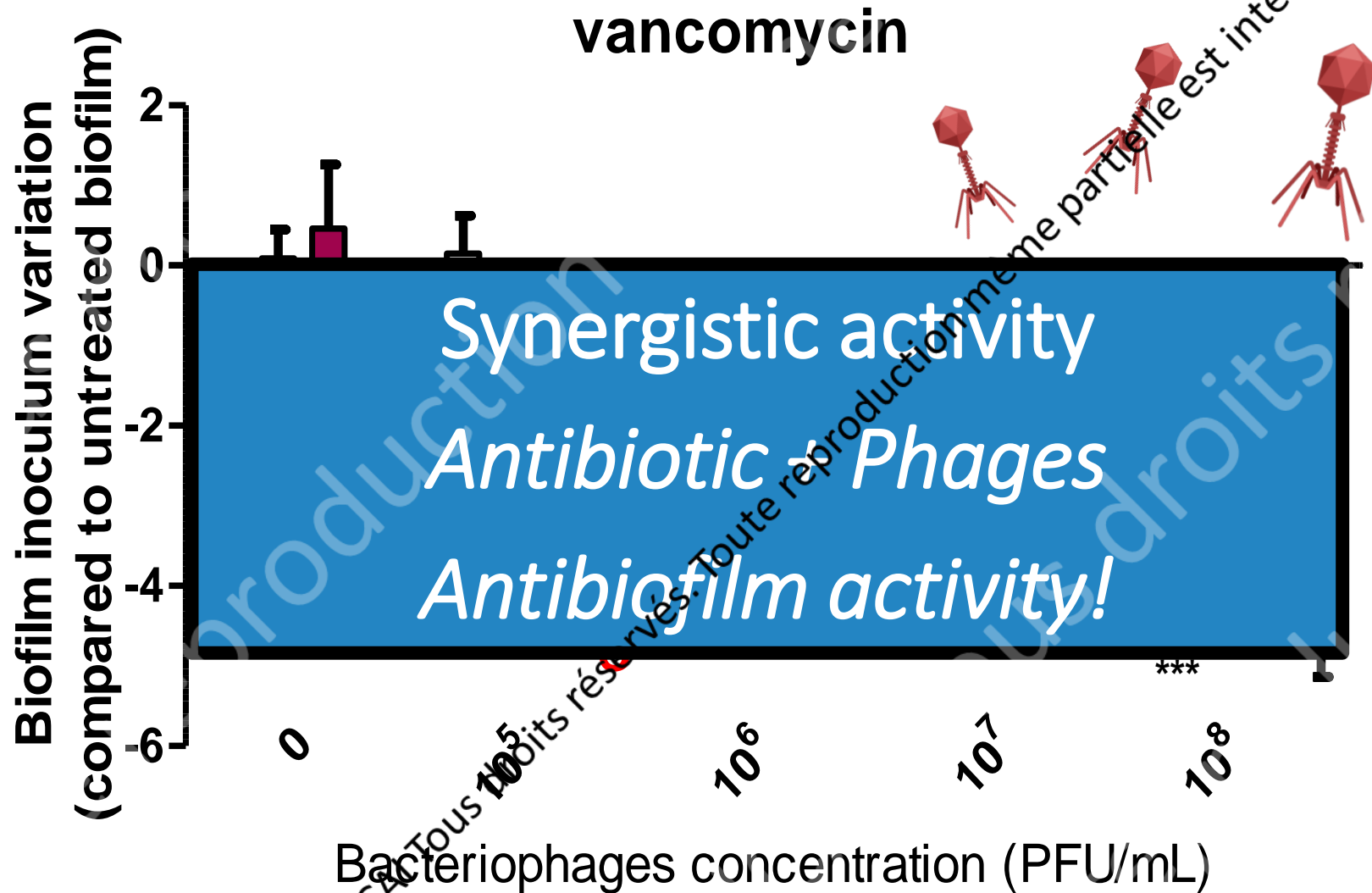


- No Antibiotic
- MIC
- C_{bone} (4*MIC)
- 10*MIC



Phages have antibiofilm activity

- No Antibiotic
- MIC
- C_{bone} (4*MIC)
- 10*MIC



Polenda et al. Antimicrob Agents Chemother 2019



viruses

Lyon BJI
study group

PHAGEinLYON



Review

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

REVIEW ARTICLE

OPEN ACCESS

Tristan Ferry
Jérôme Josse
Frédéric Laurent
On behalf

Medical innovations to maintain the function in patients with chronic PJI for whom explantation is not desirable: a pathophysiology-, multidisciplinary-, and experience-based approach

Tristan Ferry^{1,2,3,4,*}, Cécile Batailler^{2,3,5}, Sophie Brosset^{2,3,6}, Camille Kolenda^{2,3,4,7},
Sylvain Goutelle^{2,3,8,9}, Elliot Sappey-Marini^{2,3,5}, Jérôme Josse^{2,3,4,7}, Frédéric Laurent^{2,3,4,7},
Sébastien Lustig^{2,3,5}, On Behalf of the Lyon BJI Study Group,^a

infection ostéoarticulaire : historique, fondements, faisabilité et perspectives en France

Phage therapy in bone and joint infection: history, rationale, feasibility and perspectives in France

Virologie

une

Case Report: Arthroscopic “Debridement Antibiotics and Implant Retention” With Local Injection of Personalized Phage Therapy to Salvage a Relapsing *Pseudomonas Aeruginosa* Prosthetic Knee Infection

Tristan Ferry^{1,2,3,4*}, Camille Kolenda^{2,3,4,5}, Cécile Batailler^{2,3,6}, Romain Gaillard^{3,6}, Claude-Alexandre Gustave^{2,3,4,5}, Sébastien Lustig^{2,3,6}, Cindy Fevre⁷, Charlotte Petitjean⁷, Gilles Leboucher⁸, Frédéric Laurent^{2,3,4,5} and the Lyon BJI Study group

3,743

TOTAL VIEWS



Open Forum Infectious Diseases

BRIEF REPORT

VIEWS

3,770

Salvage Debridement, Antibiotics and Implant Retention (“DAIR”) With Local Injection of a Selected Cocktail of Bacteriophages: Is It an Option for an Elderly Patient With Relapsing *Staphylococcus aureus* Prosthetic-Joint Infection?

Tristan Ferry,^{1,2,3,4} Gilles Leboucher,⁵ Cindy Fevre,⁶ Yannick Herry,^{2,4,7} Anne Conrad,^{1,2,3,4} Jérôme Josse,^{2,3,4,8} Cécile Batailler,^{2,4,7} Christian Chidiac,^{1,2,3,4} Mathieu Medina,⁶ S. Lustig,⁷ and Frédéric Laurent^{2,3,4,8}, on behalf of the Lyon BJI Study Group

Phage Therapy as Adjuvant to Conservative Surgery and Antibiotics to Salvage Patients With Relapsing *S. aureus* Prosthetic Knee Infection

Tristan Ferry^{1,2,3,4*}, Camille Kolenda^{2,3,4,5}, Cécile Batailler^{2,3,6}, Claude-Alexandre Gustave^{2,3,4,5}, Sébastien Lustig^{2,3,6}, Matthieu Malatray^{3,6}, Cindy Fevre⁷, Jérôme Josse^{2,3,4,5}, Charlotte Petitjean⁷, Christian Chidiac^{1,2,3,4}, Gilles Leboucher⁸ and Frédéric Laurent^{2,3,4,5} on behalf of the Lyon BJI Study group

5,711

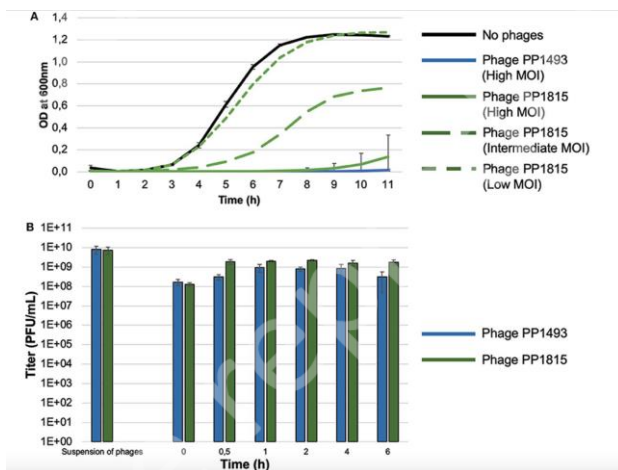
TOTAL VIEWS



The Potential Innovative Use of Bacteriophages Within the DAC® Hydrogel to Treat Patients With Knee Megaprosthesis Infection Requiring “Debridement Antibiotics and Implant Retention” and Soft Tissue Coverage as Salvage Therapy

Tristan Ferry^{1,2,3,4*}, Cécile Batailler^{2,3,5}, Charlotte Petitjean⁶, Joseph Chateau⁷, Cindy Fevre⁶, Emmanuel Forestier⁸, Sophie Brosset⁷, Gilles Leboucher⁹, Camille Kolenda^{2,3,4,10}, Frédéric Laurent^{2,3,4,10} and Sébastien Lustig^{2,3,5} on behalf of the Lyon BJI Study Group

4,970
TOTAL VIEWS



J Antimicrob Chemother 2018; **73**: 2901–2903
doi:10.1093/jac/dky263
Advance Access publication 27 July 2018

Innovations for the treatment of a complex bone and joint infection due to XDR *Pseudomonas aeruginosa* including local application of a selected cocktail of bacteriophages

Tristan Ferry^{1–4*}, Fabien Boucher^{1,4,5}, Cindy Fevre⁶, Thomas Perpoint^{1,4}, Joseph Chateau^{1,2,4,5}, Charlotte Petitjean⁶, Jérôme Josse^{2–4,7}, Christian Chidiac^{1,2–4}, Guillaume L’hostis⁶, Gilles Leboucher⁸ and Frédéric Laurent^{2–4,7} on behalf of the Lyon Bone and Joint Infection Study Group[†]

CITATIONS




VIEWS



ALTMETRIC



More metrics information

Case series  procedure called « PhagoDAIR »

Phage Therapy as Adjuvant to Conservative Surgery and Antibiotics to Salvage Patients With Relapsing *S. aureus* Prosthetic Knee Infection

5,711

TOTAL VIEWS



Tristan Ferry^{1,2,3,4*}, Camille Kolenda^{2,3,4,5}, Cécile Batailler^{2,3,6},
Claude-Alexandre Gustave^{2,3,4,5}, Sébastien Lustig^{2,3,6}, Matthieu Malatray^{3,6}, Cindy Fevre⁷,
Jérôme Josse^{2,3,4,5}, Charlotte Petitjean⁷, Christian Chidiac^{1,2,3,4}, Gilles Leboucher⁸ and
Frédéric Laurent^{2,3,4,5} on behalf of the Lyon IJL Study group



#PhagoDAIR

Debridement Antibiotics and Implant Retention

CASE REPORT
published: 16 November 2020
doi: 10.3389/fmed.2020.570572



Clinical cases (2nd treated patient)

80-year-old man

Relapsing *S. aureus* prosthetic left knee infection (past revision)

Fracture

Complex orthopaedic situation with past femoral fracture

Impossible to walk (painful knee)



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Septic arthritis



PHAGE*in***LYON**



Fistula and purulent discharge



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"PhagoDAIR"



**One shot peroperative phage
application after "DAIR"**



PHAGE*in* **LYON**



"The bacteriophages saved my life, he insists. I never thought one day to walk again. And to say that doctors were talking about cutting my leg off!" R.N.

**Favorable outcome
at 2 years**



PHAGE*in***LYON**



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Management of relapsing infections with bacterial persistence



30 months after the PhagoCAIR procedure
Under cefalexin as suppressive therapy

	<i>Staphylococcus aureus</i> CMI (mg/l)
Pénicilline G	R
Oxacilline	S
Kanamycine	S
Gentamicine	S
Tobramycine	S
Erythromycine	S
Lincomycine	S
Pristinamycine	S
Tétracycline	S
Ofloxacine	S
Cotrimoxazole	S
Nitrofurantoïne	S
Rifampicine	S
Fosfomycine	S
Acide Fusidique	S
Vancomycine	S
Teicoplanine	S
Linézolide	S

Management of relapsing infections with bacterial persistence



Management of bacterial persistence

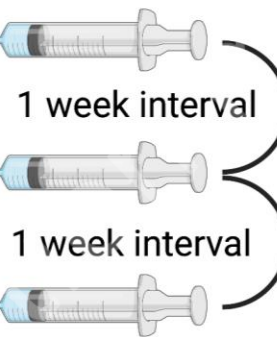


tions with

Cefalexin PO
500 mg tid
même partielle est interdite.

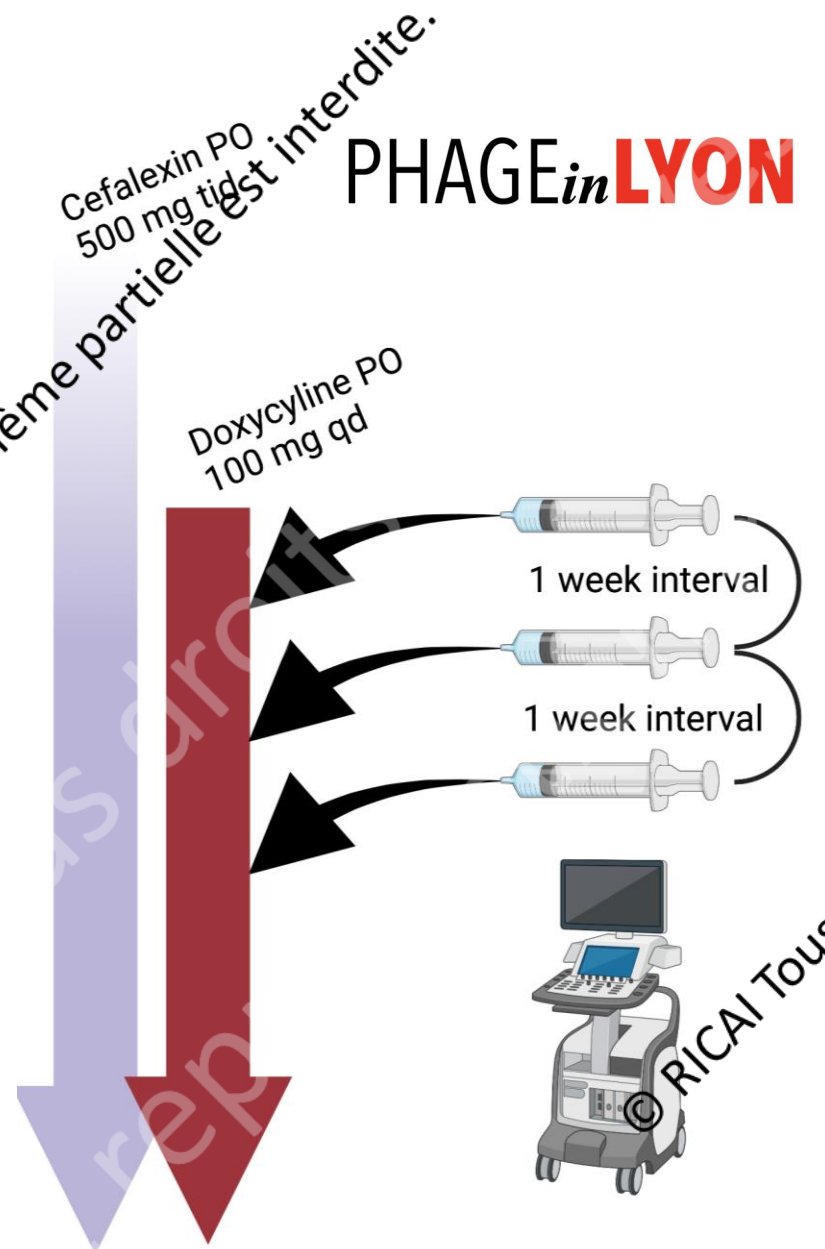
PHAGEⁱⁿLYON

Doxycycline PO
100 mg qd



© RICAI Tous

Management of relapsing infections with bacterial persistence



PhagoDAIR I

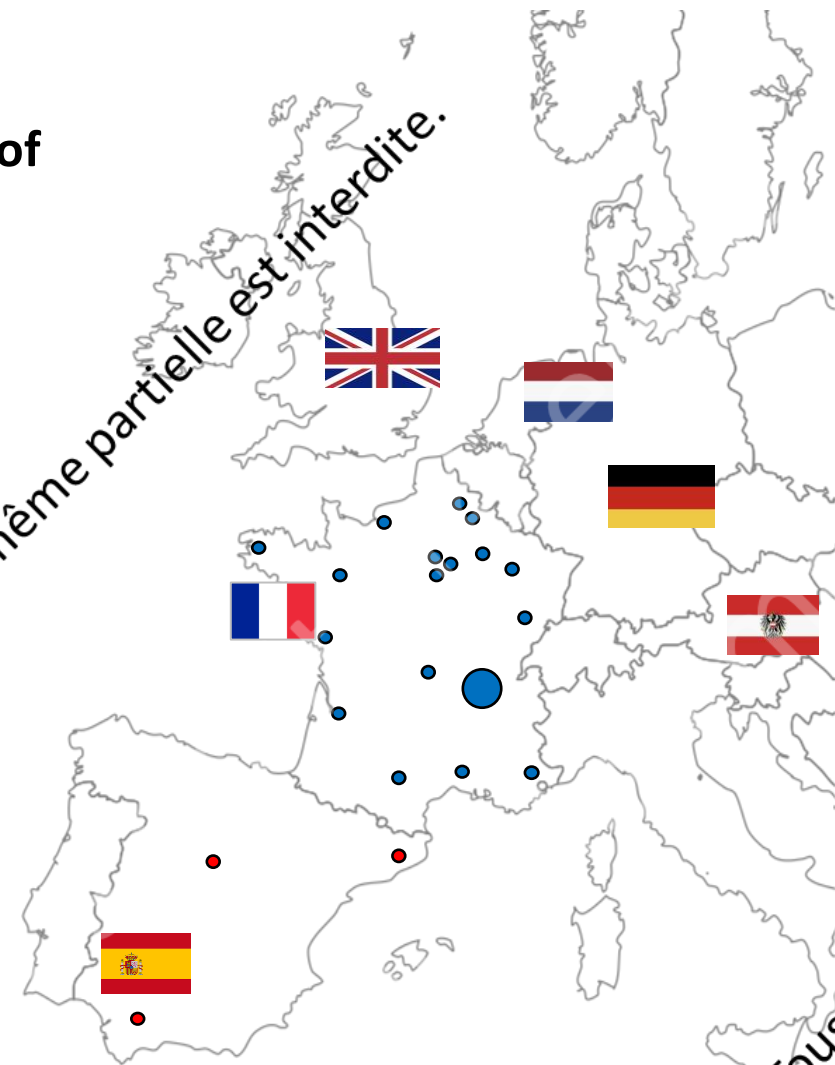
A Pilot, Multicenter, Randomized, Non-Comparative, Double-Blind Study of
Phage Therapy in Patients with Hip or Knee PJI due to *S. aureus*
Treated with DAIR and Antibiotic Therapy

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 \pm 2 which will allow to calculate the sample size for future comparative studies.

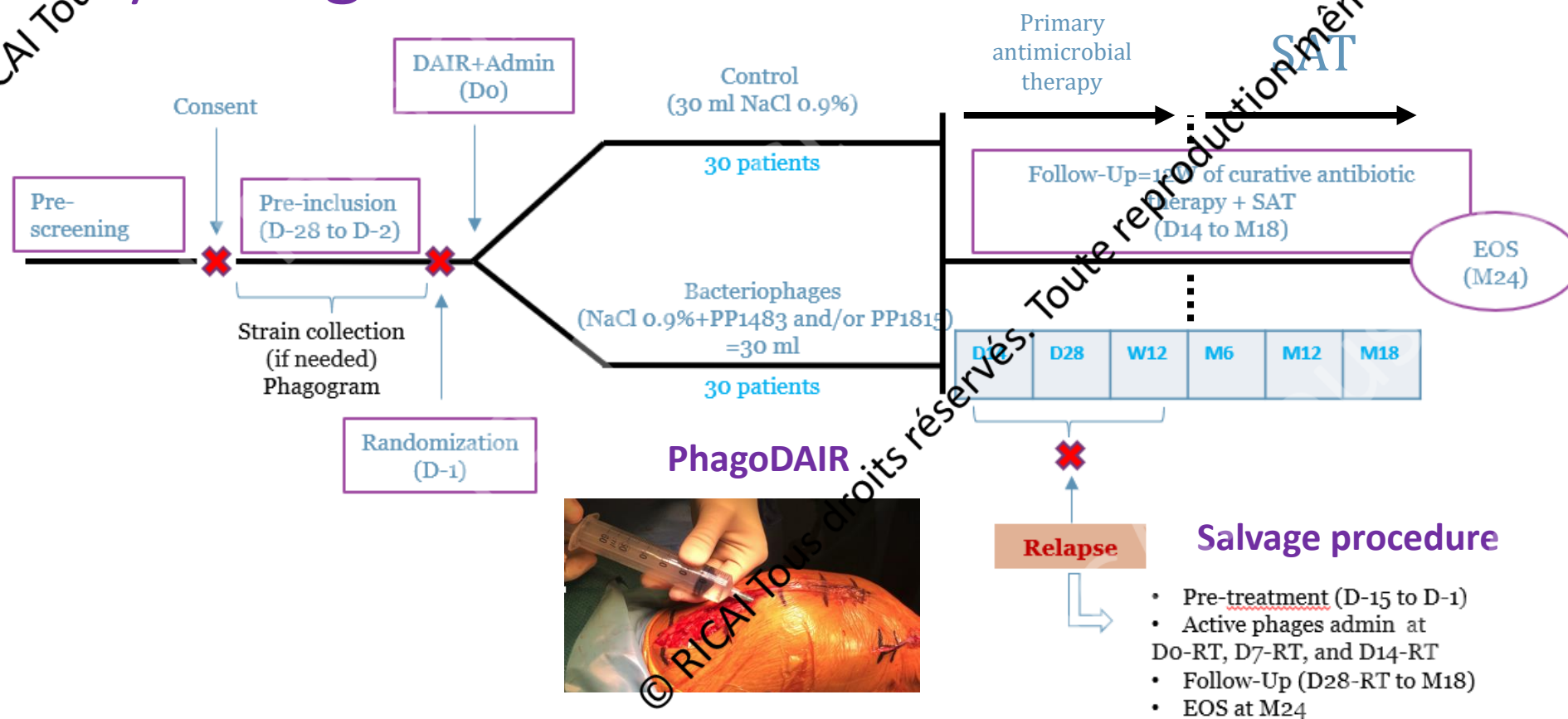


PHARECYDES
PHARMA

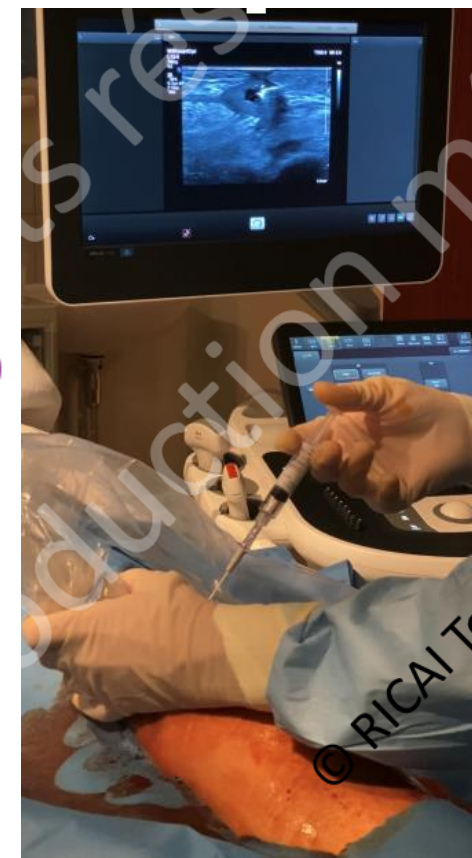
PhagoDAIR I

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



Salvage procedure



Phage Therapy for Limb-threatening Prosthetic Knee *Klebsiella pneumoniae* Infection: Case Report and In Vitro Characterization of Anti-biofilm Activity

Edison J. Cano,^{1,2} Katherine M. Cafilisch,^{2,3} Paul L. Bollyky,⁴ Jonas D. Van Belleghem,⁴ Robin Patel,^{1,2,5} Joseph Fackler,⁶ Michael J. Brownstein,⁶ Bri'Anna Horne,⁶ Biswajit Biswas,⁷ Matthew Henry,^{7,8} Francisco Malagon,⁷ David G. Lewallen,⁹ and Gina A. Suh¹

¹Division of Infectious Diseases, Mayo Clinic, Rochester, Minnesota, USA, ²Infectious Diseases Research Laboratory, Mayo Clinic, Rochester, Minnesota, USA, ³Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, Minnesota, USA, ⁴Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California, USA, ⁵Division of Clinical Microbiology, Mayo Clinic, Rochester, Minnesota, USA, ⁶Adaptive Phage Therapeutics, Gaithersburg, Maryland, USA, ⁷Genomics and Bioinformatics Department, Biological Defense Research Directorate, Naval Medical Research Center-Frederick, Fort Detrick, Maryland, USA, ⁸Geneva Foundation, Tacoma, Washington, USA, and ⁹Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota, USA

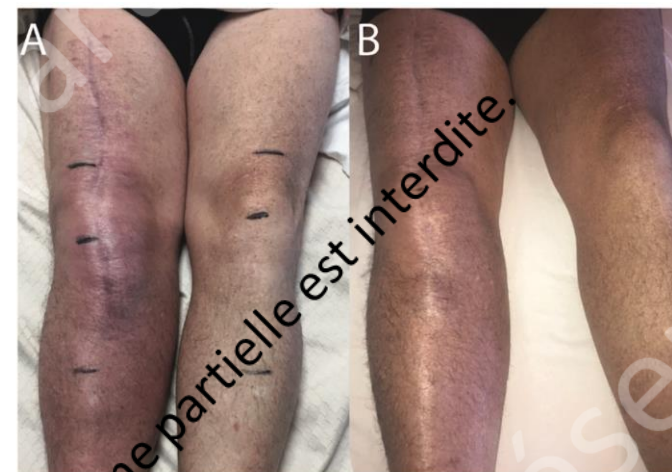


Figure 3. Phage therapy resulted in reduced erythema and swelling. Images are shown of the patient's lower extremities (A) before and (B) after completion of phage therapy.

NO SURGERY! 40 doses of exclusive INTRAVENOUS phages (1 injection each weekday)



pharmaceuticals

2021



Case Report

Successful Treatment of a Recalcitrant *Staphylococcus epidermidis* Prosthetic Knee Infection with Intraoperative Bacteriophage Therapy

James B. Doub^{1,*}, Vincent Y. Ng², Eleanor Wilson¹, Lorenzo Corsini³  and Benjamin K. Chan⁴

Single LOCAL injection during DAIR





U.S. National Library of Medicine

ClinicalTrials.gov

A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of Phage Therapy Versus Placebo in Conjunction With DAIR in Patients With Chronic Prosthetic Joint Infection Who Previously Failed Surgery for PJI



adaptive phage
THERAPEUTICS

An Open-Label Multicenter Study to Evaluate the Safety and Efficacy of PhageBank™ Phage Therapy in Conjunction With Debridement, Antibiotics, and Implant Retention (DAIR) for Patients With First Time Culture Proven Chronic Prosthetic Joint Infection



adaptive phage
THERAPEUTICS

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



PHERECYDES
PHARMA

Etc.

Clinical case (3rd treated patient)

Arthroscopic DAIR with phages to salvage *P. aeruginosa* prosthetic knee infection

88-year-old man

Relapsing *P. aeruginosa* prosthetic left knee infection

End-stage cardiac failure

Contraindicated to open DAIR



PHAGEin LYON



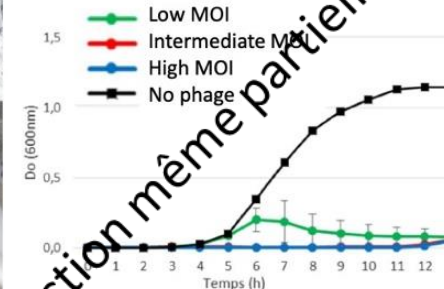
A



Left PKI with purulent joint effusion

B

Phage 1450



Phagogram (Killing assay)



Arthroscopic DAIR

C

D



Favorable outcome at 1 year

Clinical case (not published; 21th treated patients)



72-year-old man

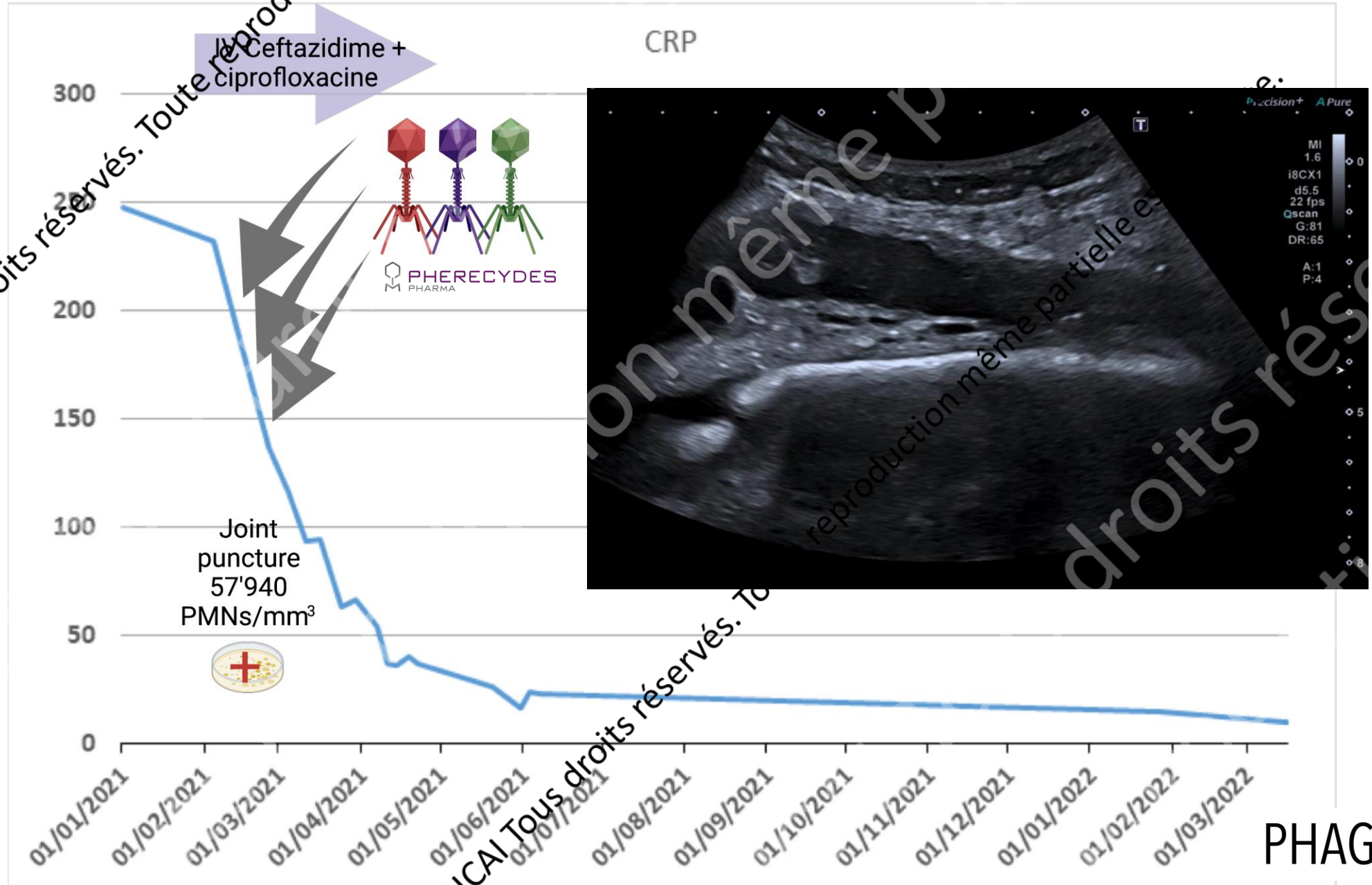
Relapsing *P. aeruginosa* prosthetic right hip PJI with femoral osteomyelitis and large abscess

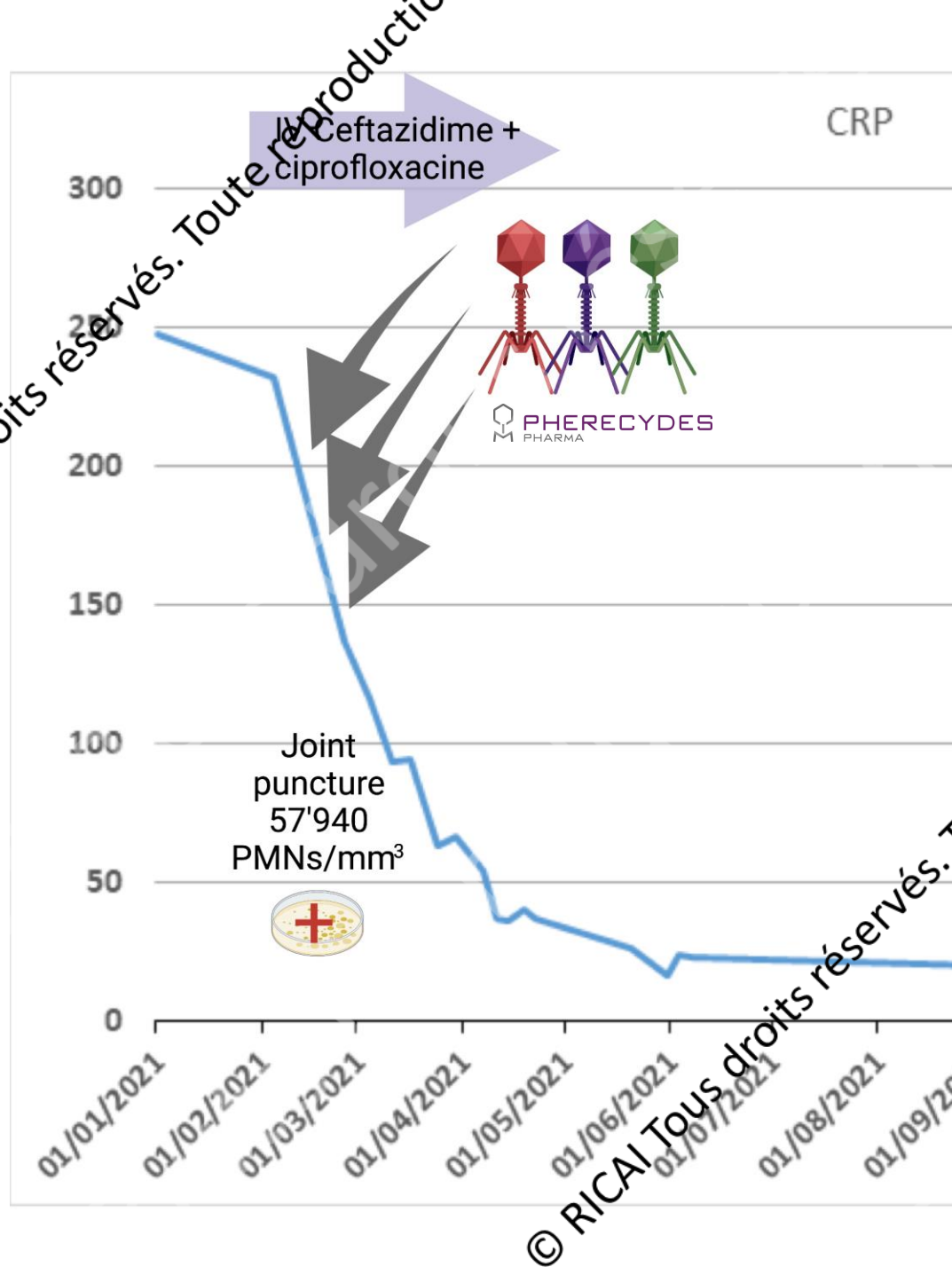
Disarticulation was proposed

Local?
IV?

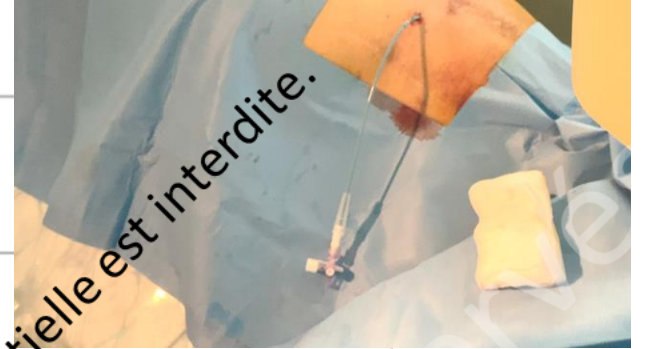
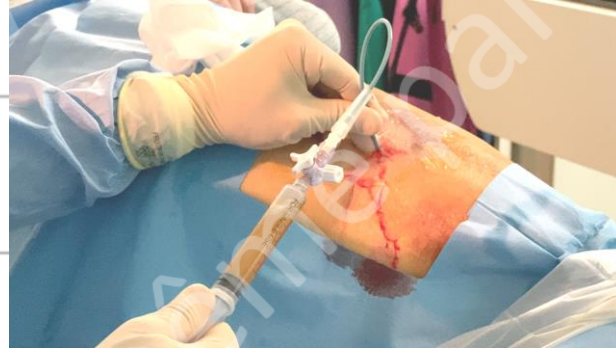
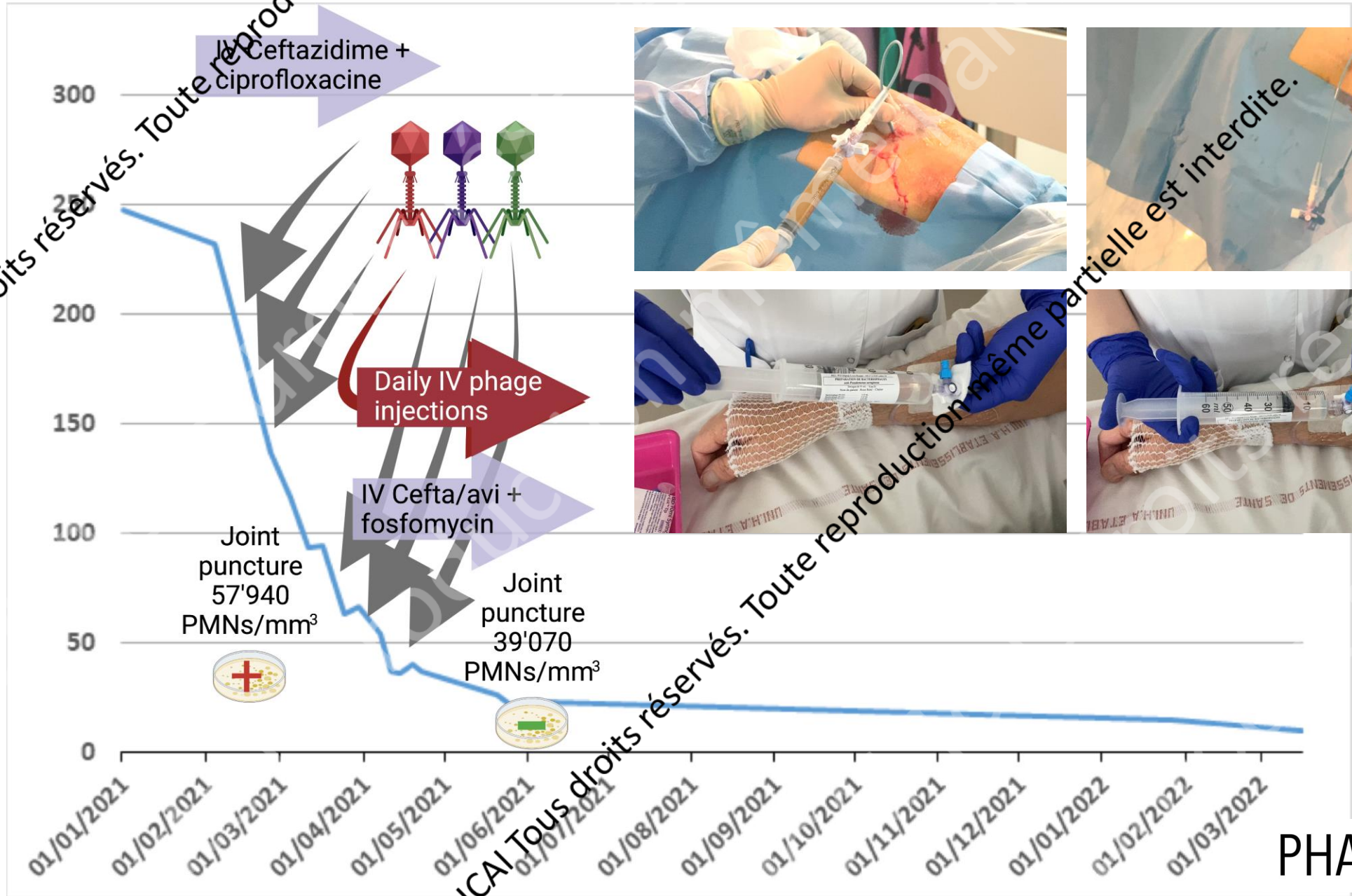
Local + IV?

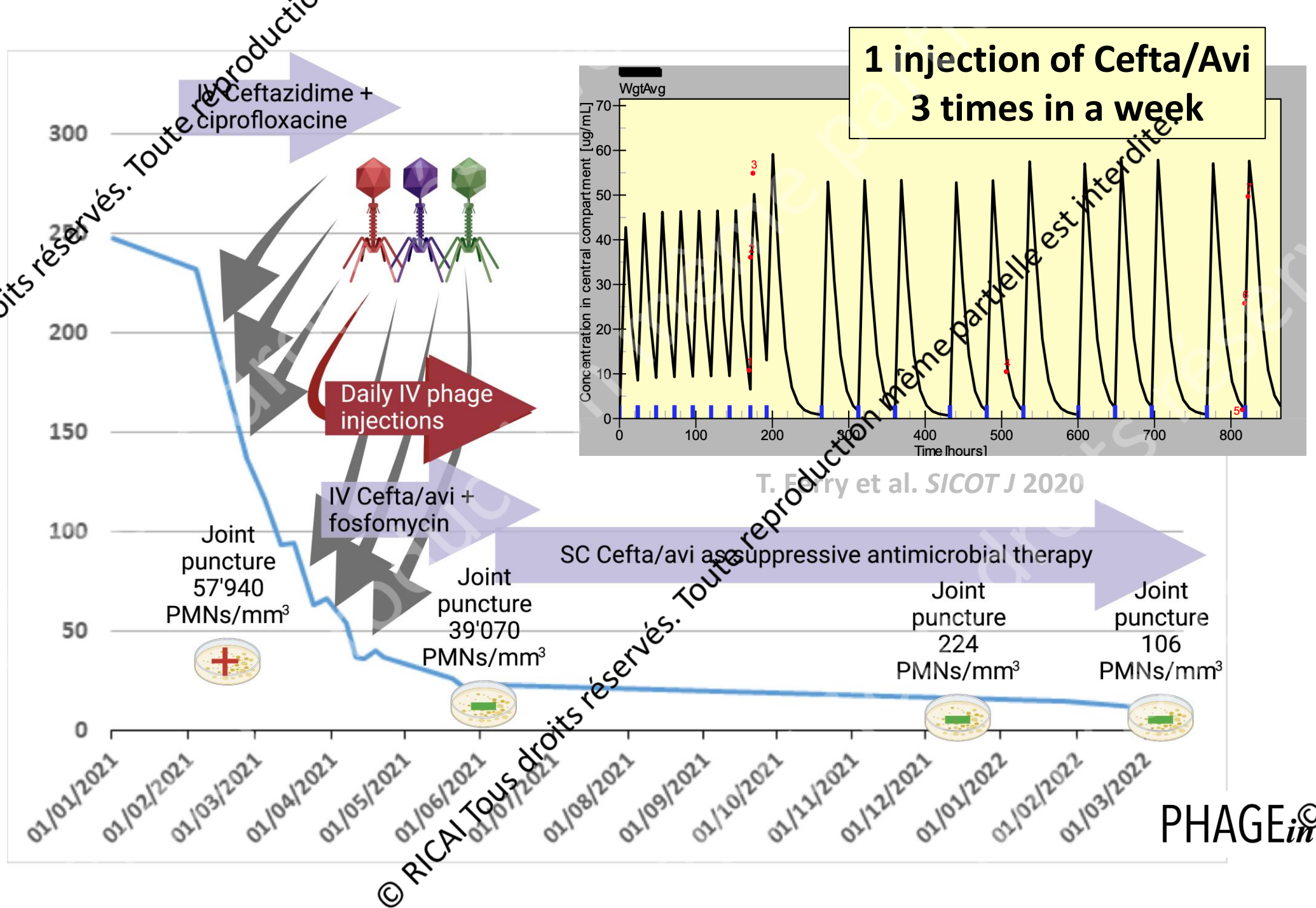


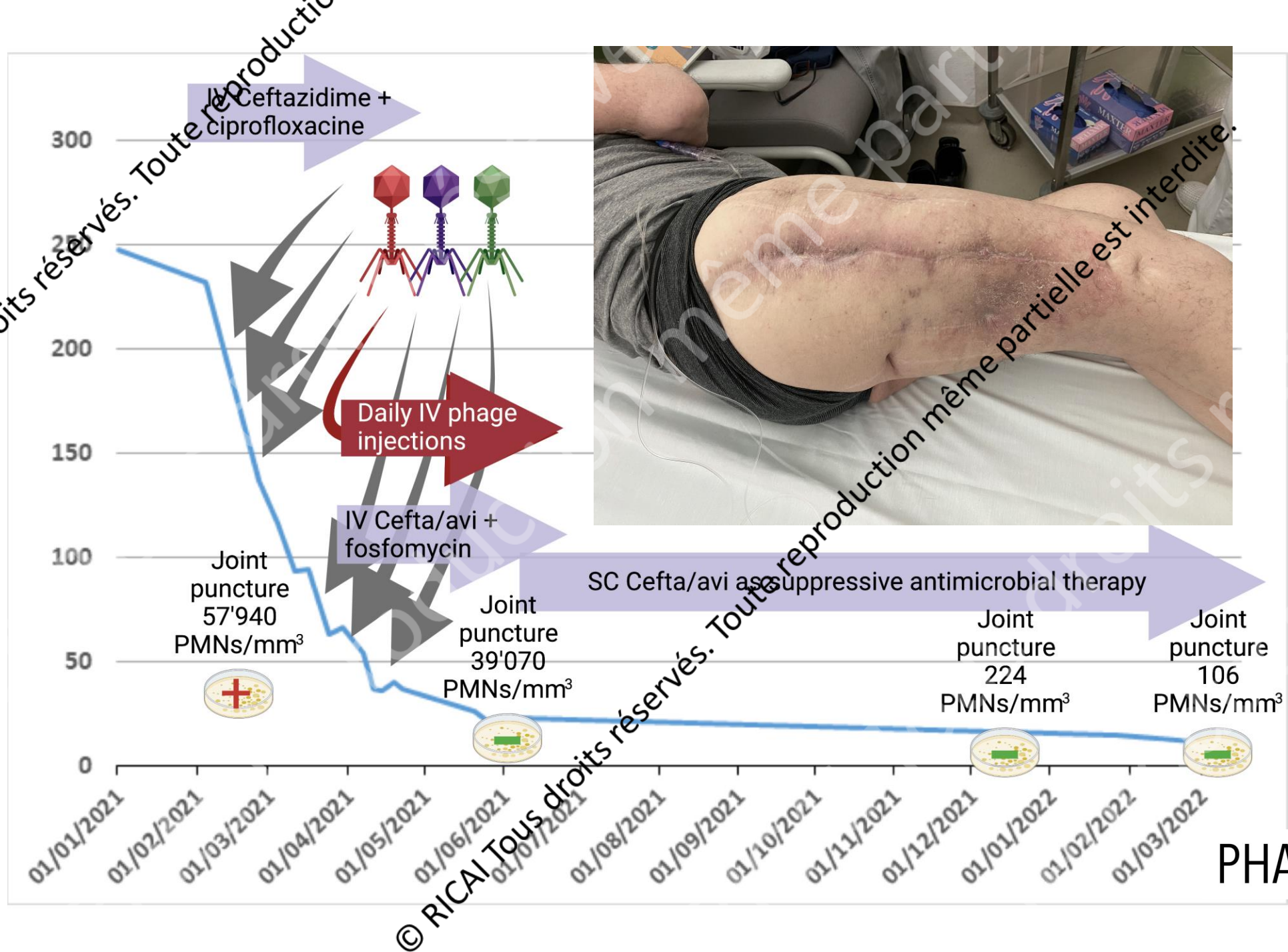


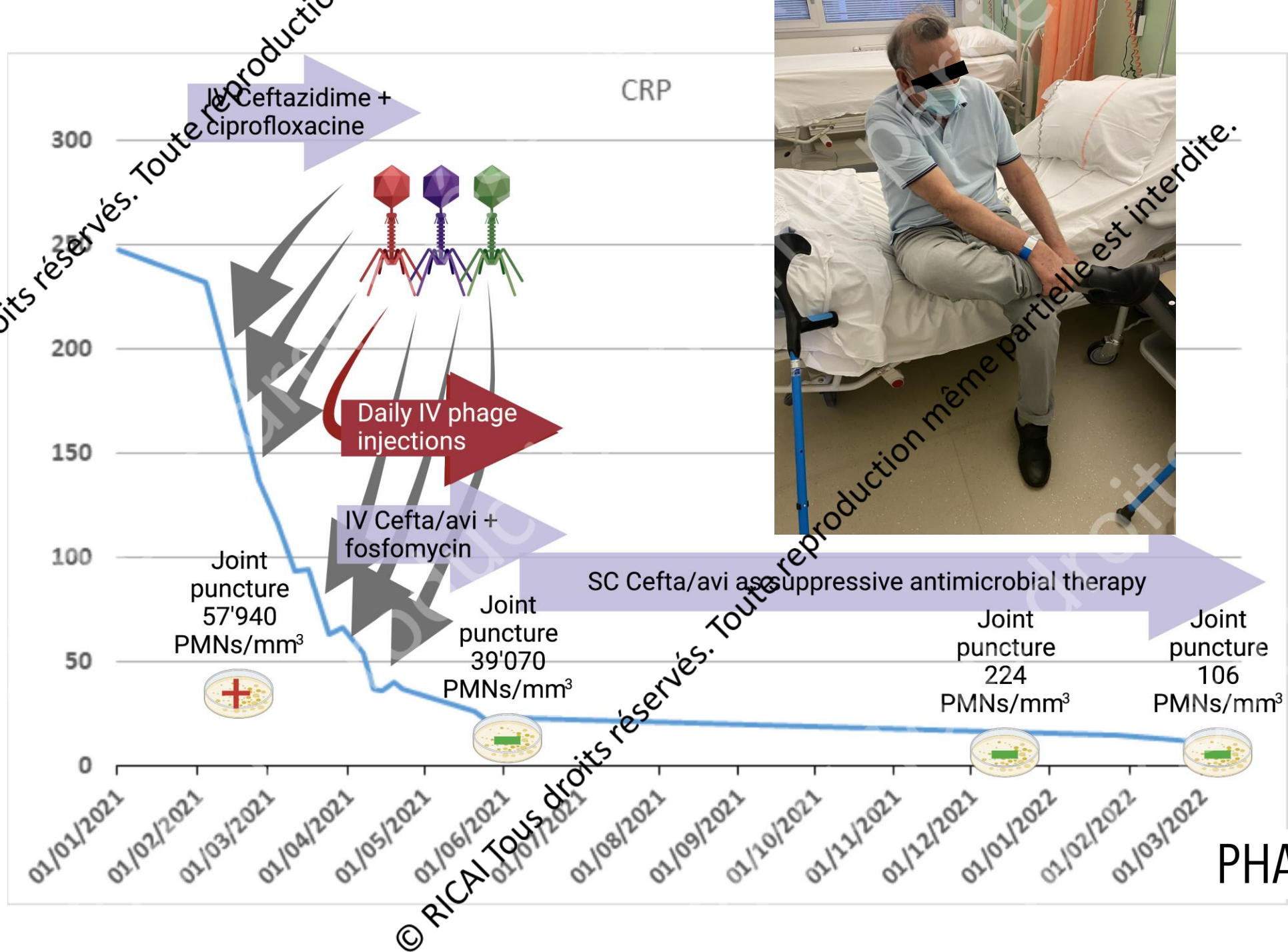


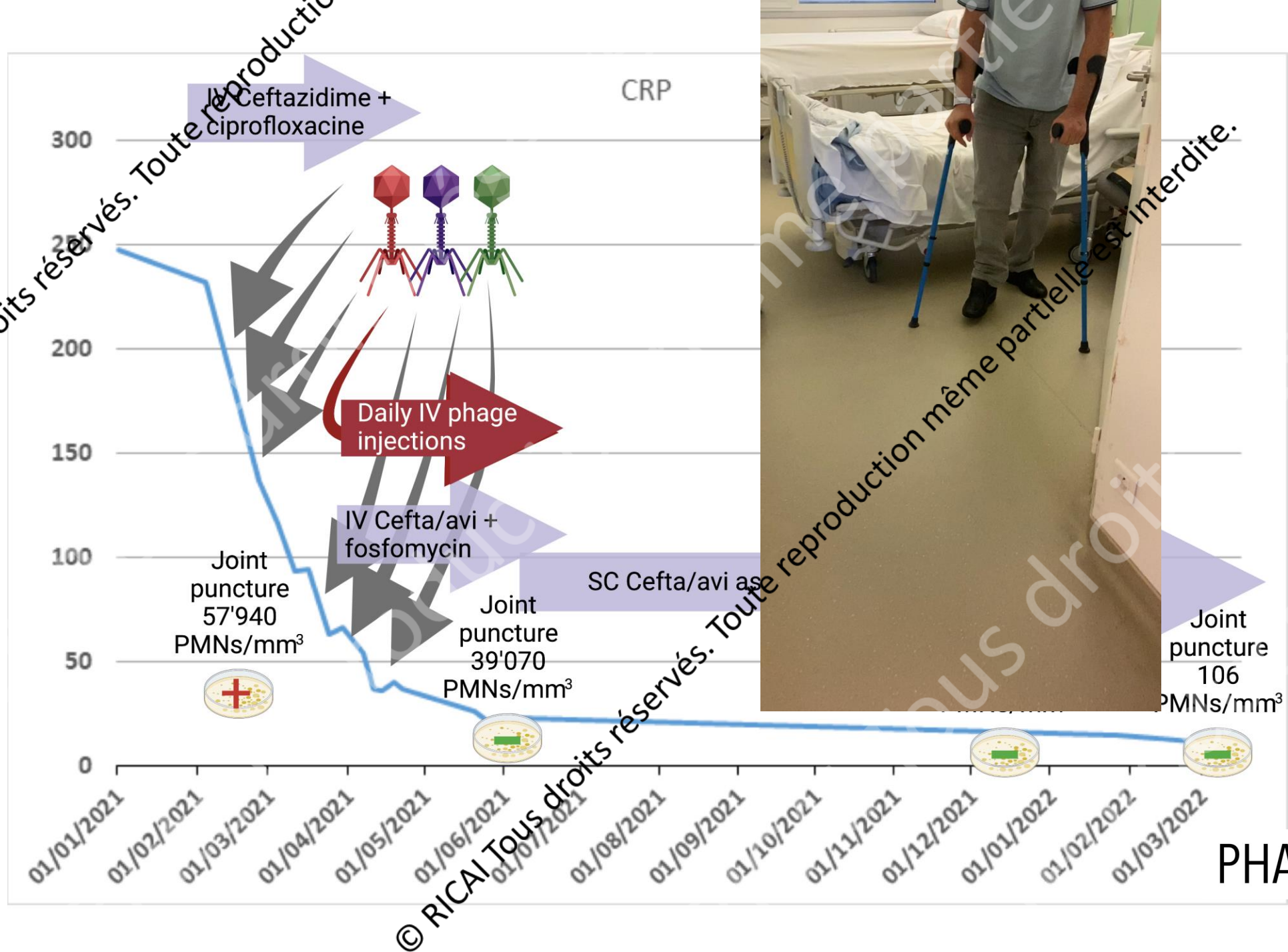
Pseudomonas aeruginosa	
	CMI (mg/l)
Ampicilline	R
Amoxicilline	R
Amoxicilline + Ac.Clavulanique	R
Ticarcilline	R
Ticarcilline + Ac. Clav	R
Pipéracilline	R
Pipéracilline + Tazobactam	R
Céfoxitine	R
Céfotaxime	R
Ceftazidime	R
Ceftazidime-Avibactam	S
Ceftolozane-tazobactam	S
Céfépime	R
Cefiderocol	S
Aztréonam	I
Ertapénème	R
Imipénème	R
Meropenem	R
Tobramycine	S
Amikacine	S
Clécycline	R
Ciprofloxacine	S
Acide Nalidixique	R
Cotrimoxazole	R
Ceftazidime (Etest)	R
	CMI : 12
Ceftazidime-Avibactam (Etest)	S
	CMI : 6
Ciprofloxacine (Etest)	S
	CMI : 0.250
Fosfomycine (Etest)	V
	CMI : 24
Colistine (UMIC)	R
	CMI : 4



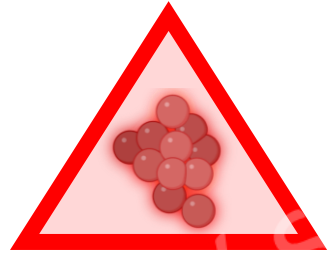








A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

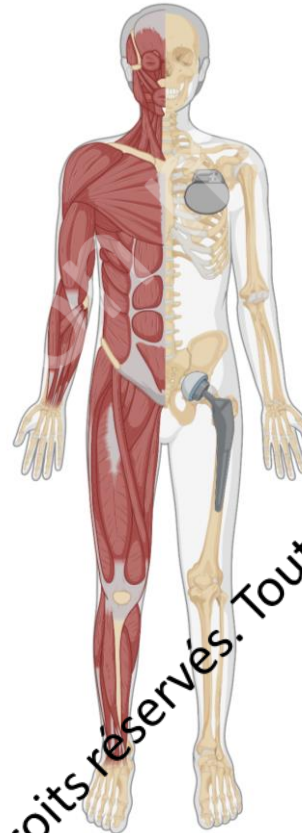
Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection

Digestive-tract infection

Typhoid fever, shigellosis
Cholera



Cardiovascular infections

Endocarditis
Cardiac electronic device infection
Prosthetic valve endocarditis
Vascular graft infection

Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection

Clinical case (12th treated patient)

74-year-old man

Melanoma treated with anti-PD1

Catheter-related *P. aeruginosa* bacteriemia in
January 2018

Spinal pain summer 2018

Spondylodiscitis with **spinal abscess**

Pandrug-resistant *P. aeruginosa* in culture!



Clinical case (12th treated patient)

74-year-old man

Melanoma treated with anti-PD1

Catheter-related *P. aeruginosa* bacteriemia in January 2018

Spinal pain summer 2018

Spondylodiscitis with spinal

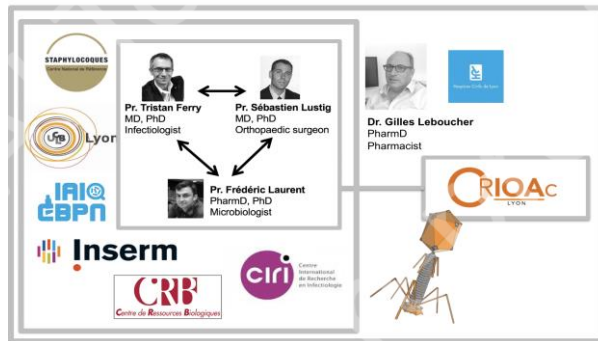
Pandrug-resistant

The strain was also spontaneously resistant to bacteriophages !!!

<i>Pseudomonas aeruginosa</i>	
	CMI (mg/l)
Ticarcilline + Ac. Clav	R (> 64)
Pipéracilline	R (> 64)
Pipéracilline + Tazobactam	R (> 64)
Ceftazidime	R (> 32)
Céfépime	R (> 32)
Aztréonam	R (> 32)
Imipénème	R (> 8)
Meropenème	R (> 8)
Gentamicine	R (> 8)
Tobramycine	R (> 8)
Amikacine	R (> 32)
Ciprofloxacine	R (> 2)
Flévoxacine	R (> 4)
Isotrizoxazole	R
E-test : 1	S (8) ⇒ R
E-test : 1	S ⇒ R
E-test : > 256	R
E-test : 64	R

Unique European academic collaboration

Lyon Phage team



Under the supervision of



French Health Authority

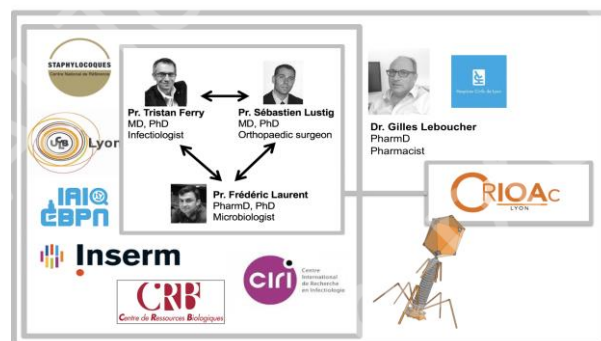
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Jean-Paul Pirnay



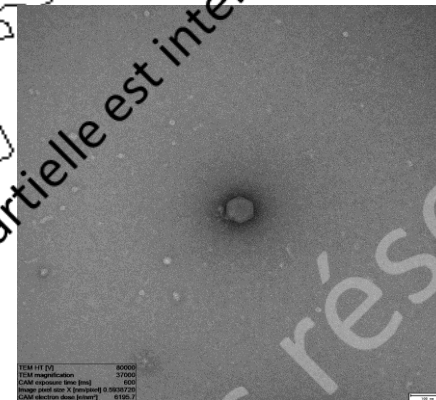
Gregory Resch



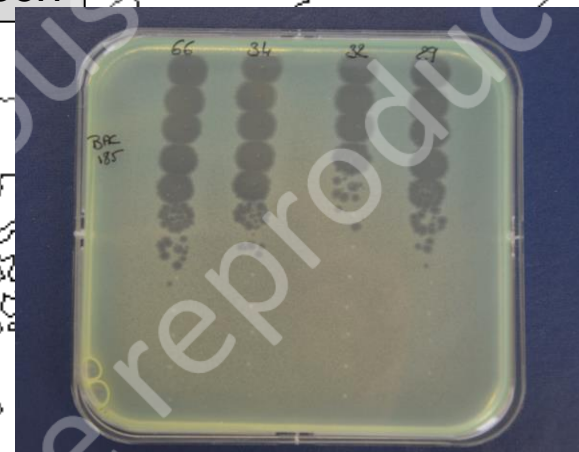
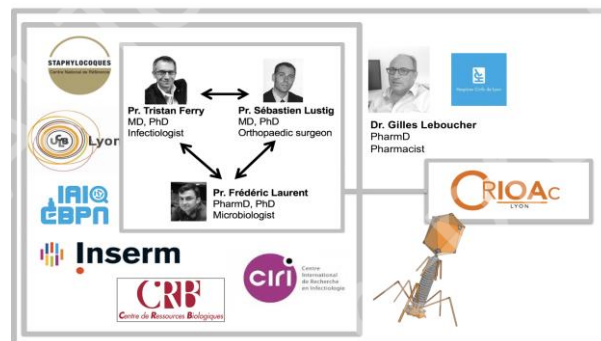
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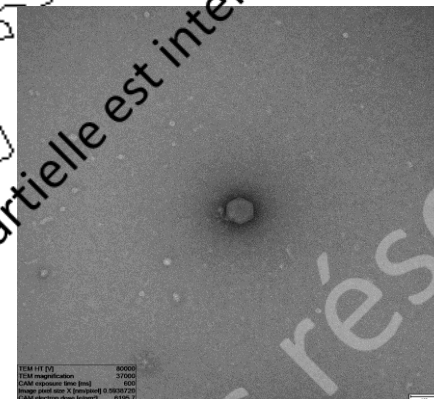


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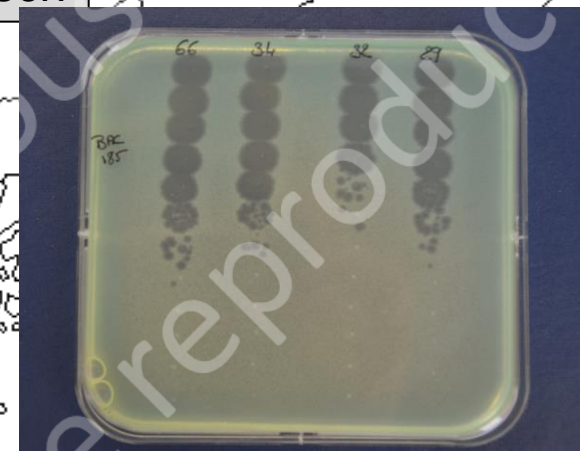
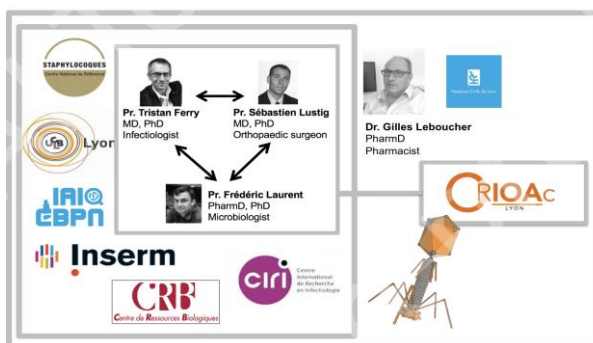


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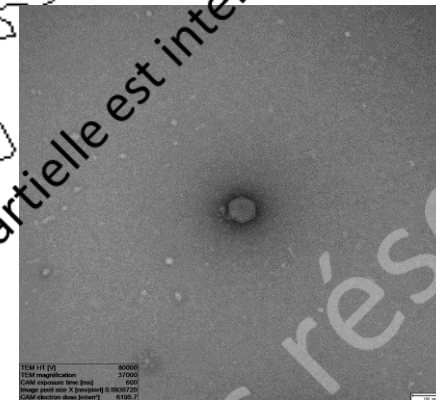


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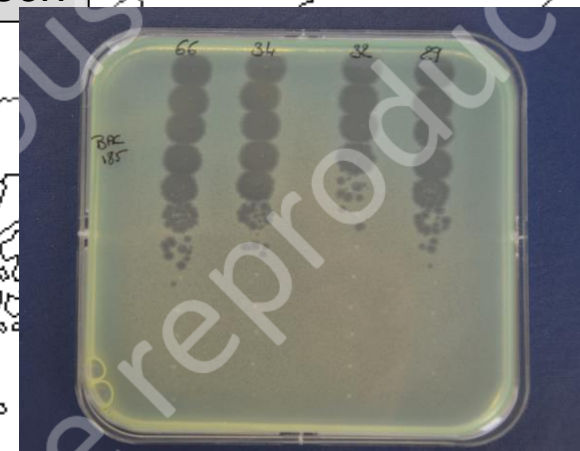
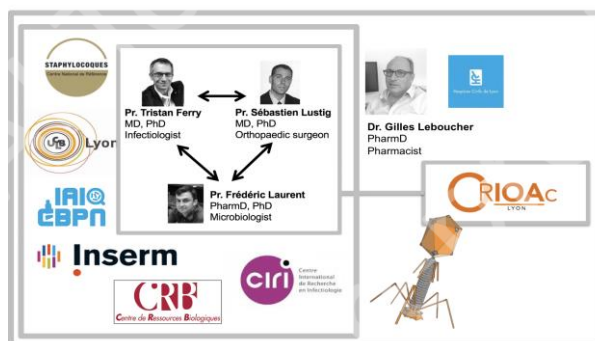
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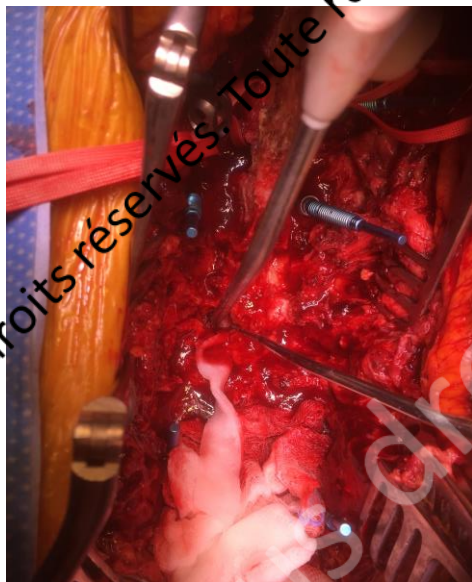
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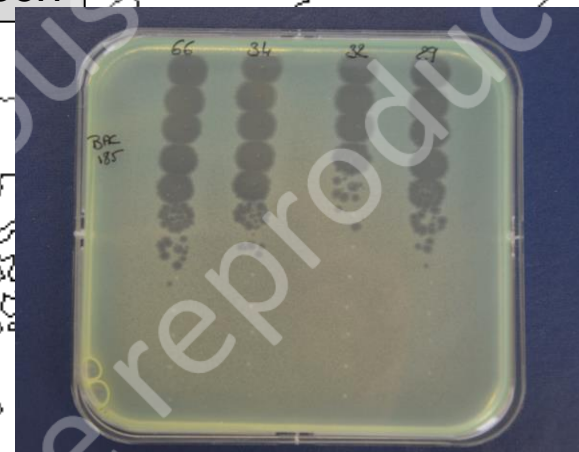
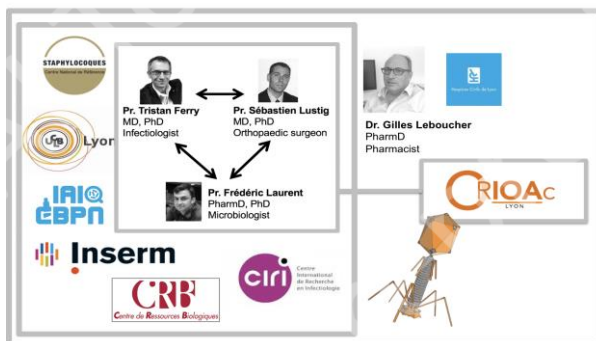
Lyon Phage team



Jean-Paul Pirnay



Gregory Resch



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T. FERRY et al. 2022



PHAGEⁱⁿLYON



Conclusions: Personalized phage therapy is a potential adjuvant treatment for patients with complex BJI due to pandrug-resistant bacteria. **In addition to industrial phages under development, academic collaborative research is crucial to develop personalized phage therapy.**

Implementation of a Phage Therapy Center in a CRIOAc



FERRY T. *et al.* 2022

Updated



PHAGEinLYON



47 patients in Lyon since 2017

~80% of the whole patients treated in France



• 14 with phages from



3 with phages from



½ Multidrug resistance

½ *S. aureus*

½ *P. aeruginosa*

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●○BJI

●○Endocarditis

●○Pneumonia

●○Burn

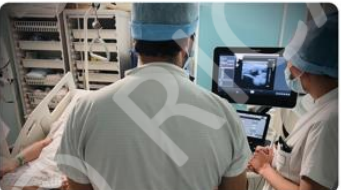
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Implementation of a Phage Therapy Center in a CRIOAc



FERRY T. *et al.* 2022

Updated



½ Multidrug resistance
½ *S. aureus*
½ *P. aeruginosa*

Under the supervision of



250 km



PHAGEinLYON



47 patients in Lyon since 2017

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• 14 with phages from



3 with phages from



• 40 **BJI** (including 34 **PJI**)

• 4 **endocarditis/vascular graft**

• 3 **lung infections** (VAP + bacteremia, pneumonia in lung graft bronchiectasia, cystic fibrosis exacerbation)



+ 11 patients managed outside Lyon

including 1 in and 1 in

●○ BJI

●○ Endocarditis

●○ Pneumonia

●○ Burn

Implementation of a Phage Therapy Center in a CRIOAc



FERRY T. *et al.* 2022

Updated



PHAGEin **LYON**



250 km



+ 15 Patients

Treated with Lysins
CF-301 (PJI)

S. epidermidis

Visio RCP CRIOAc
Thérapie innovante



RCP Phagothérapie

½ Multidrug resistance
½ *S. aureus*
½ *P. aeruginosa*

47 patients in Lyon since 2017

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●○ **Burn**

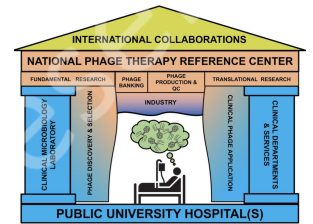
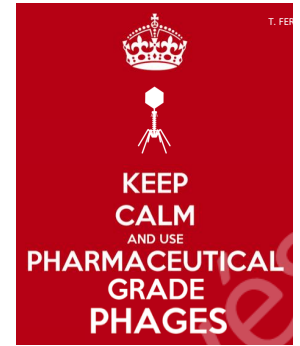
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Conclusion

- La phagothérapie est une **thérapie innovante et réémergente**
- Indications paraissant pertinentes : infections pulmonaires, endocardites sur prothèse valvulaire, IOAc dont les infections de prothèse articulaire
- En ADJUVANT à l'antibiothérapie (et potentiellement la chirurgie)
- Modalités d'administration doivent être personnalisées en fonction de l'expérience clinique, des phages à disposition et de la présentation clinique
- Nécessité d'une **mission nationale « CRIOAc thérapie innovante »**
 - Pour valider les indications pertinentes de phages/lysines dans les IOA
 - Pour orienter les prises en charge vers les essais thérapeutiques
 - Ou enfin pour orienter et accompagner le recours à des phages en « compassionnel » (nécessité d'une mission nationale **« RCP Phagothérapie »** pour préciser les modalités)
- Poser les jalons d'un centre national de phagothérapie
- Conception et réalisation d'essais thérapeutiques



THE MYTHOLOGY
OF IMAGE THERAPY



T. FERRY

EBM
Clinical
Trials



T. FERRY

Lyon BJI Study group



Coordinator: Tristan Ferry

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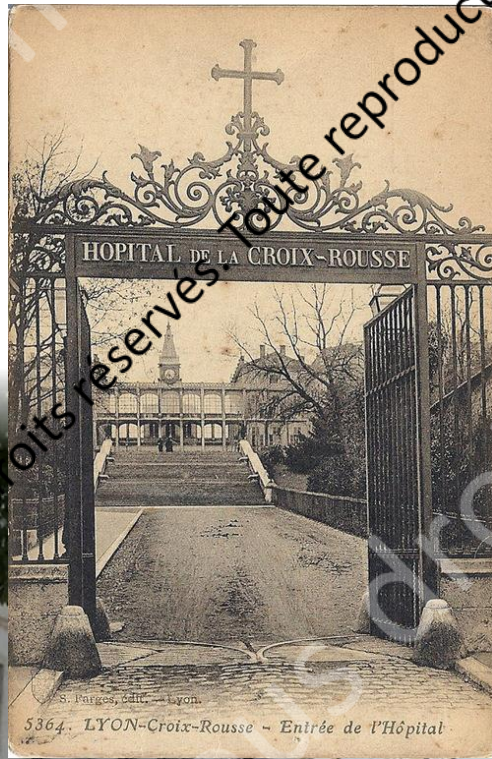
PHAGE_{in}LYON

Coordinator: Tristan Ferry (clinic); and Frederic Laurent (lab)

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Croix-Rousse Hospital



<http://www.crioac-lyon.fr>



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