

Infection ostéo-articulaire complexes, place de la phagothérapie

Phage therapy in severe bacterial infections: The French experience

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 @FerryLyon 

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Clinical officer ESCMID Study group for Non-Traditional Antibacterial therapy (ESGNTA)

Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

Conflict of interest

- **Phaxiam (ex-Pherecydes)** : Expert (Board), research grant, investigator coordinator of clinical trials (contract with hospital, no direct funding)
- **Armata** : Punctual expert (contract with university, no direct funding)
- **Contrafect** : Expert investigator coordinator of clinical trial (contract with hospital, no direct funding)

This presentation contains bloody images/videos for the operating rooms that can disturb sensitive people

All photos are my property

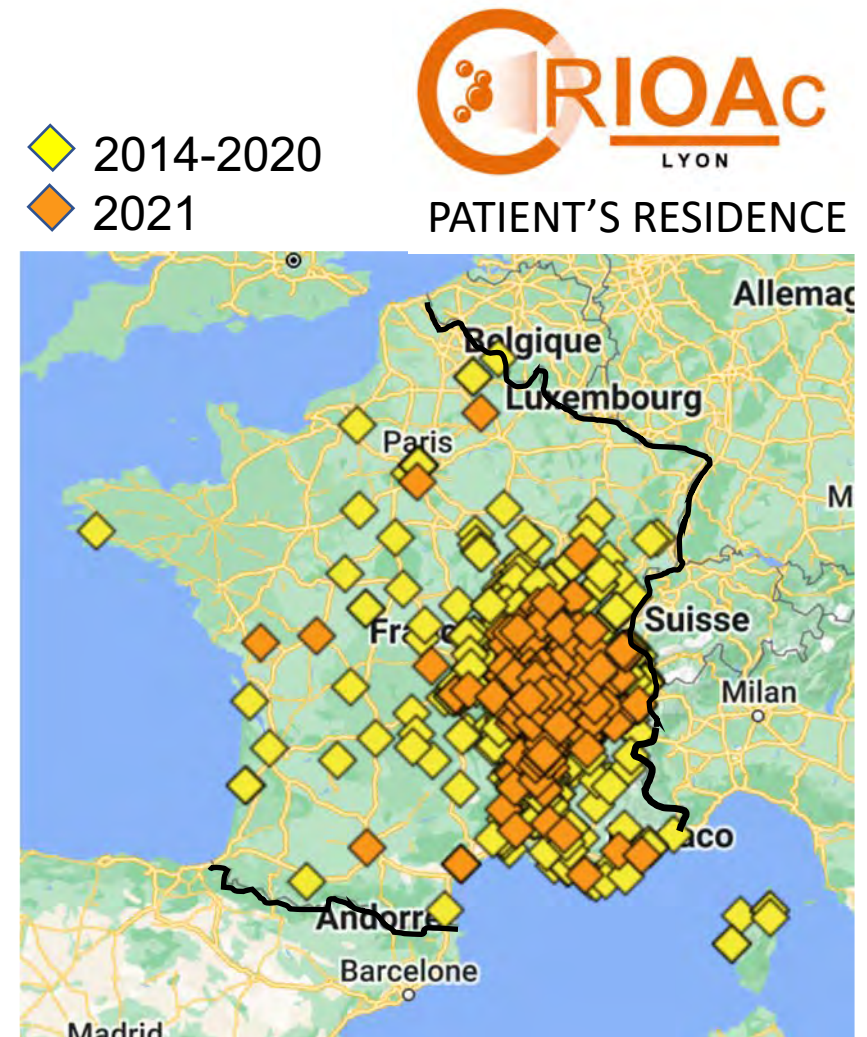
All cases are not (yet) published, keep this presentation confidential, please

I am infectious disease physician (with a PhD)

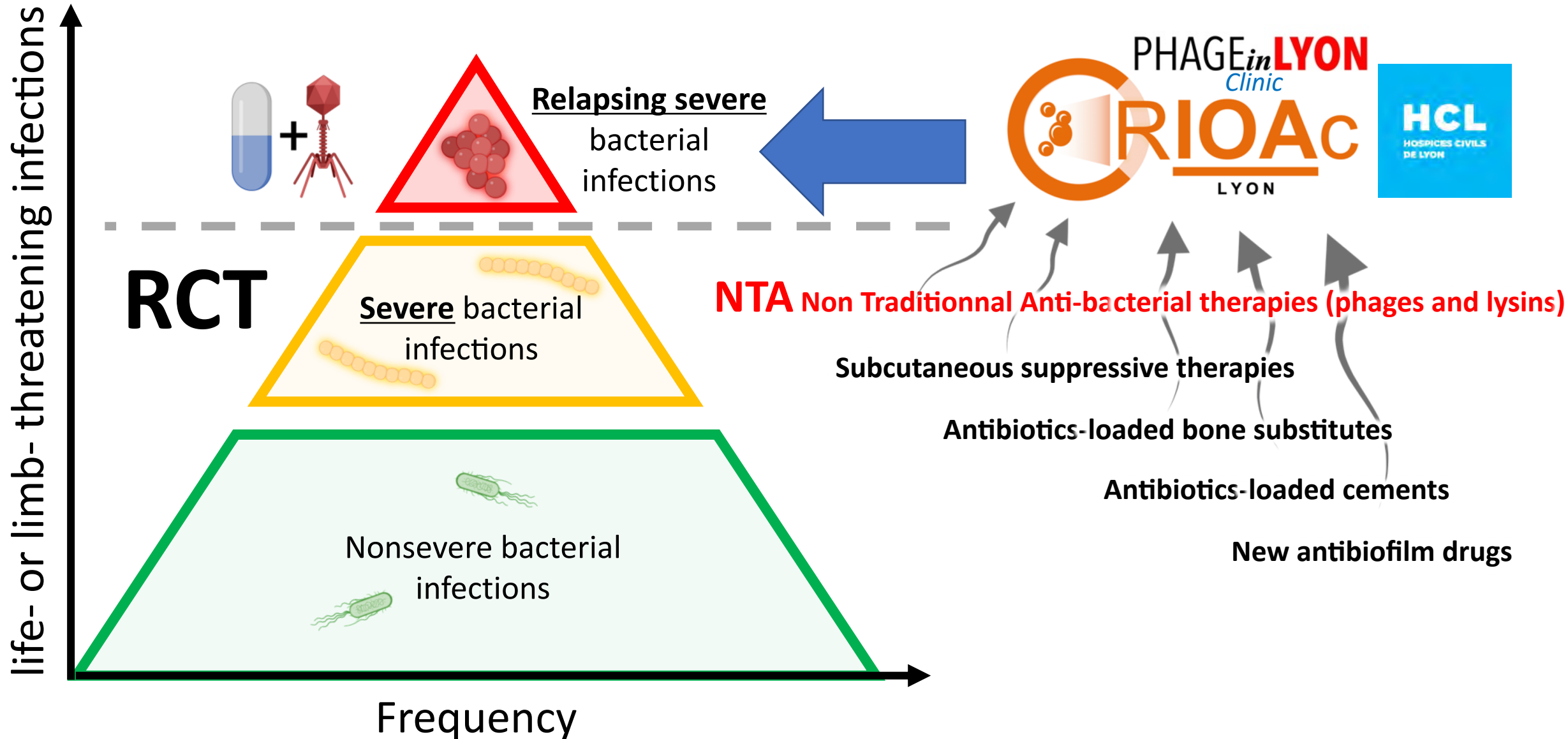


I have conflict of interest with the patients!

Referral center for the management of complex bone and joint infections (BJI)



The pyramid of bacterial infectious diseases



P Bone and joint infections: Lyon becomes the national expert center for phage therapy

The reference center for complex bone and joint infections, based at the Hospices Civils de Lyon, will centralize all requests concerning this last resort treatment, using viruses against resistant bacteria.

Le Progrès - 23 Feb. 2023 at 17:51 | updated 23 Feb. 2023 at 18:08 - Reading time: 2 min



National online
multidisciplinary meetings



Dedicated to innovative
anti-infective therapies



PHAGEⁱⁿLYON *Clinic*



Photo: Tristan Ferry



Infectious diseases department

Clinical development

Multidisciplinary meetings

Identifying relevant indications

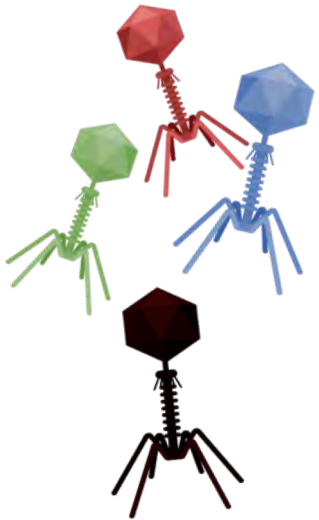
Managing the patient

Compassionate use

Cohort studies

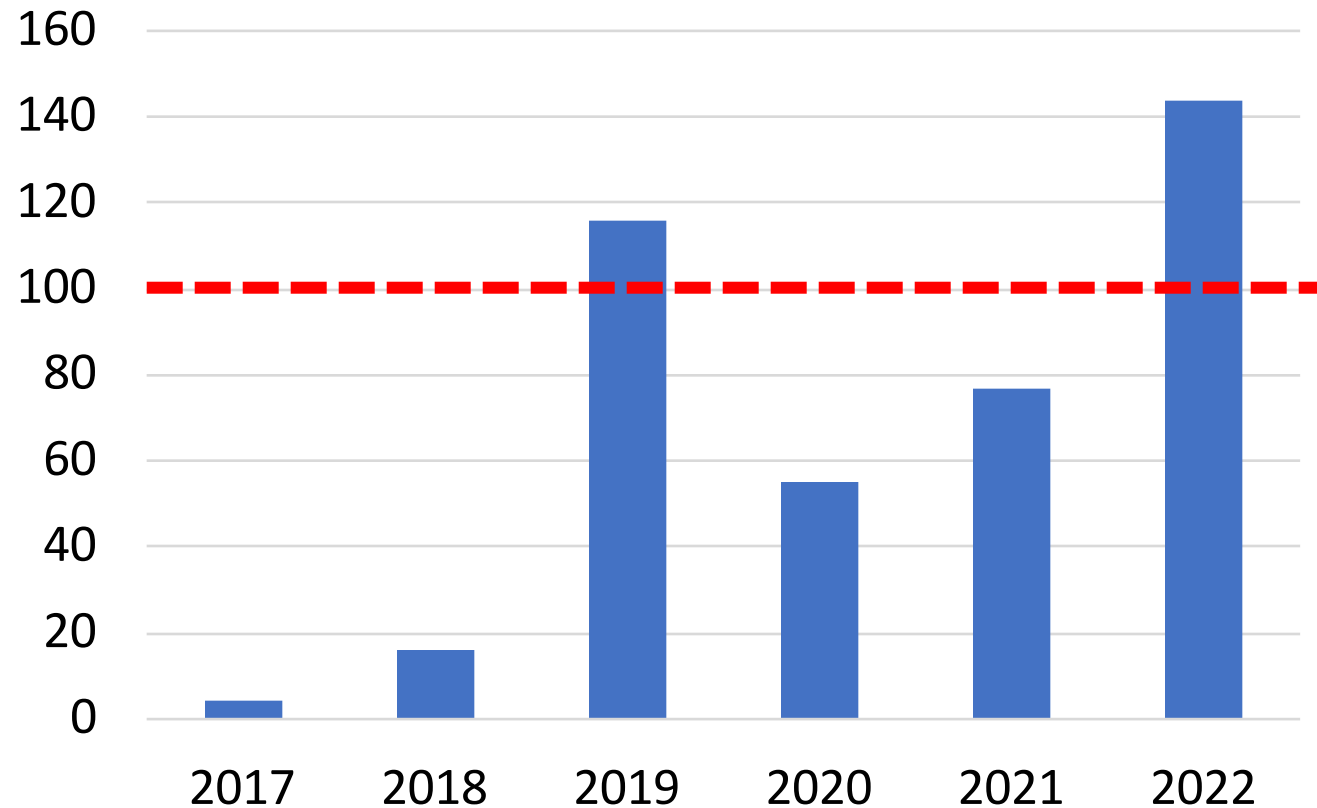
Pharmacokinetic in humans

Clinical trials



Phage requests

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Involved bacteria

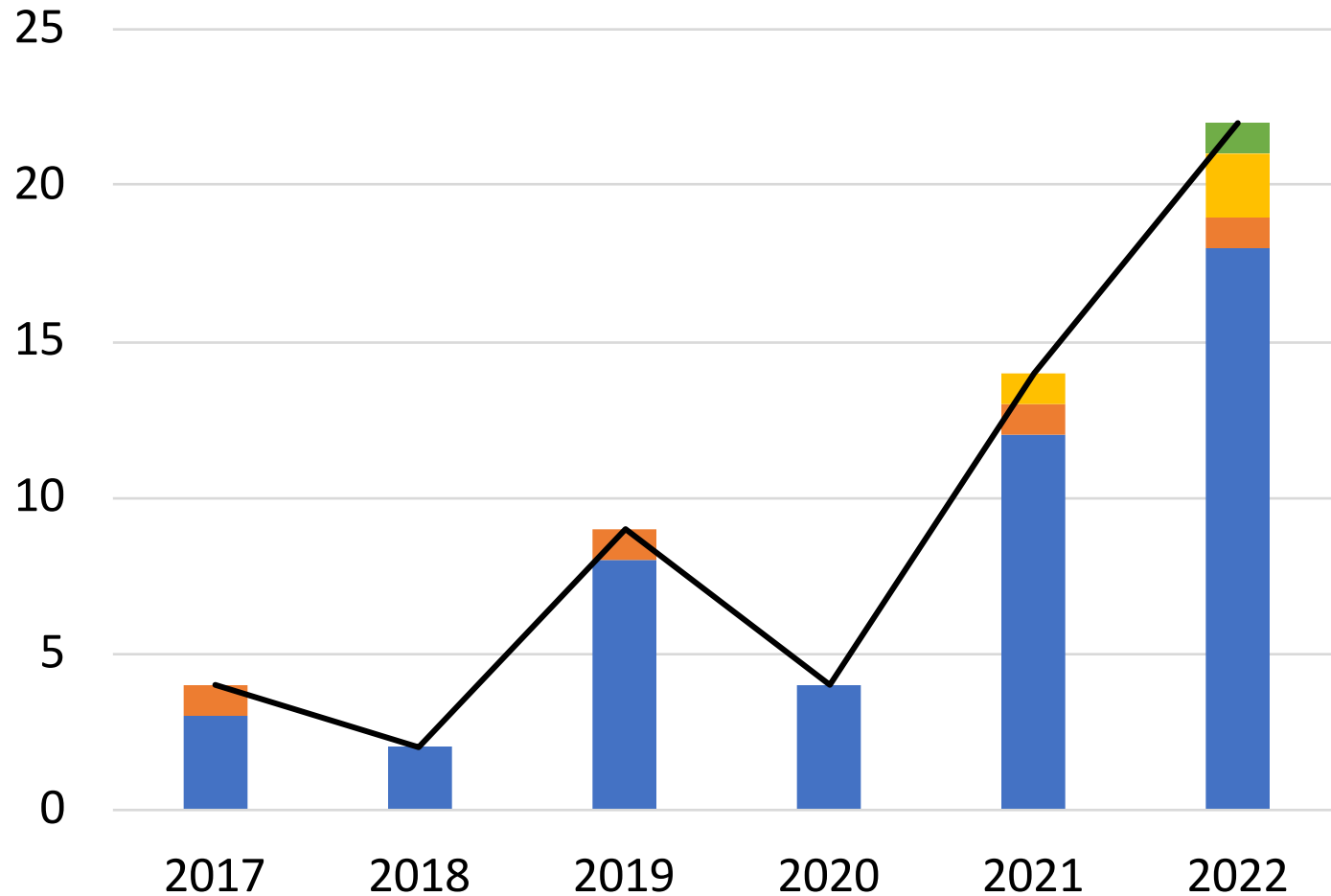
32 % *Staphylococcus aureus*
16 % *Pseudomonas aeruginosa*
6 % *Staphylococcus epidermidis*

Type of infection

37% Prosthetic-joint infection
27% Other bone and joint infection
8% Lung infection

Source : T. Ferry

Treated patients



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- Bone and joint
- Endocarditis
- Other
- Lung
- Vascular graft infection

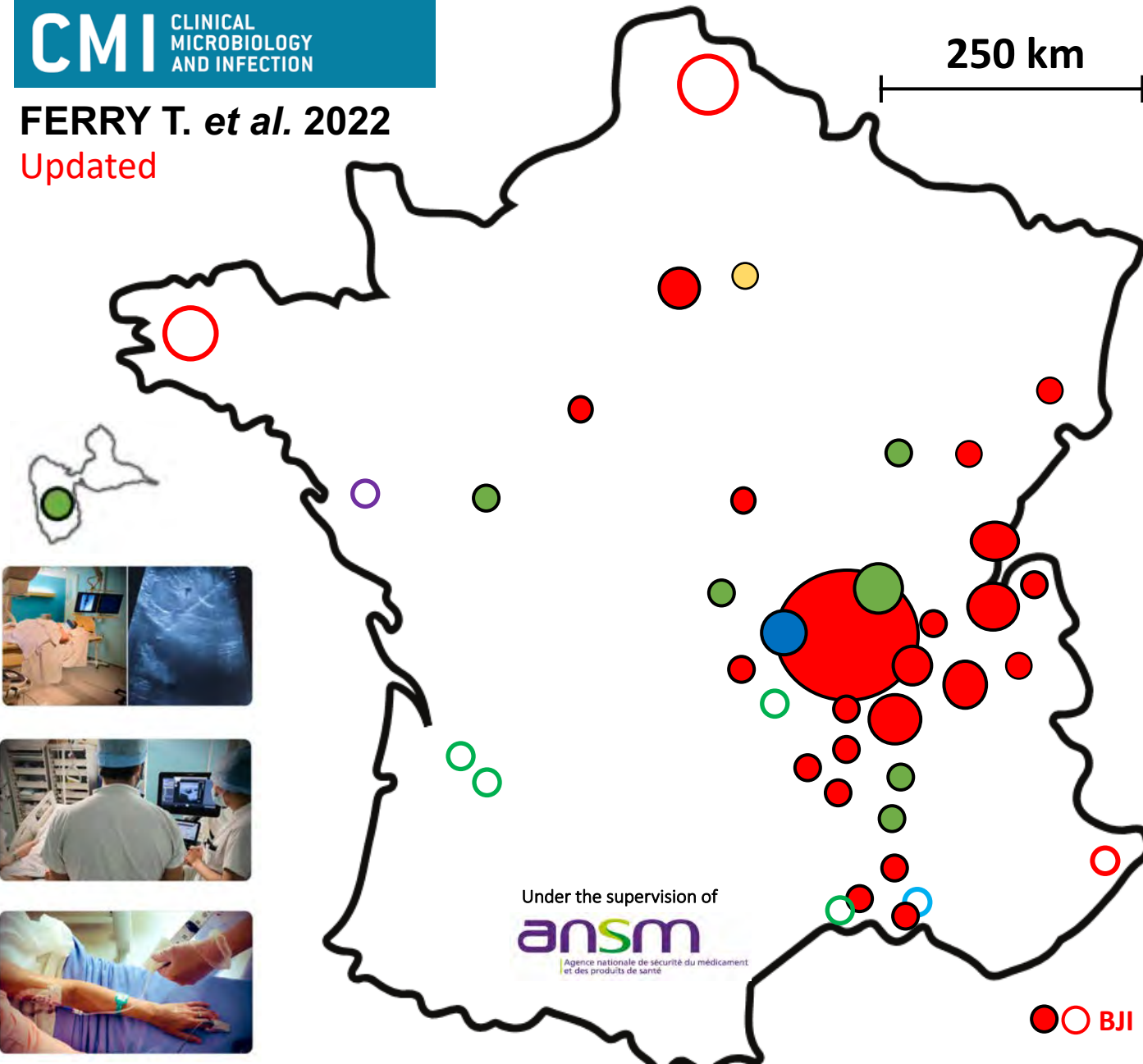
Source : T. Ferry

Implementation of a Phage Therapy Center in a CRIOAc

CMI CLINICAL
MICROBIOLOGY
AND INFECTION

FERRY T. *et al.* 2022

Updated



PHAGE*in***LYON**



59 patients in Lyon since 2017
~75% of the whole patients treated in France



- 55 with phages from
- 4 with phages from



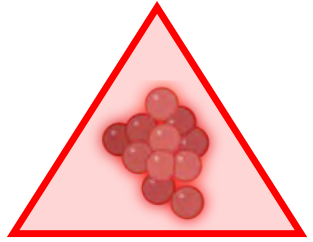
- 46 **BJI** (including 38 **PJI**)
- 10 **endocarditis/vascular graft**
- 3 **lung infections** (VAP + bacteremia, pneumonia in lung graft bronchiectasia, cystic fibrosis exacerbation)



+ 14 patients managed outside Lyon ○
including 1 in  and 1 in 

●○ BJI ●○ Endocarditis ●○ Pneumonia ●○ Burn ●○ Abscess

A large panel of severe bacterial infections



Central nervous system infections

Implant-associated meningitis

Lung infections

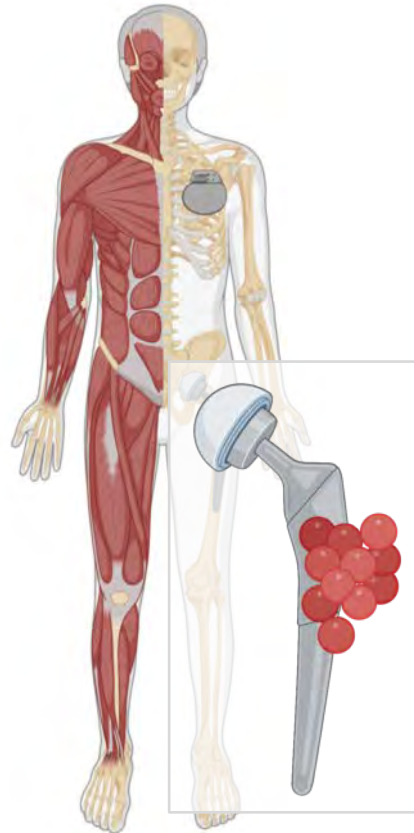
Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

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

Book chapter in press

A review of phage therapy for bone and joint infections

Tristan Ferry^{1,2,3,4,5}

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⁵ Education and Clinical Officer of the ESCMID Study Group for Non-traditional Antibacterial Therapy (ESGNTA)

Springer 2023 In press

Bacteriophage Therapy: From Lab to Clinical Practice
Joana Azeredo and Sanna Sillankorva (eds.)

Phages have anti-biofilm activity



World Health
Organization

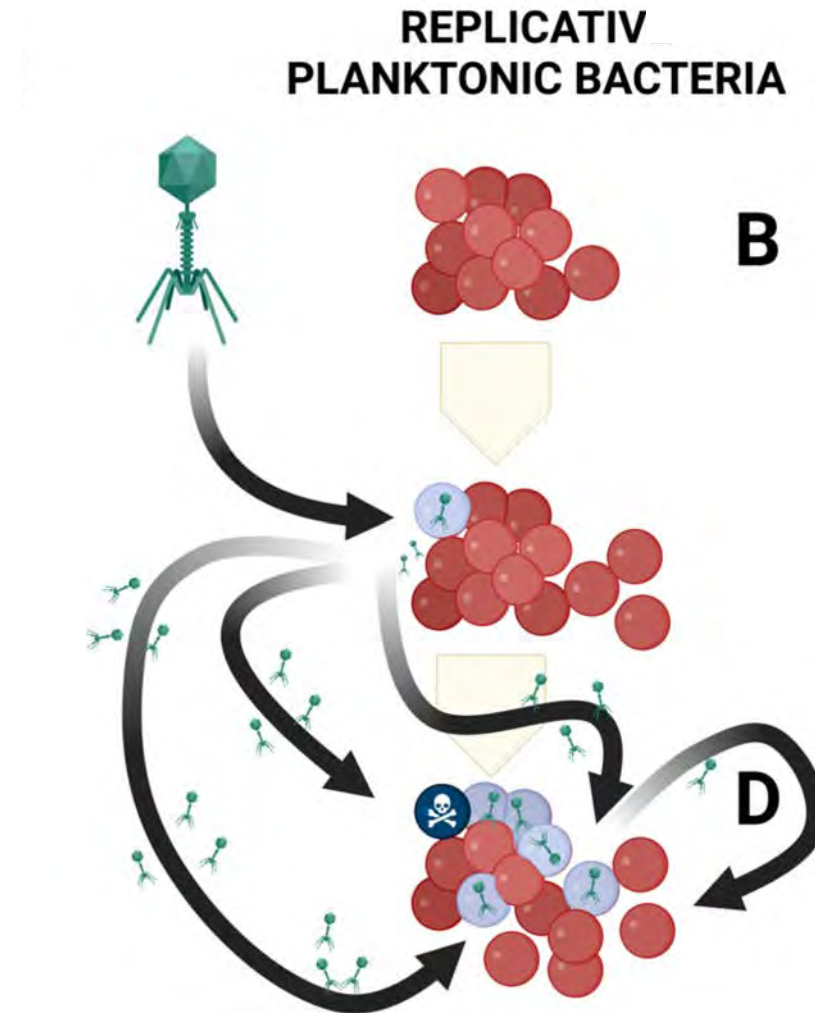
Non-**T**raditional
Antibacterial
therapy



ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY



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Clinic

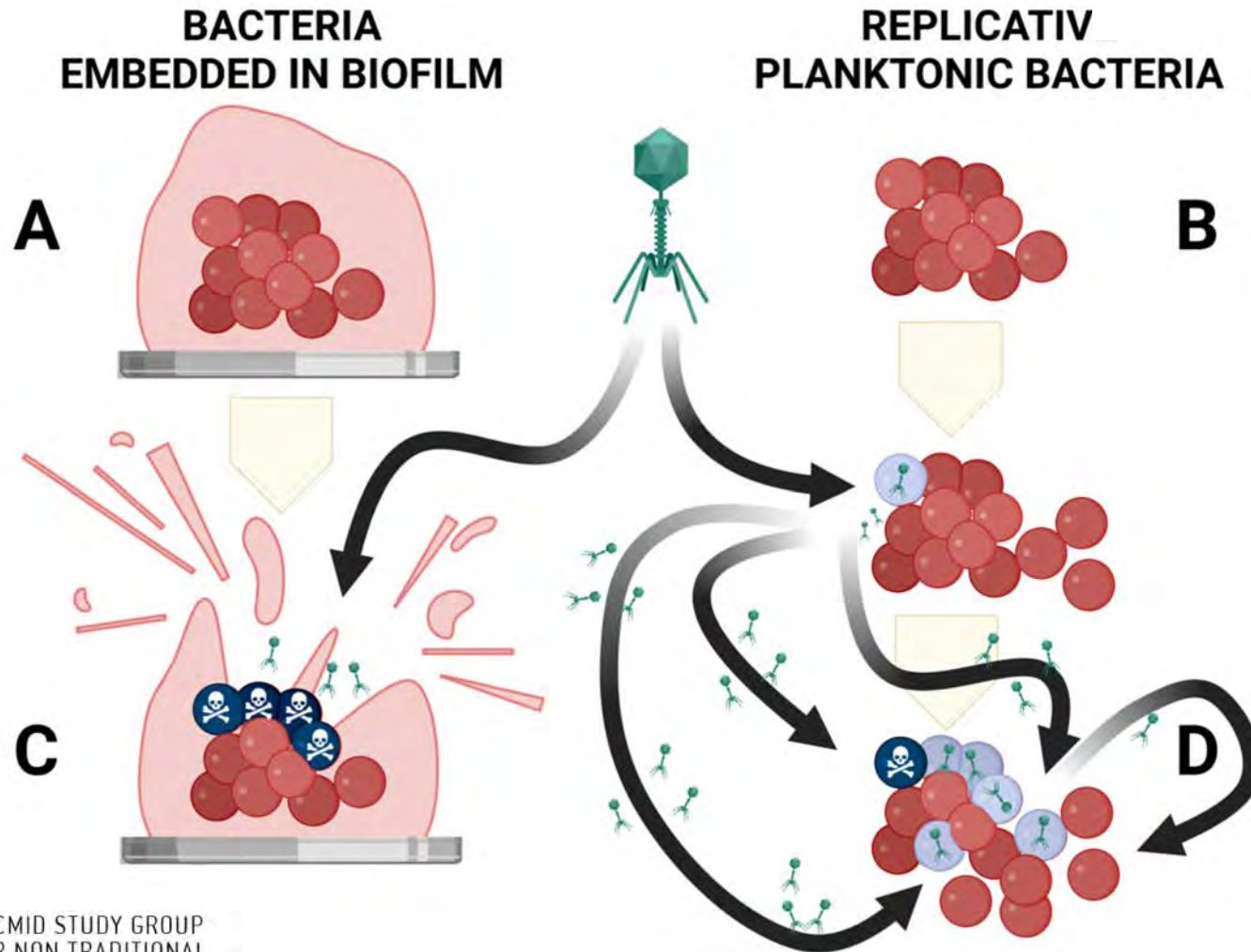
T. Ferry. Springer 2023 In press

Phages have anti-biofilm activity



World Health Organization

Non-**T**raditional
Antibacterial
therapy



PHAGE_{in}**LYON**
Clinic



ESGNTA

ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY

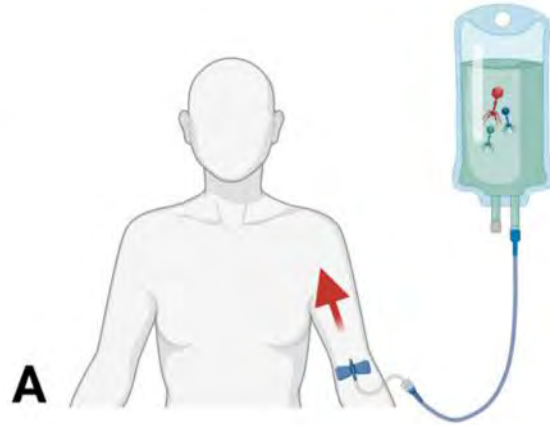
European Society of Clinical Microbiology and Infectious Diseases

T. Ferry. Springer 2023 In press

What are “conventional” ways of administration to treat bone and joint infections

CONVENTIONAL ADMINISTRATIONS

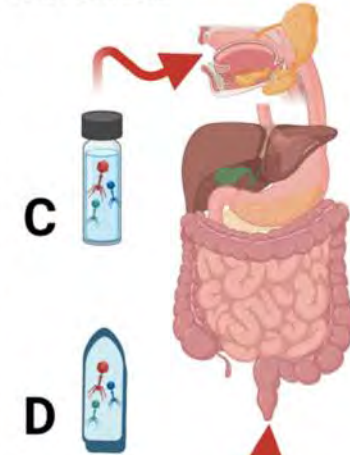
SYSTEMIC



LOCAL



HISTORICAL



Intra articular injection(s) of active bacteriophages as adjuvant therapy in patients with PJI qualified for open or arthroscopic DAIR followed by suppressive antimicrobial therapy (SAT): the PHAGEinLYON experience at the CRIOAc Lyon referral center

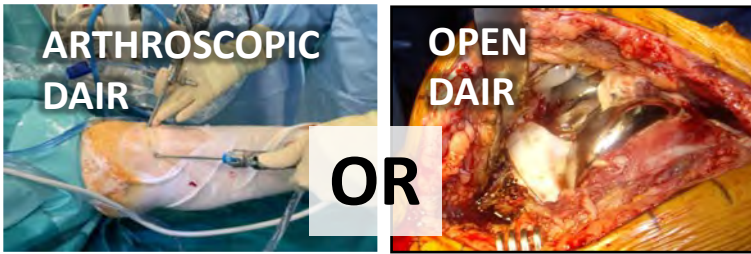


Tristan Ferry, Thomas Briot, Camille Kolenda, Clément Javaux, Gilles Leboucher, Fabien Craighero, Sébastien Lustig, Frederic Laurent, Cecile Batailler

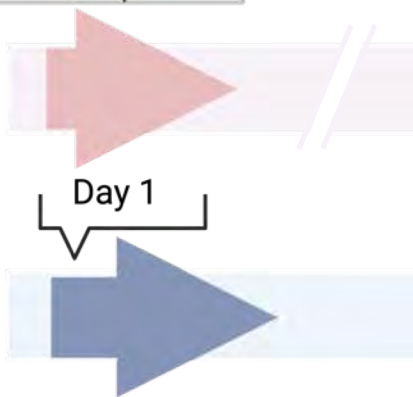
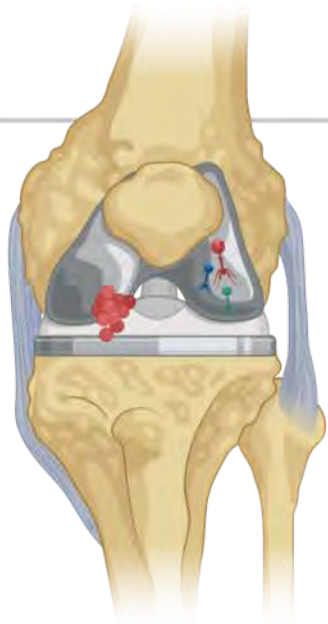
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 [@FerryLyon](https://twitter.com/FerryLyon) 

Infectious and Tropical Diseases Unit, Croix-Rousse Hospital , Hospices Civils de Lyon, Claude Bernard Lyon1 University, Lyon
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Clinical officer ESCMID Study group for Non-Traditional Antibacterial therapy (ESGNTA)
Referral center for the management of complex bone and joint infections (CRIOAc Lyon)



#PhagoDAIR procedure



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.

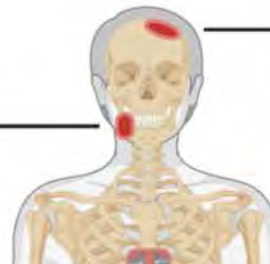


PHAXIAM

Ex-  **PHERECYDES**
PHARMA



Mandibular osteomyelitis (w/o implant)



Post-operative skull bone infection (w/o implant)



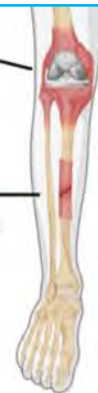
elitis



Prosthetic-joint infection (w/o loosening)



Long bone septic non-union (w/o implant)



Long bone focal endomedullar osteomyelitis (w/o implant)



focal cortical osteomyelitis (w/o implant) (w/o bone exposition)

Diabetic foot infection



Which bone and joint infections are relevant for phage therapy?

Unpublished clinical cases

Clinical case #1:

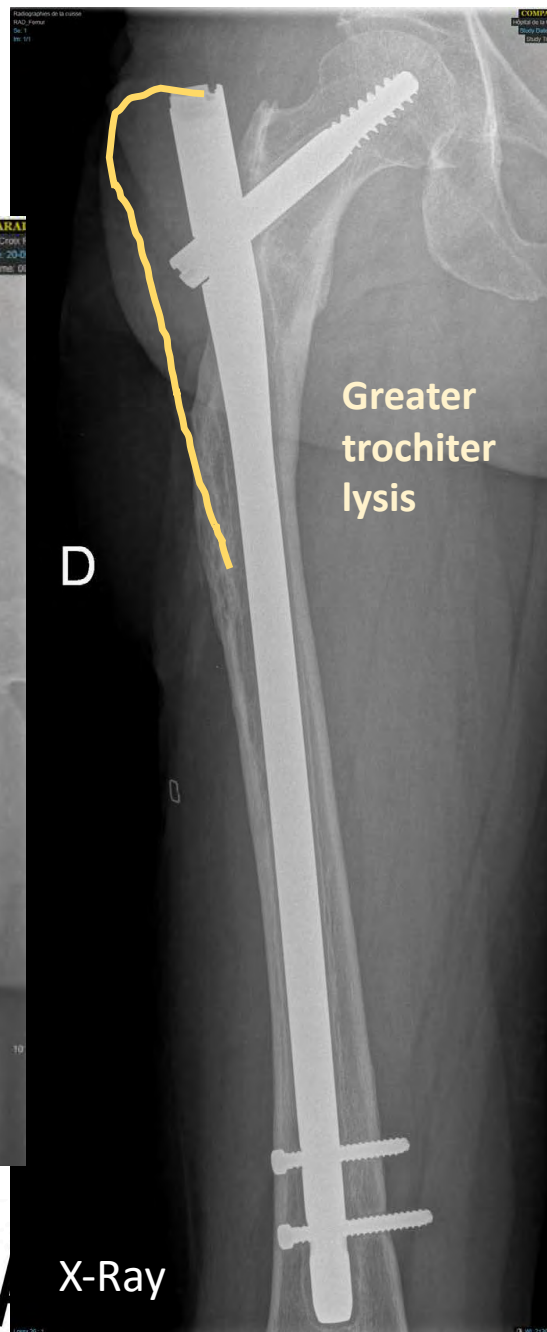
Relapsing implant-associated infection with abscesses

Clinical case #2:

Relapsing long-bone pantiaphysitis

Clinical case #1

62-year-old male with a long history of rheumatoid arthritis (RA) and osteoporosis. He presented with a 2-week history of increasing pain in the proximal femur, which was initially attributed to a stress fracture. Despite conservative management, the pain persisted, and a CT scan revealed a lytic lesion in the proximal femur. A biopsy confirmed the diagnosis of metastatic disease. The patient was started on systemic chemotherapy and received a 24-hour course of intravenous pamidronate for hypercalcemia. The pain improved significantly, and the lytic lesion showed partial resolution on follow-up imaging.



Clinical case #1

62-year-old woman

Leiomyosarcoma

Radiotherapy

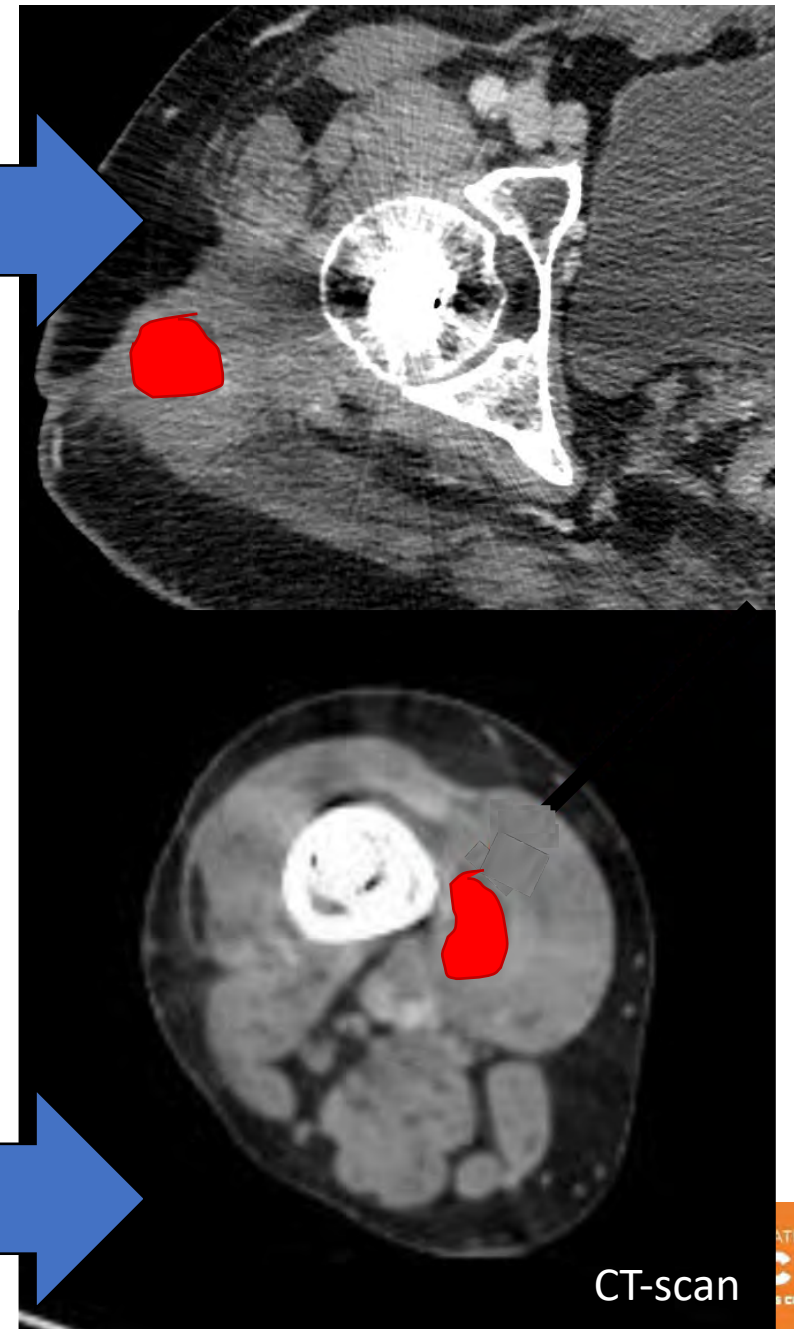
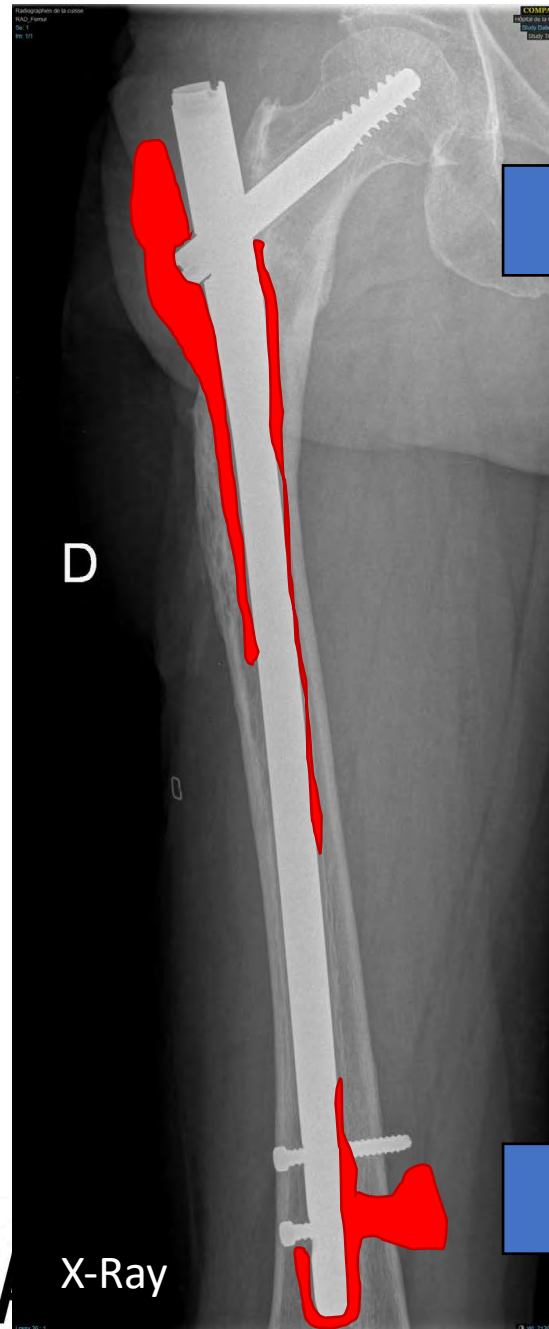
Fracture

Osteosynthesis, soft tissue flap

2-stage exchange of a nail

Recurrent *S. aureus* infection

Proximal and distal abscesses



Clinical case #1

Questions from the
MODERATORS

What is the standard of care?

- 1- Surgery with nail explantation, debridement, ATBx
- 2- Surgery with 1-stage nail exchange, debridement, ATBx
- 3- No surgery, ATBx including suppressive ATBx
- 4- No surgery, Phage therapy in combination with ATBx

Clinical case #1

What is the standard of care?

- 1- Surgery with nail explantation, debridement, ATBx
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Clinical case #1

Questions from the
MODERATORS

What would you do if you imagine phage therapy?

- 1- **Single** active phage **IV** during several weeks
- 2- **Cocktail** of active phages **IV** during several weeks
- 3- **IV** way of administration during ≥ 1 week
- 4- **locally during surgery** (1 shot)
- 4- **locally under sonography** (≥ 1 shot)
- 5- Combination with primary **ATBx**
- 6- Followed by **suppressive antimicrobial therapy** if the outcome if favorable

Multiple
Choice
Question

Clinical case #1

Questions from the MODERATORS

What would you do if you imagine phage therapy?

- 1- **Single** active phage **IV** during several weeks
- 2- **Cocktail** of active phages **IV** during several weeks
- 3- **IV** way of administration during several weeks
- 4- **locally during surgery** (1 shot)
- 4- **locally under sonography** (≥ 30 min)
- 5- Combination with primary **ABX**
- 6- Followed by **suppressive antimicrobial therapy** if the outcome is favorable

No good answer
Area of uncertainties
Experienced-based approach

Multiple
Choice
Question

Clinical case #1

What would you do if you imagine phage therapy?

- 1- **Single** active phage **IV** during several weeks
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Multiple
Choice
Question

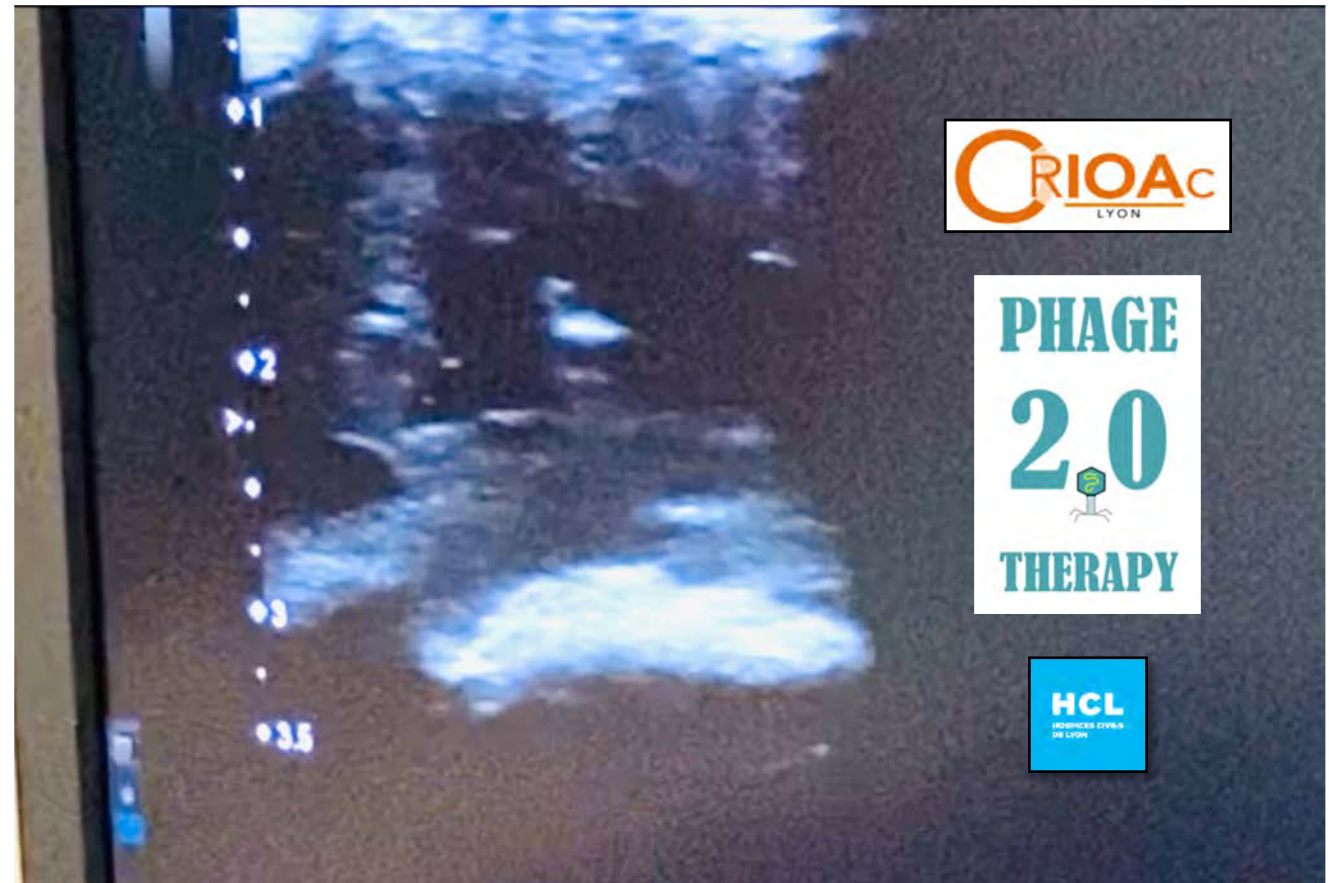


Clinical case #1

No surgery

Personalized phage cocktail

One shot phage injection in each abscess (proximal and distal)



Highly purified phage cocktail 10^9 phages/mL
PP1493, PP1815, PP1957

PHERECYDES
PHARMA
PHAXIAM



Clinical case #1

No surgery

Personalized **phage cocktail**

One shot phage injection

Primary ATBX (3 months) then suppressive antimicrobial therapy (cephalexin)

Favorable outcome at 24 months



Clinical case

No surgery

Personalized **phage cocktail**

One shot phage injection

Primary ATBX (3 months) then suppressive antimicrobial therapy (cephalexin)

Favorable outcome at 24 months



*"I acknowledge so much Pr. Ferry
and the PHAGE_{in}**LYON** team, thanks
to them, I save precious time!"*

Clinical case #2

Clinical case #2

44-year-old active woman

Past history of transfemoral amputation due to tibial sarcoma

Complication with *S. aureus* post-operative distal femur infection, treated with surgical debridement and antibiotics

Relapse with proximal and distal fistula associated with small discharge for many years, with limited functional impact



Clinical case #2

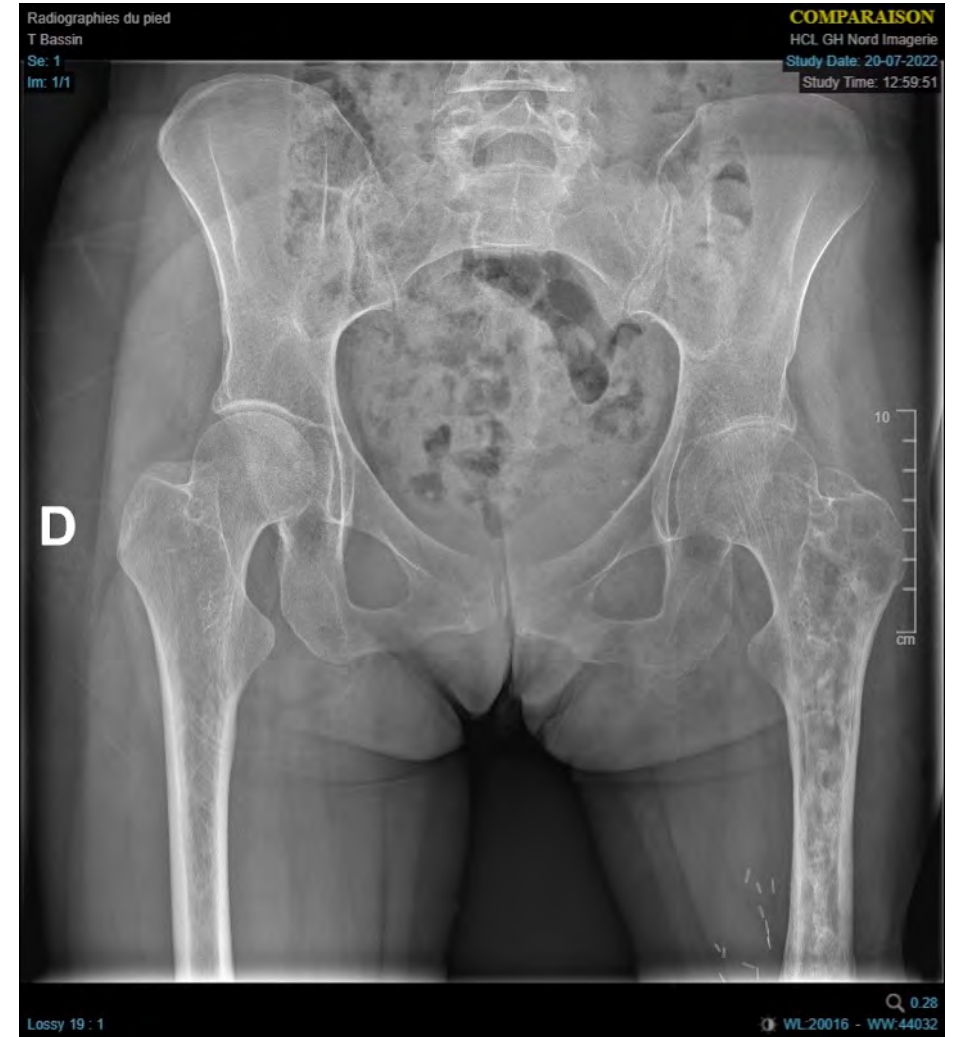
44-year-old active woman

Past history of transfemoral amputation due to tibial sarcoma

Complication with *S. aureus* post-operative distal femur infection, treated with surgical debridement and antibiotics

Relapse with proximal and distal fistula associated with small discharge for many years, with limited functional impact

Fear of the patient to loss any function



Clinical case #2

Questions from the
MODERATORS

What is your diagnosis?

- 1- Chronic distal focal femoral osteomyelitis
- 2- Chronic proximal focal osteomyelitis
- 3- Chronic pandiaphysitis

Clinical case #2

What is your diagnosis?

- 1- Chronic distal focal femoral osteomyelitis
- 2- Chronic proximal focal osteomyelitis
- 3- Chronic pandiaphysitis**

Clinical case #2

What are the treatment options?

- 1- No surgery and no ATBx
- 2- Puncture and ATBx, including suppressive ATBx
- 3- Surgery with intramedullar debridement, shortening of the femur and ATBx, without suppressive ATBx
- 4- Surgery with intramedullar debridement, shortening of the femur and ATBx, followed by suppressive ATBx
- 5- Puncture, phage therapy and ATBx including suppressive ATBx
- 6- Puncture, surgery with intramedullar debridement, phage therapy and ATBx including suppressive ATBx

Clinical case #2

What are the treatment options?

- 1- No surgery and no ATBx
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No good answer
Area of uncertainties
Experienced-based approach

Clinical case #2

Questions from the
MODERATORS

What would you do if you imagine phage therapy?

- 1- Single active phage
- 2- Cocktail of active phages
- 3- IV administrations during ≥ 1 week
- 4- Phage(s) injected locally under CT-scan or sonography (≥ 1 shot)
- 4- Phage(s) injected locally during surgery (1-shot) especially just after the intramedullar debridement
- 5- Phage(s) injected locally after surgery (≥ 1 shot) using an intramedullar catheter put in place after intramedullar debridement

Multiple
Choice
Question

Clinical case #2

Questions from the MODERATORS

What would you do if you imagine phage therapy?

- 1- Single active phage
- 2- Cocktail of active phages
- 3- IV administrations during \geq 1 week
- 4- Phage(s) injected locally under surgery
- 4- Phage(s) injected locally during surgery after intramedullary debridement
- 5- Phage(s) injected locally after surgery (≥ 1 shot) using an intramedullary catheter put in place after intramedullary debridement

Multiple
Choice
Question

No good answer
Area of uncertainties
Experienced-based approach

Clinical case #2

What are the treatment options?

- 1- No surgery and no ATBx
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Clinical case #2

What are the treatment options?

- 1- No surgery and no ATBx
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- 6- Puncture, surgery with intramedullar debridement, phage therapy and ATBx including suppressive ATBx**

Clinical case #2

What would you do if you imagine phage therapy?

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Multiple
Choice
Question

Clinical case #2

What would you do if you imagine phage therapy?

1- Single active phage

2- Cocktail of active phages

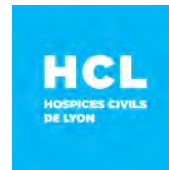
3- IV administrations during ≥ 1 week

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5- Phage(s) injected locally after surgery (≥ 1 shot) using an intramedullar catheter put in place after intramedullar debridement

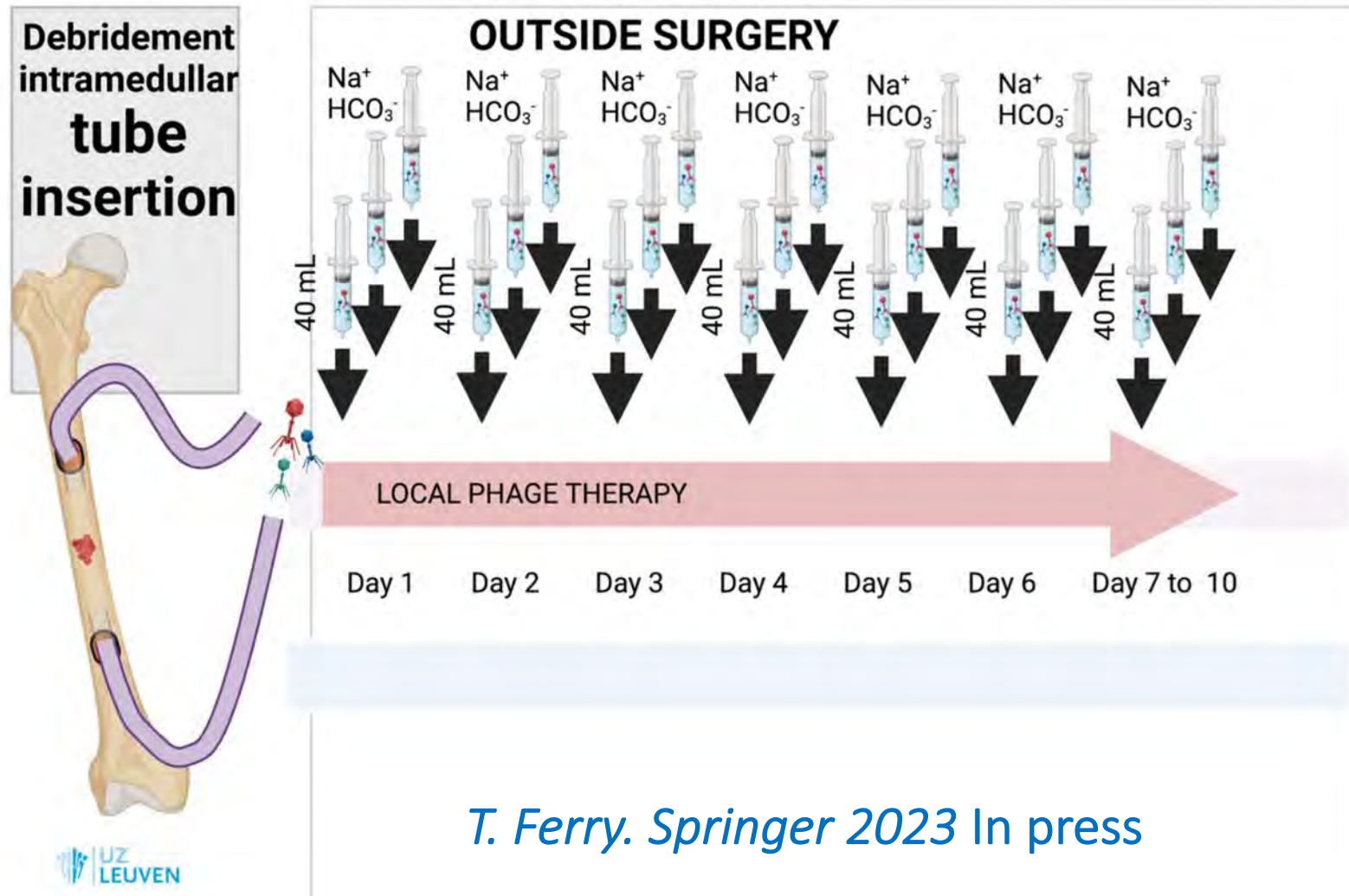
Multiple
Choice
Question



Clinical case #2

Experience in Belgium

Onsea et al. Viruses 2019



Clinical case #2

- **Puncture under sonography** of between the fistula and the bone to obtain the strain responsible for infection (no liquid)
- Susceptible *S. aureus* in culture from a swab after local disinfection
- Multidisciplinary discussion
- Strain sent by our microbiologists (C. Kolenda, T. Roussel-Gaillard)
- Highly purified phage cocktail 10^9 phages/mL
- **PP1493, PP1815, PP1957**



Orthopaedic department
CRIOAc Lyon, Croix-Rousse Hospital

Pr. S. Lustig

Dr. Axel Schmidt

Me!



Phages!



Introduce phage therapy
into the operating room

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Clinic



Orthopaedic department
CRIOAc Lyon, Croix-Rousse Hospital

Pr. S. Lustig

Dr. Axel Schmidt

Me!

PHAGE*in***LYON**
Clinic



Phages!



Intravenous phage therapy
1 injection per day during 7 days



Infectious diseases ward



Outome

- 3 months of primary ATBx
- Switch to suppressive antimicrobial therapy (clindamycin)
- Fistula closed
- Favorable outcome at 1 year
- Function kepted!

French poem

« The happiness merchant »

Finger crossed!



Lyon BJI Study group



Coordinator: Tristan Ferry

Infectious Diseases Specialists – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Pouderoux, Pierre Chauvelot, Paul Chabert, Johanna Lippman, Evelyne Braun

Surgeons – Sébastien Lustig, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schmidt, Elliot Sappey-Marinier, Quentin Ode, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Aram Gazarian, Arnaud Walch, Antoine Bertani, Frédéric Rongieras, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person, Samuel Prive, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal;

Anesthesiologists – Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo, Dana Patrascu;

Microbiologists – Laetitia Beraud, Tiphaine Roussel-Gaillard, Céline Dupieux, Camille Kolenda, Jérôme Josse;

Imaging – Fabien Craighero, Loic Boussel, Jean-Baptiste Pialat, Isabelle Morelec;

PK/PD specialists – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle;

Clinical research assistant and database manager– Eugénie Mabrut

PHAGE_{in}LYON Clinic

Acknowledgments to ANSM, Phaxiam, and QAMH!

Coordinator: Tristan Ferry

Tristan Ferry, Myrtille Le Bouar, Gilles Leboucher, Thomas Briot, Camille Kolenda, Tiphaine Roussel-Gaillard, Karine Dallosto



PHAGE *in* LYON *Clinic*

Acknowledgments to ANSM, Phaxiam, and QAMH!

See you next time!



Clinical Officer

ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP FOR
NON-TRADITIONAL
ANTIBACTERIAL THERAPY





demande phagothérapie hcl



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Hospices Civils de Lyon

<https://www.chu-lyon.fr/phagothe...> · [Translate this page](#) ⋮

Phagothérapie (Bactériophage) | Fiche santé HCL

Jun 27, 2023 — Vous souhaitez **demande**r un avis pour un éventuel traitement par bactériophages. Ce traitement exceptionnel est exclusivement envisageable dans ...



GCS Sara

<https://myhcl.sante-ra.fr/Default> · [Translate this page](#) ⋮

Demande de traitement par bactériophages / phagothérapie

Demande de traitement par bactériophages / **phagothérapie** - Hôpital de la Croix Rousse ...

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MENU



Votre espace de suivi personnel et sécurisé aux
Hospices Civils de Lyon

Demande de traitement par bactériophages / phagothérapie - Hôpital de la Croix Rousse

Vous souhaitez demander un avis pour un éventuel traitement par bactériophages.

Ce traitement exceptionnel est exclusivement envisageable dans certaines situations précises où le pronostic fonctionnel ou vital est engagé.

Certains phages peuvent être à disposition, mais ils restent rares et ils ne couvrent malheureusement pas toutes les situations cliniques.

Merci de répondre de façon la plus précise possible aux questions posées dans les pages suivantes et de joindre les documents demandés.

Phagothérapie demande patient
Maladies infectieuses et tropicales (HOP. CROIX-ROUSSE)



ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP
FOR NON-TRADITIONAL
ANTIBACTERIAL THERAPY

Join us!

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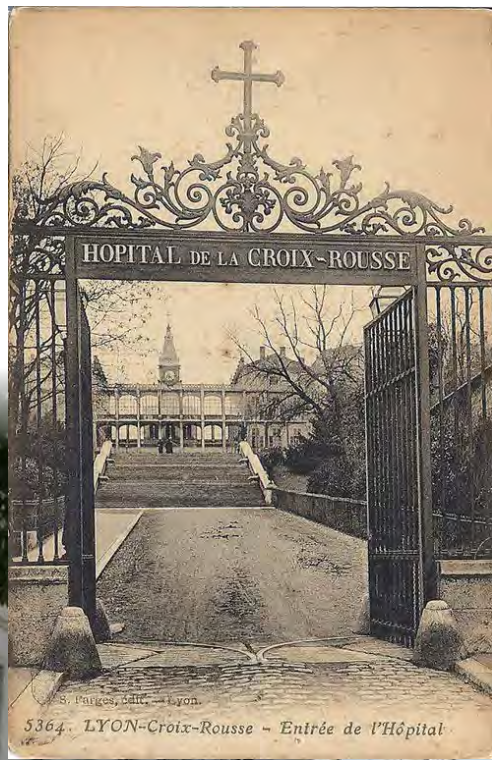
Zuzanna Drulis-kawa, Poland



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MANAGING INFECTIONS
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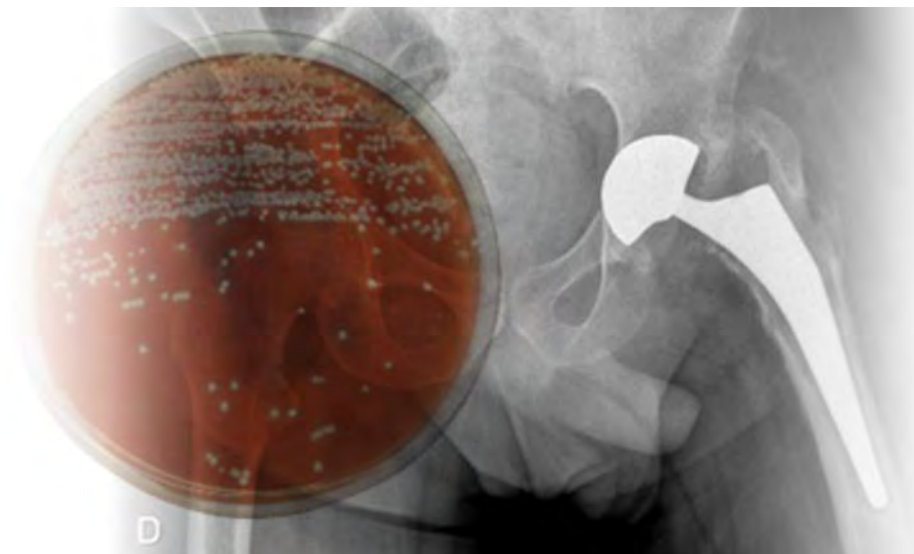
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