

Phagothérapie et Infections pulmonaires

Résultats précliniques

Études cliniques prévues

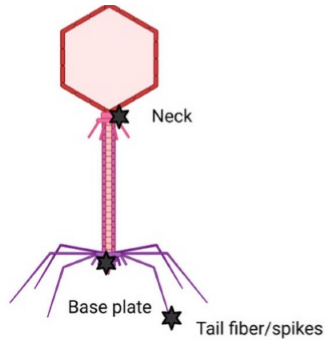
Dr Alexandre Bleibtreu

S^{vce} Maladies Infectieuses et Tropicales
Hôpital de la Pitié Salpêtrière AP-HP Sorbonne Université

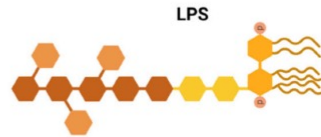
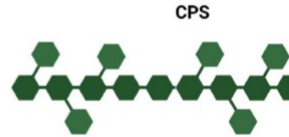
Déclaration d'intérêts de 2014 à 2021

- Intérêts financiers :
- Liens durables ou permanents : Bill Gates, Apple, APHP
- Interventions ponctuelles : Gilead, Astellas, InnoVIIV,
- Intérêts indirects : Pfizer, MSD, Ipsen, Sanofi, NeuTiger, Shionogi, Pherecydes, Astellas, Eumedica, Menarini,

Not Phake just Phages



TARGET: Bacterial polysaccharide structures



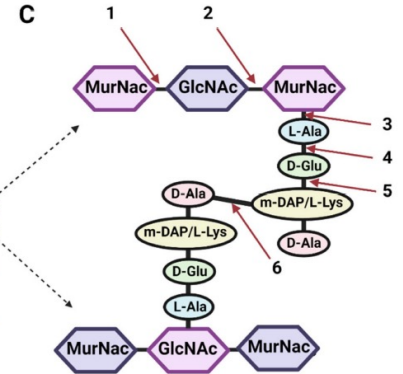
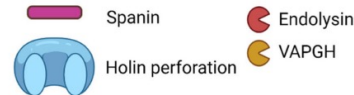
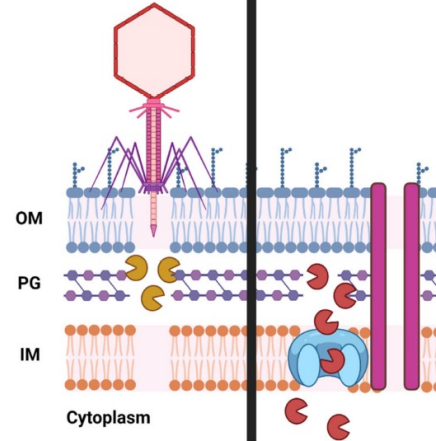
Hydrolases

- ★ Sialidase
- ★ Rhamnosidase
- ★ Levanase
- ★ Xylanase
- ★ Dextranase
- ★ LPS deacetylase

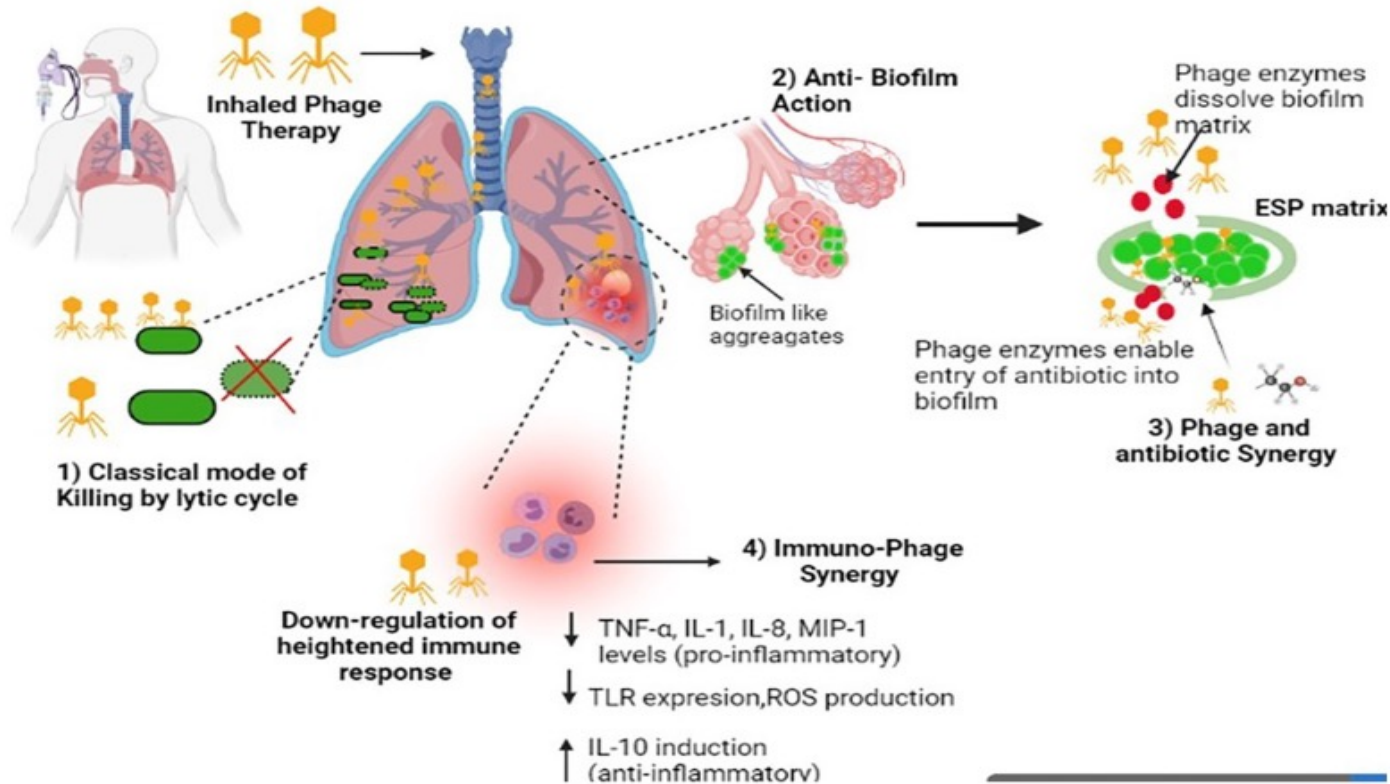
Lyases

- ★ Hyaluronate lyase
- ★ Pectate lyase
- ★ Alginate lyase
- ★ K5 lyase
- ★ O-specific polysaccharide lyase

A Beginning of infection **B End of infection**



Mécanismes d'action putatifs de la phagothérapie intra-pulmonaire



23^{es} JN1, B **FIGURE 1** | Diagrammatic illustration of the multiple mechanisms of phages against respiratory infections. Image created in Biorender.

Un phage = une bactérie

Phagothérapie pour quelles infections

- **Infection monobactérienne**
 - Complexe
 - Résistance bactérienne
 - Matériel étranger inextirpable
 - Site infectieux avec mauvaise diffusion des ATB
- **Absence d'alternative**
- **En association avec**
 - Geste de drainage/réduction de l'innoculum
 - Antibiothérapie

Mais des Phages = des bactéries => cocktails



La solution liquide de phages n'est pas toujours la solution

Polymeric microparticles

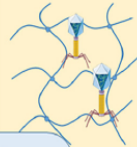


- Methacrylic acid and methyl methacrylate (1 – 10 μm) [48]
- Alginate (50 – 200 μm) [39, 56]
- PLGA (8 – 10 μm) [105, 106]

Bacteriophages

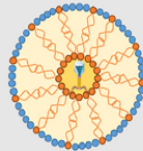


Hydrogel



- Alginate-nanohydroxyapatite [86]
- Peptides [87]
- Hyaluronic acid and polylactic acid [88]

Cationic liposomes



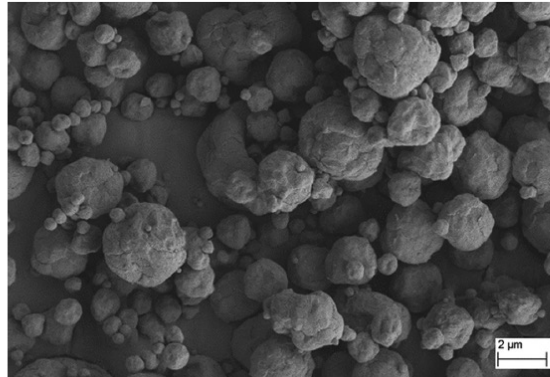
- 309 – 326 nm [57]
- 120 – >1000 nm [67, 69, 107]
- > 5 μm [101]



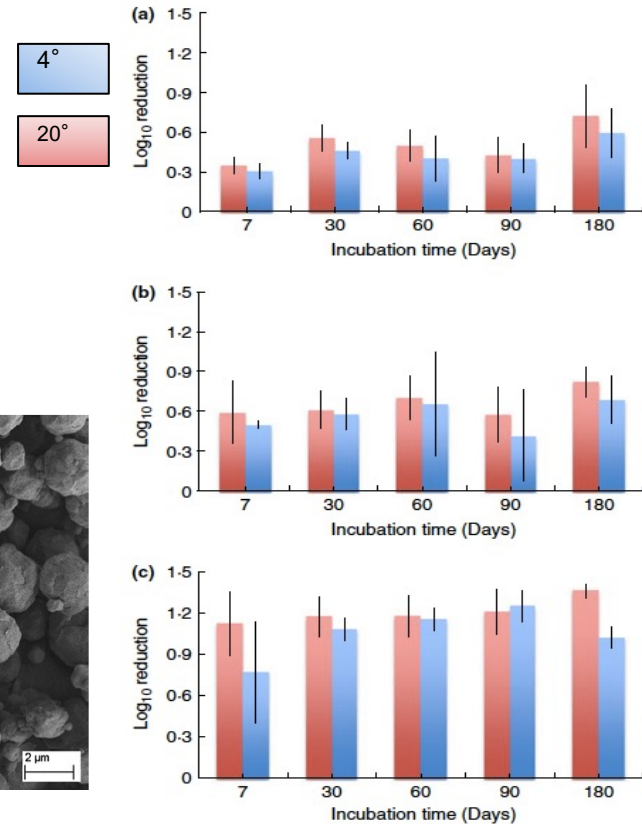
BRIOT T. Journal of Controlled Release 347 (2022) 414–424

Plusieurs formulations, des stabilités variables

- **Suspension**
 - Conservation à -80°C
 - Conservation à 4°C
- **Lyophilisation**
 - Reconstitution en suspension
 - Administration sous forme de poudre inhalée



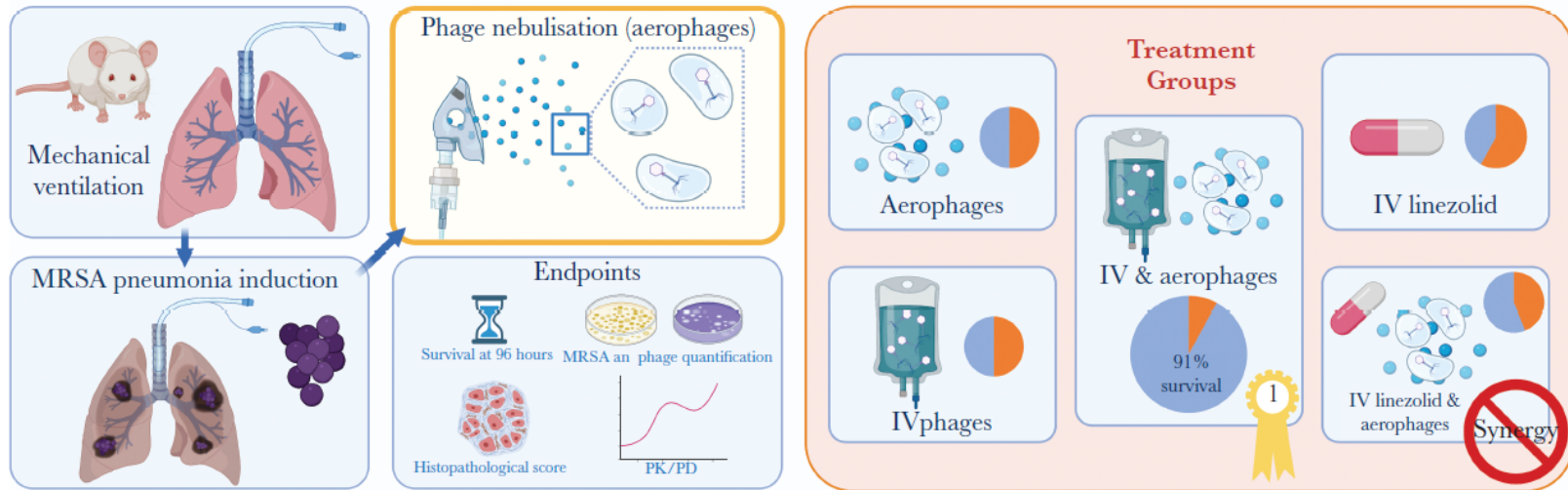
Chang et al AAC 2018



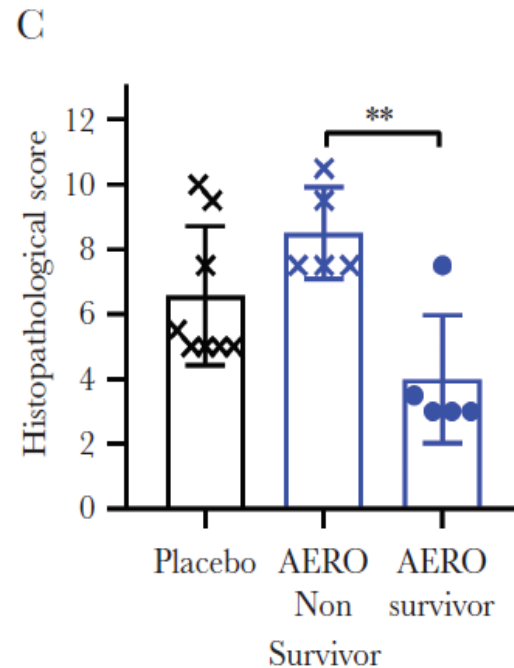
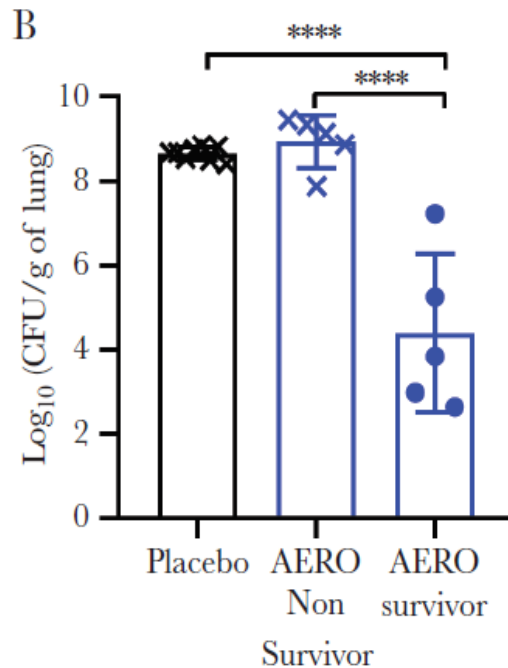
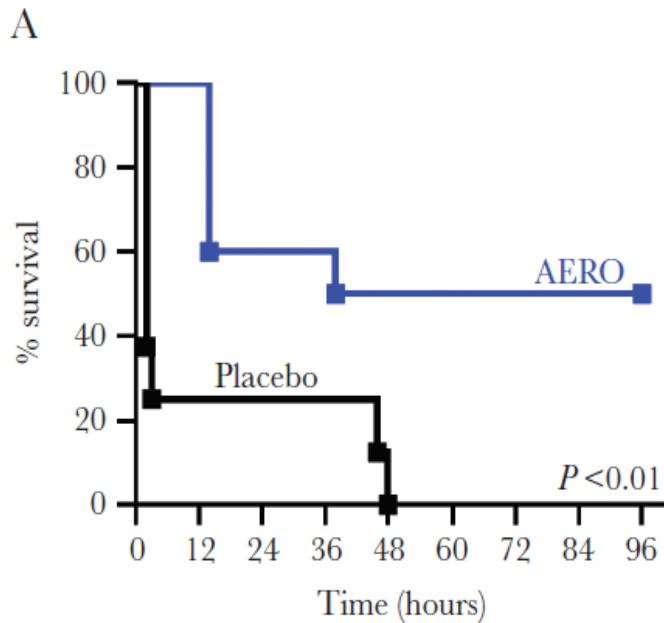
PAVM SARM Phages +/- Linezolid IV

Graphical abstract

Benefits of Aerosolized Phages for the Treatment of Pneumonia due to methicillin-resistant *Staphylococcus aureus* (MRSA):
an Experimental study in Rats

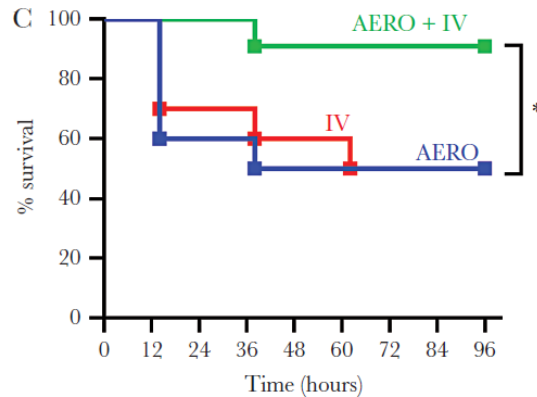
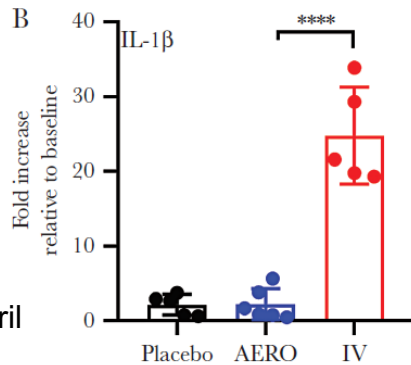
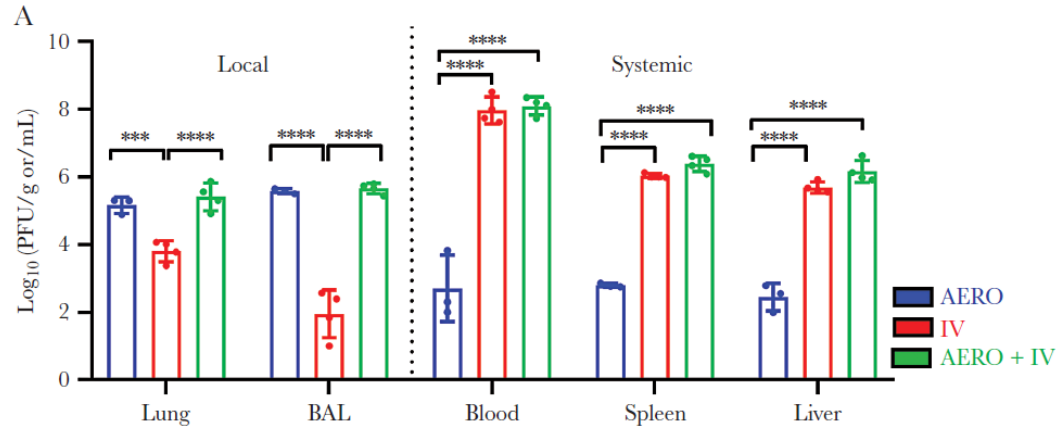


PAVM SARM Phages +/- Linezolid IV



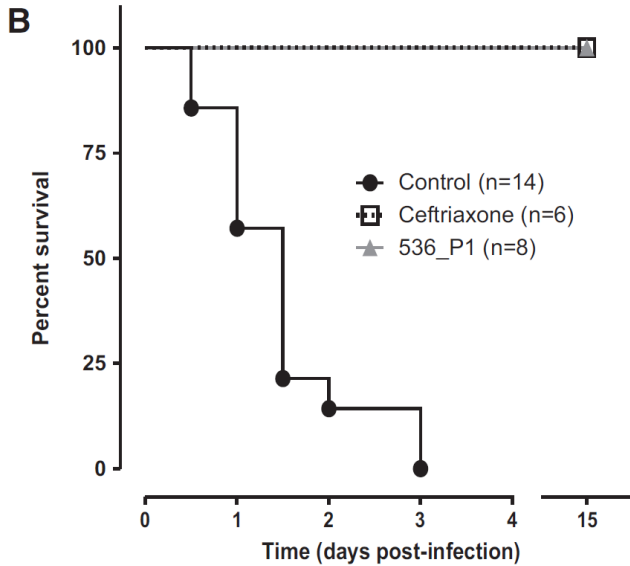
PAVM SARM Phages +/- Linezolid IV

Diffusion des phages

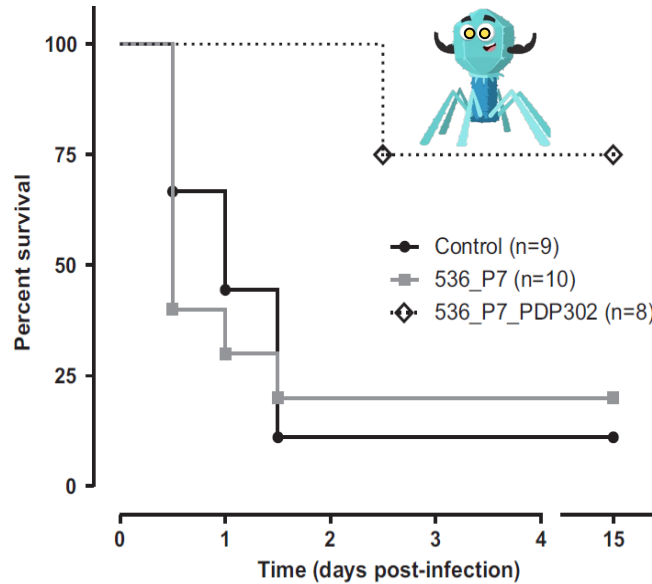


Prazak *et al.* jid 2022:225 15 April

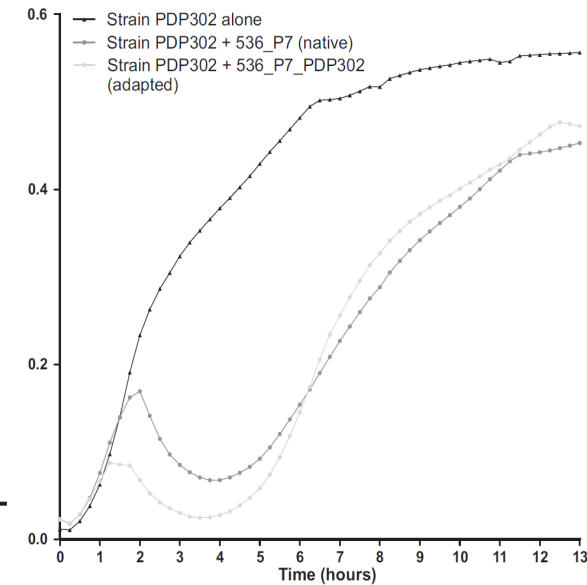
Phagothérapie efficace dans la PNP murine à *E. coli*



Phage = Ceftriaxone



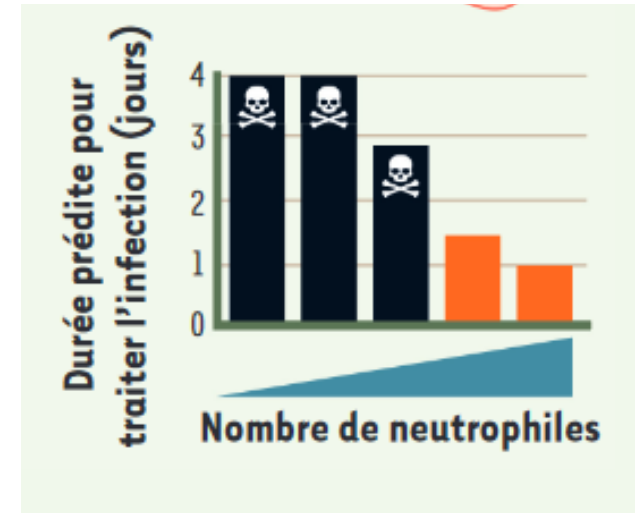
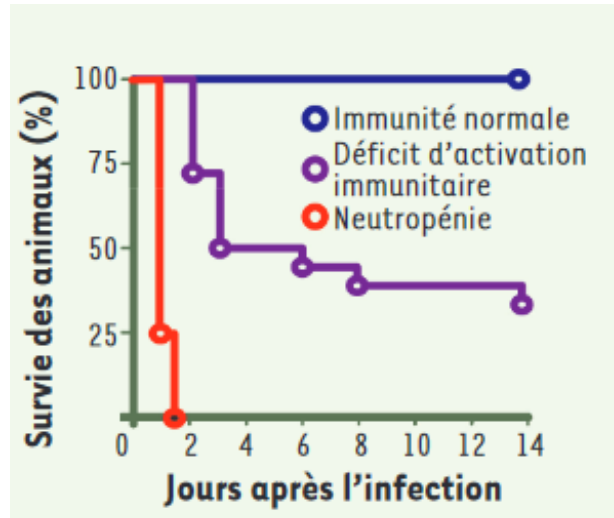
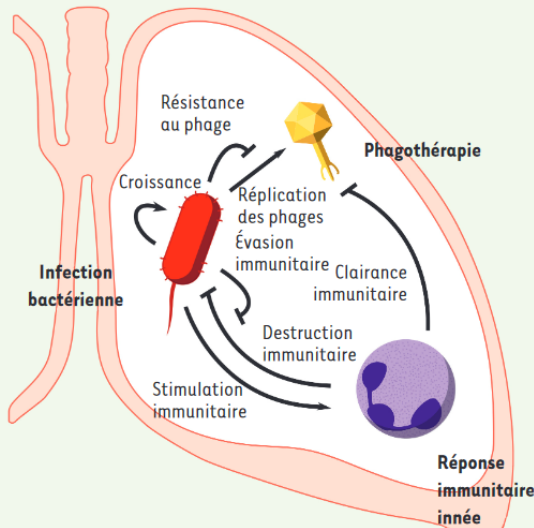
Phage adapté > Phage sauvage



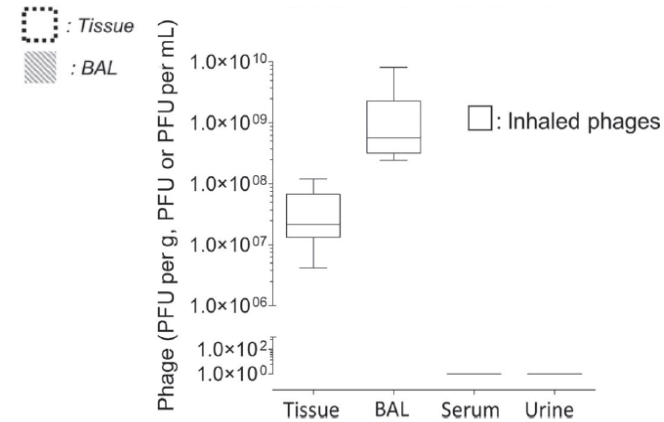
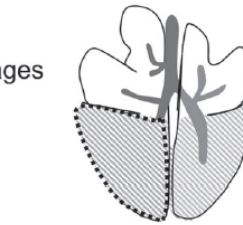
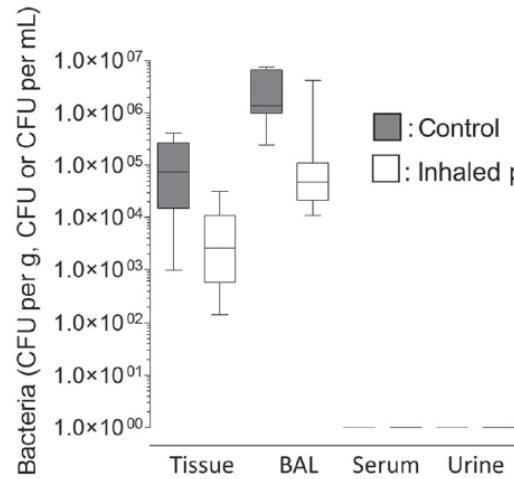
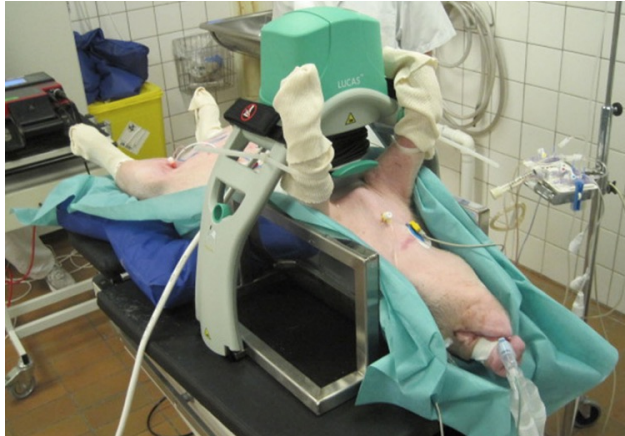
Pas de différence en termes de Fitness

Un système immunitaire fonctionnel améliore l'efficacité dans les modèles animaux

Interactions Hôte-Pathogène-Traitement



PAVM à *P. aeruginosa* phagothérapie nébulisée



Kjærgaard et al. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine (2016) 24:67

PAVM à *P. aeruginosa* phagothérapie nébulisée

(b)



PHAGES

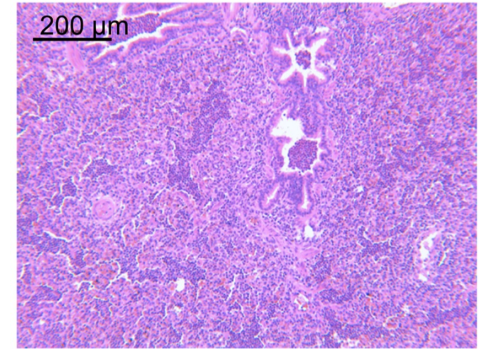
PAK-Lux strain,
sensitivity

MIX B : 5 phages

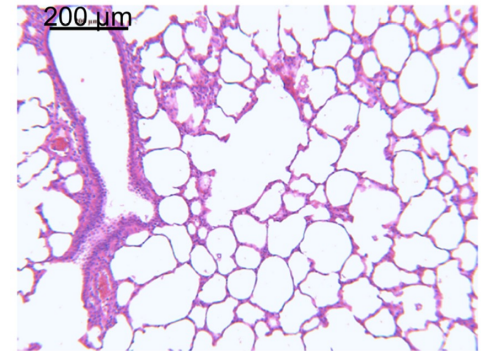
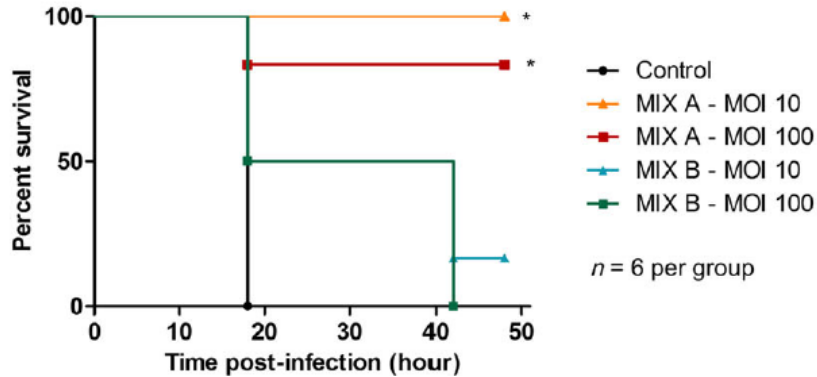
MIX A : 3 phages

PP1777 PP1450 PP1902 PP1797 PP1792

+ + + +/- +/-



(c)



De la fiole à l'avéole une déperdition de phages

Optimization of aerosol output –
Prediction of aerosol deposition for mechanical ventilation with pig parameters

T piece ($n=3$)	Inhalation chamber (CombiHaler®, $n=3$)
$69.5 \pm 2.7\%$	$75.2 \pm 3.3\%$

Aerosol aerodynamic properties at the tube outlet using pig ventilation parameters ($n=3$)

Particle size (MMAD) : $1.13 \pm 0.03 \mu\text{m}$

FPF_{5 μm} : $99.6 \pm 0.2\%$

FPF_{2 μm} : $91.7 \pm 1.2\%$

Viability of phages in MIX A after
nebulization in experimental conditions ($n=3$)

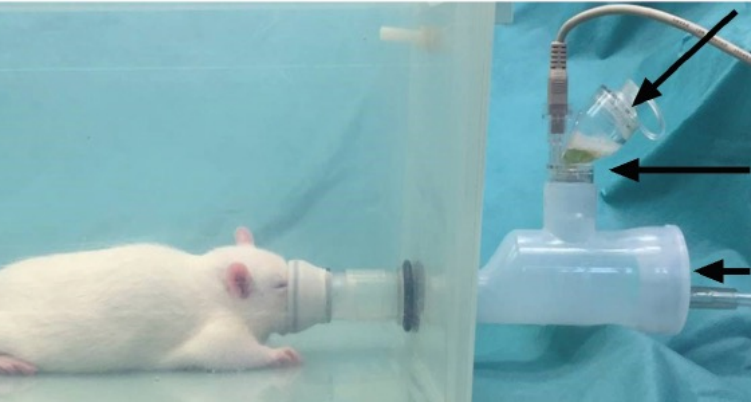
$5.3 \pm 1.9\%$

Nous partîmes 3000; mais par un prompt renfort
- Nous nous vîmes 500 en arrivant au port

EI DIC NeilleCor

Guillon A Br J Pharmacol. 2021;1–14.

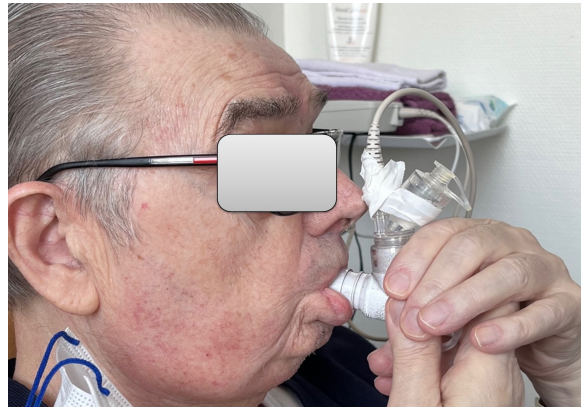
Nous ne sommes pas des souris ou des porcs Quoique?



Phage cocktail
(2×10^{10} PFU in 2ml)

Nebulizer
(Aerogen[®])

Sevoflurane + O₂
(Fi Sevo 1–3%)



Cas cliniques et ttt passionnels

	Patient population	Causative pathogen	Phage preparation	Administration	Dose (PFU/mL)	Regimen	Concomittant treatment	Adverse events	Efficacy	
									Clinical improvement	Bacterial eradication
Case reports										
Kvachadze et al ¹³	Chronic colonisation in a 7-year-old child with cystic fibrosis (n=1)	<i>Pseudomonas aeruginosa</i> and <i>Staphylococcus aureus</i>	Pyophage plus single phage Sb-1	Nebuliser	NS	14 applications, NS	Antibiotics	No	Improvement	Yes, negative at 2-month follow-up
Hoyle et al ¹²	Chronic colonisation in a patient with cystic fibrosis (n=1)	<i>Achromobacter xylooxidans</i> *	<i>Achromobacter</i> cocktail, NS	Oral plus nebuliser	3 × 10 ⁸	Twice a day for 20 days, 4 cycles	Antibiotics	NS	Improvement, increased FEV ₁	NS
Law et al ¹⁶	Chronic colonisation in a patient with cystic fibrosis (n=1)	<i>P. aeruginosa</i> *	AB-PA01 cocktail	Intravenous	4 × 10 ⁹	Every 6 h for 8 weeks	Antibiotics	No	Improvement with successful weaning, normalisation of WBCs, no exacerbation within 100 days	No
Maddocks et al ¹⁷	VAP and bronchopleural fistula after thoracotomy (n=1)	<i>P. aeruginosa</i> *	AB-PA01 cocktail	Intravenous plus nebuliser	NS	Intravenous: 1 mL in 100 mL; nebuliser: 4 mL twice a day for 7 days	Antibiotics	No	Improvement with successful weaning	Yes, negative at 6-month follow-up
Dedrick et al ¹⁴	Disseminated infection in a patient with cystic fibrosis who had received a lung transplant (n=1)	<i>Mycobacterium abscessus</i> *	Muddy plus BPs33δHTH_HRM10 plus ZoeJΔ45	Intravenous plus topical	3 × 10 ⁹	Every 12 h for 32 weeks	Antibiotics	No	Improvement, improved lung function, gradual healing of sternal wound and skin lesions	Yes, negative at 5-month follow-up

(Table 1 continues on next page)

Phagothérapie pulmonaire chez l'homme

Case studies of Pulmonary Phage therapy in humans

Liquid Aerosol
(Collision-jet
nebulizer)

MDR-
Achromobacter
xylosoxidans

Cocktail of two
Achromobacter
phages
(Siphoviridae)
prepared at Eliava
Institute, Tbilisi)

- A case of 17 year old female with cystic fibrosis and chronic infection with *A. xylosoxidans* (starting at age of 12) not responding to many rounds of antibiotics.
- Phage was administered via inhalation using a compression nebulizer once daily (3×10^8 PFU/ml) and phages were also given orally twice daily for 20 days.
- The same treatment course (inhaled plus oral) was repeated four times (at 1 month, 3 months, 6 months, and 12 months).

- After the initial round of phage treatment, the patient's conditions significantly improved, dyspnea resolved, and cough reduced.
- Her lung function measured as Forced expiratory volume (FEV1) increased from an initial 1.83 L (54%) to 1.88 L (62%) in 3 months post treatment.
- After the final treatment round of *Achromobacter* phages, there was a significant improvement in lung function reaching to a final FEV1 value of 3.33 L (84%).

Hoyle
et al., 2018

Liquid Aerosol
(Vibrating
mesh
nebulizer)

Carbapenem-
resistant *A.*
baumannii
(CRAB)

Personalized lytic
pathogen-specific
single-phage
(Unnamed)

- A case of an 88-year-old man already suffering from chronic obstructive pulmonary disease developed hospital acquired pneumonia (HAP) with carbapenem-resistant *A. baumannii* as the etiological agent.
- A personalized single-phage preparation was nebulized to the patient continuously for 16 days in combination with tigecycline and polymyxin E.

- The treatment was well tolerated and resulted in clearance of the infection from patient's lung with clinical improvement in lung function.

Tan et al.,
2021

Liquid Aerosol
(Vibrating
mesh
nebulizer)

Achromobacter
xylosoxidans

Cocktail of three
lytic phages ((JW
Delta, JWT, and 2-
1)- APC 1.1
And another
cocktail mix (APC

- A 12-year-old lung-transplanted cystic fibrosis patient with persistent lung infection with pandrug-resistant *A. xylosoxidans*
- Patient received two rounds of phage therapy. In first round 3

- Clinical tolerance was perfect after each round of therapy with no observed side effects.
- However, the culture was positive with bronchoalveolar lavage (BAL) showing low densities of *A. xylosoxidans*.

Lebeaux
et al., 2021

PNP à *P. aeruginosa* IV + Nebulisation de phages

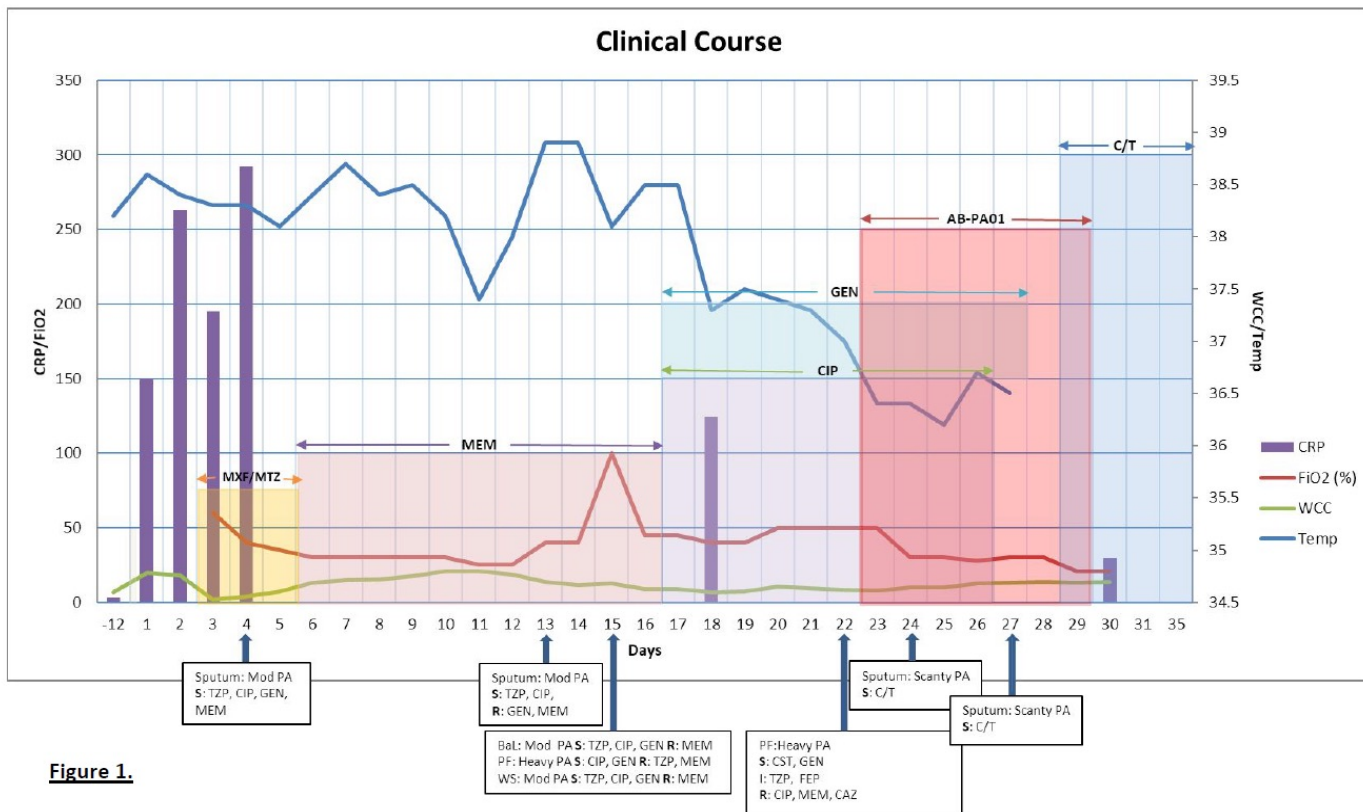


Figure 1.

PNP à *A. baumannii* ttt par ATB IV + Phagothérapie IV et Nébulisée

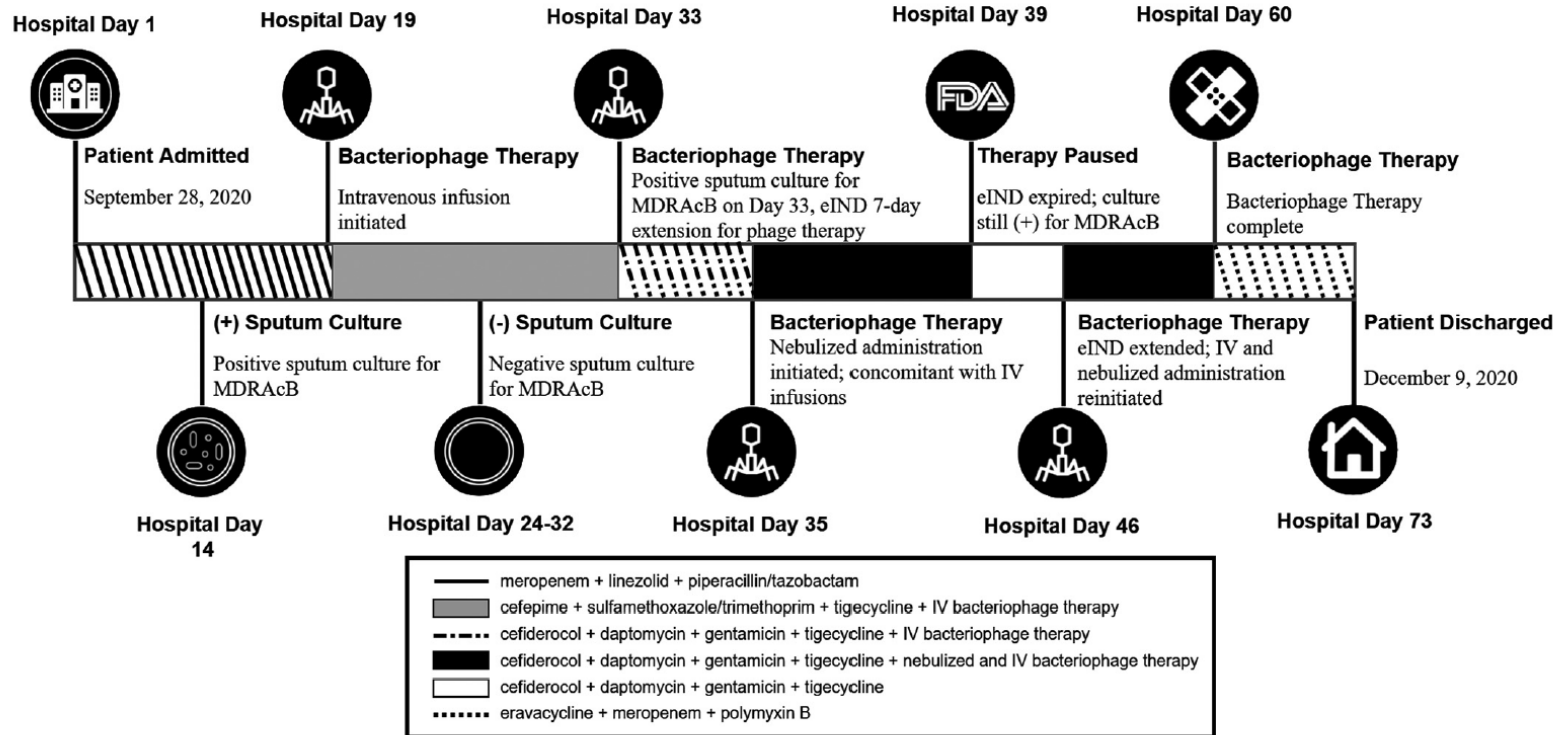


FIG 1 Timeline for the treatment in a patient with multidrug-resistant *Acinetobacter baumannii* lung infection with strain-reactive bacteriophages and antibiotics.

Phage In Paris

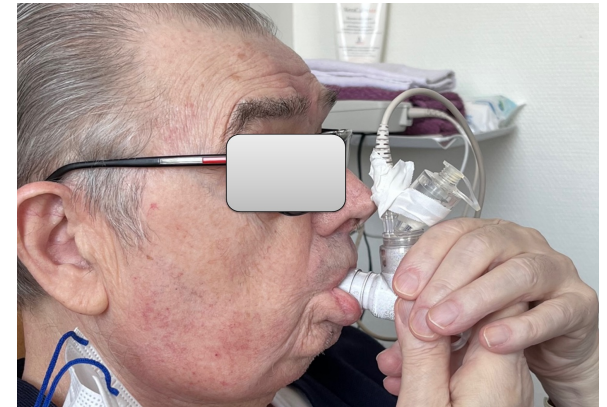
DDB colonisé et infections à *P. aeruginosa* XDR

22 MARS 2022

Aerogen® ultra
Tamis vibrant



Nébulisation de 2 phages anti *P. aeruginosa*
2 nébulisation/j pendant 7 j
+ ATB IV



Amélioration clinique et ↘ charge PA démasque autre bactéries, pas de récurrence à M3

	1.Pseudomonas aeruginosa 1.10e6 2.Corynebacterium striatum > 1.10e7 3.Stenotrophomonas maltophilia > 1.10e7 4.Achromobacter xylosoxidans > 1.10e7 5.Streptococcus constellatus > 1.10e7	1.Pseudomonas aeruginosa > 1.10e7 2.Achromobacter xylosoxidans > 1.10e7 3.Flore de type oropharyngée > 1.10e7	1.Achromobacter xylosoxidans 1.10e7 2.Pseudomonas aeruginosa 1.10e7 3.Flore de type oropharyngée > 1.10e7 4.Stenotrophomonas maltophilia 1.10e6	1.Pseudomonas aeruginosa > 1.10e7 2.Flore de type oropharyngée 1.10e5
Identification via spectro d...				Maldi-Tof,...
Méthode : Diffusion	V			
Amoxicilline				
Amoxicilline+ac. clavulanique				
Ticarcilline	R			R
Ticarcilline+ac. clavulanique	R			R
Pipéracilline (30 µg)	R			R
Pipéracilline+tazobactam (...)	R			R
Céfotaxime (5 µg)				
Ceftazidime (10 µg)	R			R
Ceftazidime+avibactam				
Aztréonam	R		S 8.0 S 2.0	S 6.0 S 2.0
Céfépime	R		R	R
Imipénème	R		R	R
Méropénème	R		R	R
Gentamicine (10 µg)	S		R	S
Tobramycine	S		R	S
Amikacine	S		R	S
Minocycline			S	S
Acide nalidixique			R	
Ciprofloxacine	R		R	R
Lévofloxacine			R	S
Triméthoprim+ sulfamétho...			R 0.5	S

30 MARS 2022

27 MARS 2022

25 MARS 2022

22 MARS 2022

05 MAI 2022

Bactériologie

Cultures POSITIVES :

Pseudomonas aeruginosa : 10 puissance 6 UFC/ml
A confronter au contexte clinique

Numération inférieure au seuil significatif.

Achromobacter xylosoxidans : 10 puissance 7 UFC/ml
Corynebacterium striatum : 4.10 puissance 7 UFC/ml

Essais cliniques ou en est-on ?

	Title	Status	Study Results	Conditions	Interventions	Locations
12	Bacteriophage Therapy in Patients With Urinary Tract Infections	Recruiting	No Results Available	•Urinary Tract Infection Bacterial	•Biological: Bacteriophage Therapy	<ul style="list-style-type: none"> •Universal Axon Clinical Research, Doral, Florida, United States •AMP Research Clinic, Miami Gardens, Florida, United States •AdMed Research, Miami, Florida, United States •Innovation Medical Research Center, Inc, Palmetto Bay, Florida, United States •Henry Ford Hospital, Detroit, Michigan, United States •James J. Peters VA Medical Center, Bronx, New York, United States •University of Texas Southwestern Medical Center, Dallas, Texas, United States •DHR Health Institute for Research and Development, Edinburg, Texas, United States
13	Bacteriophage Therapy in Tonsillitis	Active, not recruiting	No Results Available	•Acute Tonsillitis	•Drug: Nebulizer inhalation irrigation of the mucous membranes of the tonsils with a bacteriophage.	•Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan
14	PrePhage - Faecal Bacteriophage Transfer for Enhanced Gastrointestinal Tract Maturation in Preterm Infants - Donor Study	Recruiting	No Results Available	•Feeding Patterns •Microbial Colonization		•Gustav R Jakobsen, Copenhagen, Denmark
15	PrePhage - Faecal Bacteriophage Transfer for Enhanced Gastrointestinal Tract Maturation in Preterm Infants	Not yet recruiting	No Results Available	•Necrotizing Enterocolitis •Microbial Substitution	•Other: Fecal Filtrate Transfer •Other: Placebo	•Rigshospitalet, Copenhagen, Denmark
16	Nebulized Bacteriophage Therapy in Cystic Fibrosis Patients With Chronic Pseudomonas Aeruginosa Pulmonary Infection	Not yet recruiting	No Results Available	•Chronic Pseudomonas Aeruginosa Infection •Cystic Fibrosis	•Drug: BX004-A •Drug: Placebo	
17	Phage Therapy for the Prevention and Treatment of Pressure Ulcers	Not yet recruiting	No Results Available	•Pressure Ulcer	•Combination Product: Bacteriophage-loaded Microcapsule Spray •Combination Product: Placebo •Procedure: Standard of Care	
18	Bacteriophage Therapy TP-102 in Diabetic Foot Ulcers	Recruiting	No Results Available	•Diabetic Foot Ulcer •Pseudomonas Aeruginosa Infection •Staphylococcus Aureus Infection •Acinetobacter Infection	•Biological: TP-102	•Hadassah Medical Center, Ein Kerem, Jerusalem, Israel
19	Ph 1/2 Study Evaluating Safety and Tolerability of Inhaled AP-PA02 in Subjects With Chronic Pseudomonas Aeruginosa Lung Infections and Cystic Fibrosis	Recruiting	No Results Available	•Cystic Fibrosis •Pseudomonas Aeruginosa •Pseudomonas •Lung Infection •Lung Infection Pseudomonal	•Biological: AP-PA02 •Other: Placebo	<ul style="list-style-type: none"> •Children's Hospital Los Angeles, Los Angeles, California, United States •University of South Florida, Tampa, Florida, United States •St. Luke's Cystic Fibrosis Center of Idaho, Boise, Idaho, United States •Northwestern University, Chicago, Illinois, United States •University of Iowa, Iowa City, Iowa, United States •Johns Hopkins University, Baltimore, Maryland, United States •Massachusetts General Hospital, Boston, Massachusetts, United States •Boston Children's Hospital, Boston, Massachusetts, United States •Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, United States •Nationwide Children's Hospital, Columbus, Ohio, United States

Urinaire

OS

Respiratoire

Peau et tissus mous

Bactériémie

microbiote/
digestif

Essais cliniques ou en est-on ?

ClinicalTrials.gov Search Results 05/13/2022

	Title	Status	Study Results	Conditions	Interventions	Locations
1	Mayo Clinic Phage Program Biobank	Enrolling by invitation	No Results Available	•Bacteriophage Therapy		•Mayo Clinic Rochester, Rochester, Minnesota, United States
2	Phage Safety Cohort Study	Not yet recruiting	No Results Available	•Prosthetic Joint Infection •Severe Infection	•Other: Adverse event after injection of phages	•Hospices Civils de Lyon, Lyon, France
3	Standard Treatment Associated With Phage Therapy Versus Placebo for Diabetic Foot Ulcers Infected by S. Aureus	Not yet recruiting	No Results Available	•Diabetic Foot •Staphylococcal Infections	•Drug: Topical anti-Staphylococcus bacteriophage therapy •Drug: Topical placebo corresponding to anti-Staphylococcus bacteriophage therapy	•CHU de Bordeaux - Hôpital Pellegrin, Bordeaux, France •CHRU de Nîmes - Hôpital Universitaire de Réadaptation du Grau du Roi, Le Grau du Roi, France •CHU de Nantes - Hôtel Dieu, Nantes Cedex 1, France •APHP - Groupe Hospitalier Pitié-Salpêtrière, Paris Cedex 13, France •APHP - Hôpital Lariboisière, Paris, France •CHRU de Toulouse - Hôpital de Rangueil, Toulouse Cedex 9, France •CH de Tourcoing, Tourcoing, France •Institut Robert Merle d'Aubigné, Valenton, France •CH Intercommunal de Villeneuve-Saint-Georges, Villeneuve-Saint-Georges, France
4	Phage Safety Retrospective Cohort Study	Recruiting	No Results Available	•Bone and Joint Infection •Prosthetic Joint Infection	•Other: patients having had adverse event after phagotherapy for bone or joint or implant infection	•Hospices Civils de Lyon, Lyon, France
5	Phage Therapy for the Prevention and Treatment of Wound Infections in Burned Patients	Not yet recruiting	No Results Available	•Wound Infection	•Biological: Bacteriophage cocktail spray •Drug: Xeroform	
6	Phage Therapy in Prosthetic Joint Infection Due to Staphylococcus Aureus Treated With DAIR	Not yet recruiting	No Results Available	•Infection of Total Hip Joint Prosthesis •Infection of Total Knee Joint Prosthesis	•Biological: Anti-Staphylococcus aureus Bacteriophages	
7	Bacteriophage Therapy in Patients With Diabetic Foot Osteomyelitis	Recruiting	No Results Available	•Osteomyelitis •Diabetic Foot Osteomyelitis	•Biological: Phage Therapy •Other: Placebo	•Martin Foot and Ankle, York, Pennsylvania, United States •Futuro Clinical Trials, LLC, McAllen, Texas, United States
8	Cystic Fibrosis bacterioPhage Study at Yale (CYPHY)	Recruiting	No Results Available	•Cystic Fibrosis	•Drug: Standard Dose YPT-01 •Other: Placebo	•Yale New Haven Hospital, New Haven, Connecticut, United States
9	Bacteriophage Therapy in First Time Chronic Prosthetic Joint Infections	Not yet recruiting	No Results Available	•Prosthetic Joint Infection •Bacterial Infections	•Biological: Phage Therapy	
10	Bacteriophage Therapy in Patients With Prosthetic Joint Infections Who Previously Failed Surgery for PJI	Not yet recruiting	No Results Available	•Prosthetic Joint Infection	•Drug: Bacteriophage •Drug: Placebo	
11	Safety and Efficacy of the Bacteriophage Preparation, ShigActive™, in a Human Experimental Model of Shigellosis	Not yet recruiting	No Results Available	•Shigellosis	•Biological: bacteriophage •Other: Placebo	•University of Maryland, Baltimore, University of Maryland School of Medicine, Center for Vaccine Development and Global Health, Baltimore, Maryland, United States

Urinaire

OS

Respiratoire

Peau et tissus
mous

Bactériémie

microbiote/
digestif

Essais cliniques recensés sur clinicaltrials

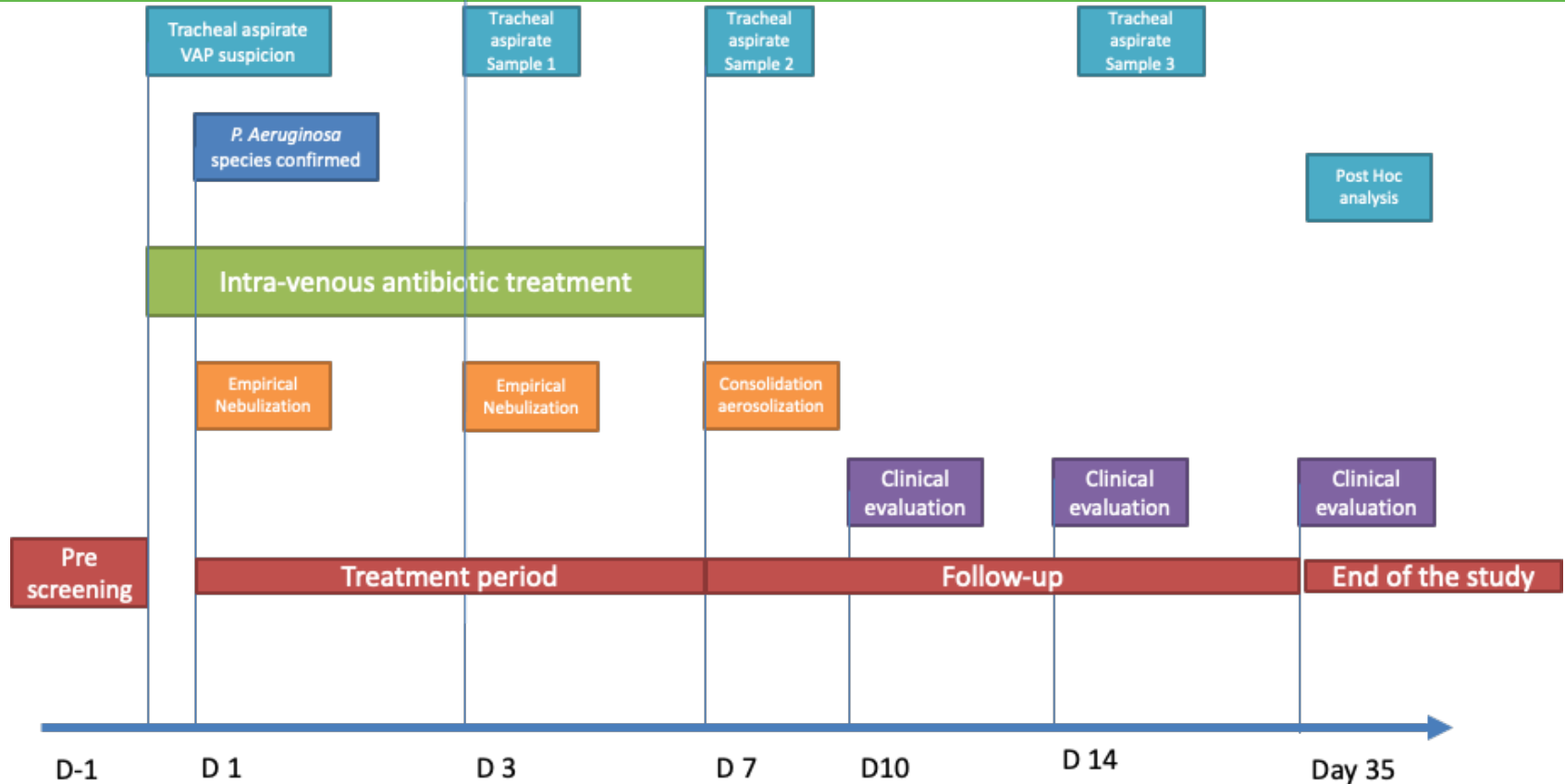
Pulmonary (nebulized)	Suspension	Liquid piobacteriophage complex (anti-staphylococcus, enterococcus, streptococcus, <i>E. coli</i> , <i>Proteus vulgaris</i> , <i>Proteus mirabilis</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , and <i>Klebsiella oxytoca</i>)	Acute tonsillitis	3	Active, not recruiting
Pulmonary (nebulized)	Suspension	Cocktail of bacteriophages (BX004-A)	Cystic fibrosis with chronic <i>P. aeruginosa</i> pulmonary infection	1 2	Not yet recruiting
Pulmonary	Suspension	Cocktail (Anti- <i>P. aeruginosa</i>)	Cystic fibrosis with chronic <i>P. aeruginosa</i> pulmonary infection	1 2	Recruiting
Pulmonary (nebulized)	Suspension	YPT-01 (Anti- <i>P. aeruginosa</i>)	Cystic fibrosis with chronic <i>P. aeruginosa</i> airway infections	1 2	Recruiting

PYOPHANEB

A Double-Blind, Placebo-Controlled Study of Nebulized Bacteriophages in Patients With Ventilator-Associated Pneumonia Due to *Pseudomonas aeruginosa*

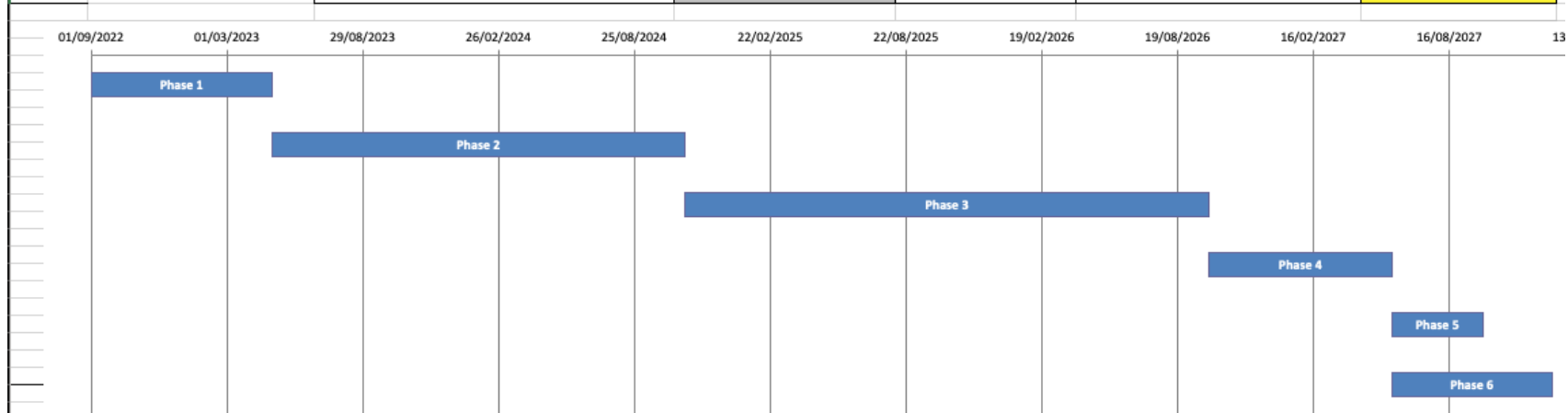
- **Superiority** trial in parallel arms 1:1, **184 Patients dans 12 centres en France**
- CJP demonstrate the efficacy of aerosolized bacteriophages therapy vs placebo (saline aerosol) in addition to IV antibiotic therapy on mortality and recurrence rate at day 28 of *Pseudomonas aeruginosa* VAP.
- Proportion of patients alive at D28 and without any recurrence of Pa-VAP after the initial episode.
 - Recurrence will be defined as:
 - A clinically suspected VAP
 - A microbiological confirmation with Pa recovered at a significant level from lung sample ($\geq 10^4$ /ml for BAL and $\geq 10^5$ /ml for tracheal aspirate).
- The primary criterion will be individually assessed by an Adjudication Committee on the basis of clinical data, in a blinded manner with respect to the randomization arm.

PYOPHANEB Flow-chart



PYOPHANEB Timeline rêvée

Phase		Etape démarrage de phase	Date étape démarrage de phase	Durée de la phase	Etape Fin de phase	Date étape fin de phase
Phase 1	Instruction du projet de recherche	Succès à l'AAP et notification des crédits	01/09/2022	241	Dates avis éthique et/ou ANSM et/ou CNIL + numéro clinical trial	30/04/2023
Phase 2	Période d'inclusion et / ou de recueil des données	Dates avis éthique et/ou ANSM et/ou CNIL + numéro clinical trial	30/04/2023	550	50 % des inclusions	31/10/2024
Phase 3	Période d'inclusion et / ou de recueil des données	50 % des inclusions	31/10/2024	699	Début de l'analyse des données ("Gel de base")	30/09/2026
Phase 4	Analyse des données	Début de l'analyse des données ("Gel de base")	30/09/2026	243	Envoi des rapports scientifiques, techniques et du résumé du rapport final de l'ANSM	31/05/2027
Phase 5	Valorisation	Envoi des rapports scientifiques, techniques et du résumé du rapport final de l'ANSM	31/05/2027	122	Soumission du manuscrit à revue à comité de lecture + accusé de réception	30/09/2027
Phase 6		Soumission du manuscrit à revue à comité de lecture + accusé de réception	31/05/2027	214	Publication princeps	31/12/2027



Points à résoudre au plan thérapeutique

- **Formulation**

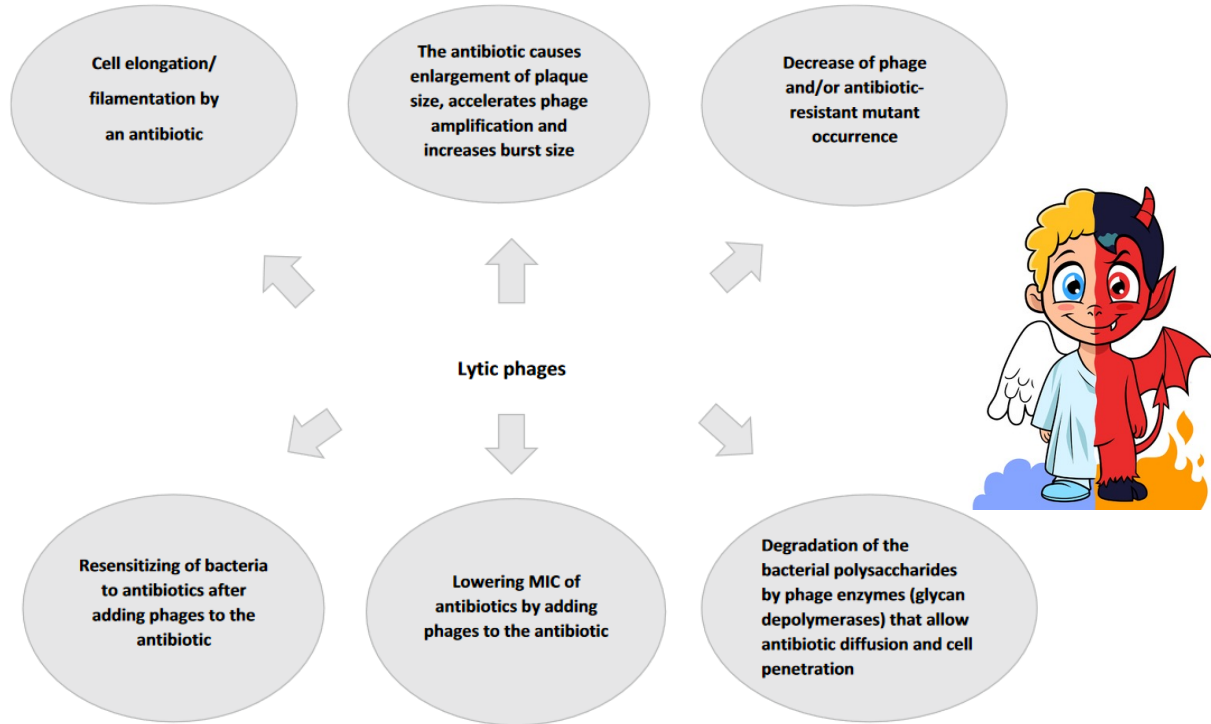
- Liquide
- Liposomal
- Lyophilisée

- **Administration**

- Directe
 - Instillée
 - Aérosolisée
 - Nebulisée
 - Tamis vibrant +++
 - Jet nebulisation (lyse les phages)
- Indirecte : IV



Phage-antibiotic synergy



Études *in vitro* soulevant la possibilité d'antagonisme entre phages et ATB agissant sur :

- La synthèse protéique ou le cycle ADN-ARN-Protéines
- Aminosides > FQ > Macrolides > Rifam

La phagothérapie n'est pas magique mais revient du mythe vers la réalité

- De nombreuses expériences à travers le monde
- Tendance à rapporter ce qui a fonctionné
- Quelques essais cliniques
- Beaucoup de questions à résoudre
- Thérapeutique ancienne mais innovante
- Thérapeutique à la fois naturelle et hautement technologique
- Un espoir à protéger de nos erreurs du passé

Merci

alexandre.bleibtreu@aphp.fr

Twitter : @BleibtreuAlexa1



ESCMID Study Group for Non-traditional
Antibacterial Therapy – ESGNTA



Réseau Bactériophage France

