

## INTRODUCTION

Lytic bacteriophages trigger bacterial lysis through their multiplication in an exponential and self-sustained reaction. They have a high therapeutic potential in patients with implant-associated infection, as they have a synergistic activity with antibiotics on biofilm-embedded bacteria.

## MATERIALS- METHODS

We managed 2 patients (64, 67 yo) with relapsing *P. aeruginosa* bacteremia associated with intravascular implants (biologic aortic valve, coil infection following bronchial artery embolization) for whom surgery was impossible or at risk of death. Both of them experienced >6 relapses in the previous year.

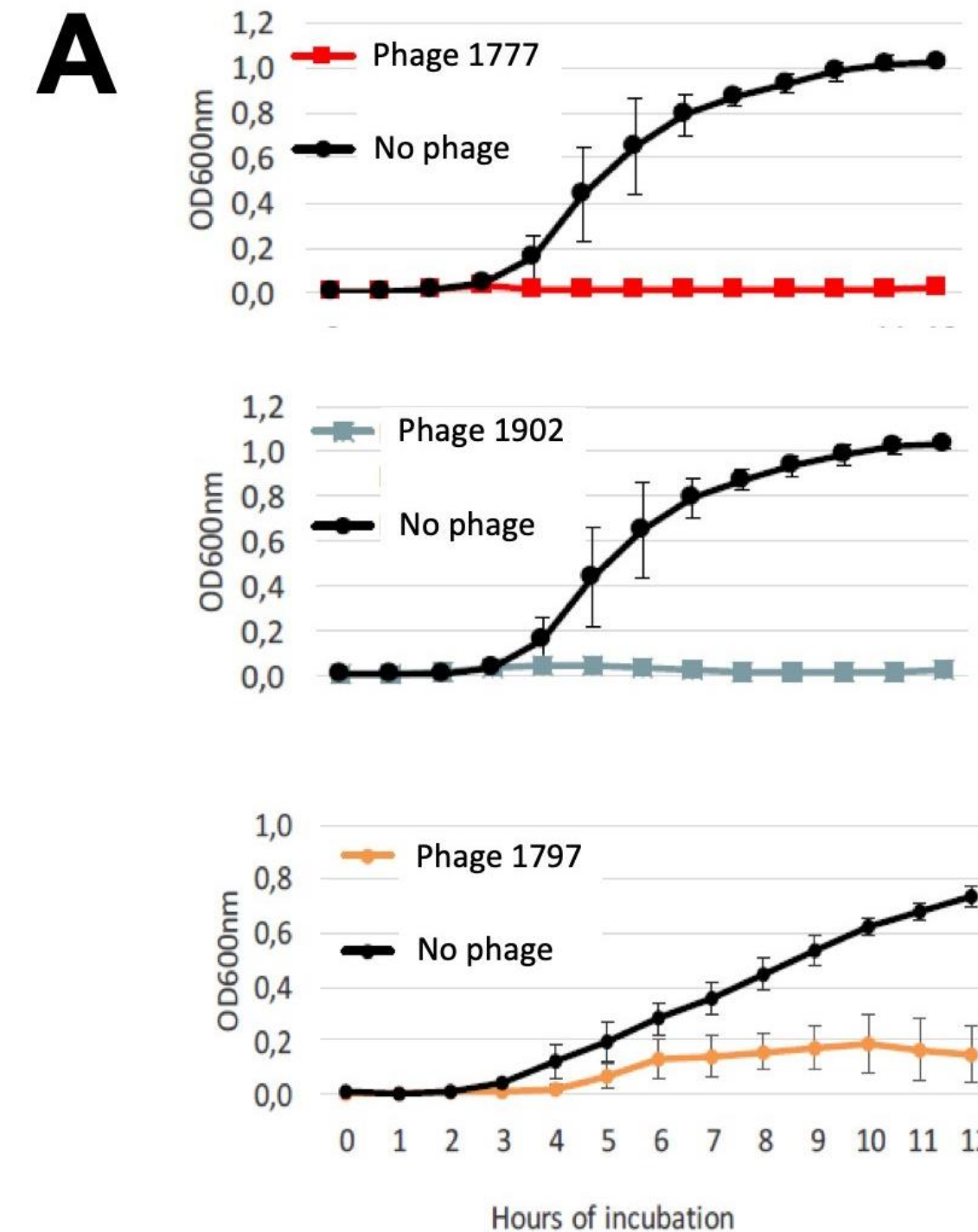
After discussion with the French health authority, 3 bacteriophages produced following Good Manufacturing Practice (GMP) guidelines were selected by Pherecydes based on their activity (**Panel A**). Hospital pharmacist mixed each phage (1 ml of  $1 \times 10^{10}$  PFU/ml) extemporaneously as “magistral” preparation (final dilution  $1 \times 10^8$  PFU/mL).

Bacteriophages quantification before and after the mix and in the blood of the first patient were performed to determine the optimal way of preparation and administration. Phages were administered every 2 or 3 days, during 10 to 21 days in combination with ceftazidime/avibactam prescribed during 6 weeks, if possible in combination with another active drug (fosfomycin or colistin).

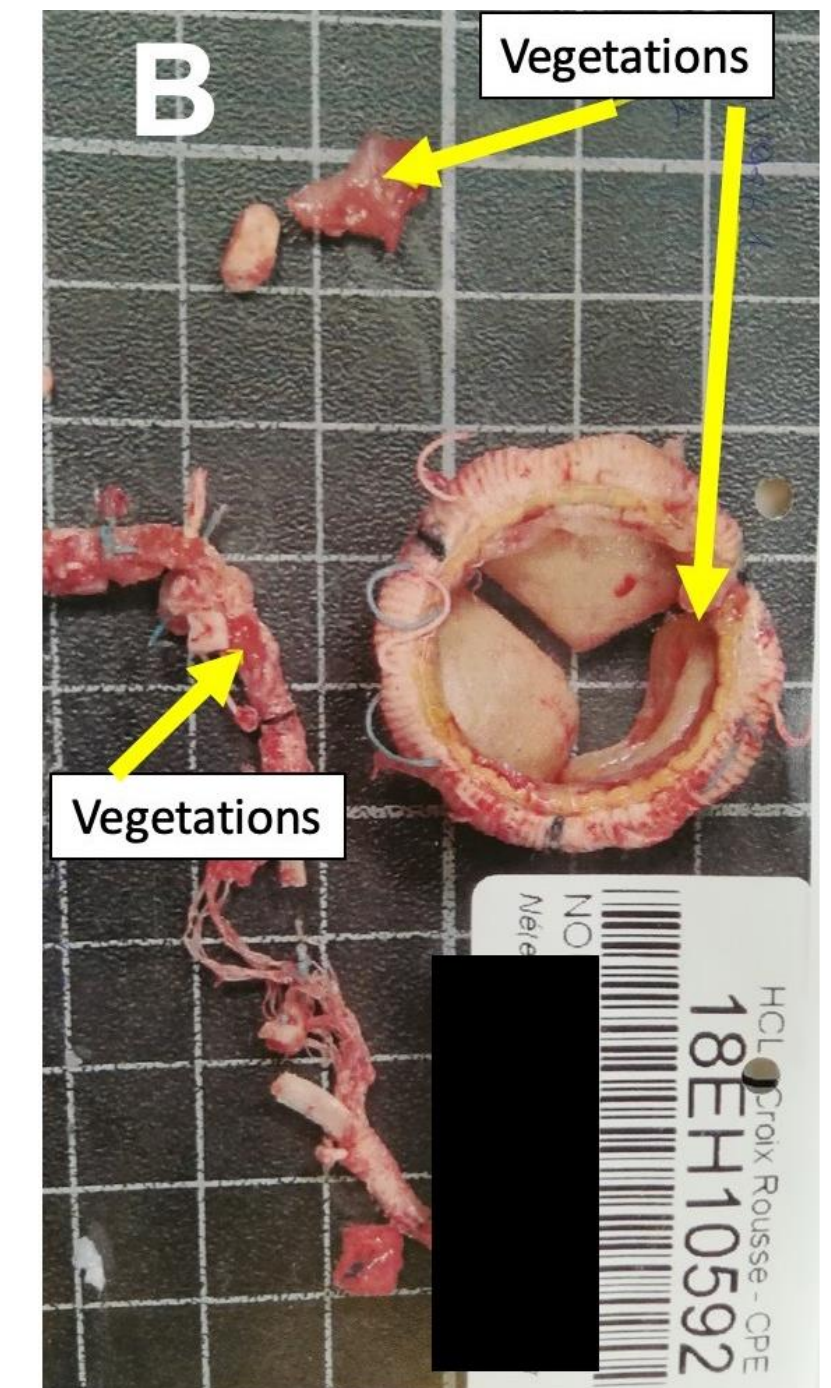
## RESULTS

Phages were administered to the first patient during a 6 hours infusion with an electronic pump. Depending on the filter used, we observed a decrease of the titer in the final solution: no bacteriophages were detected in the line, as well as in the patient’s blood. As this patient experienced a relapse, direct (5 min) intravenous injections of phages were then performed, after using the adequate filter. One bacteriophage was detected in the patient’s blood. Blood cultures became negative. A new prosthetic valve exchange was done, and peroperative cultures were now negative (**panel B**).

The second patient also received direct IV injections following the same process, and blood cultures remained negative during the three months follow-up.



**Panel A**  
Phagogram (killing curves) of the 3 bacteriophages selected to treat the patient



**Panel B**  
Macroscopic view of the infected biologic aortic valve with vegetations

## CONCLUSIONS

The type of filter used for the magistral preparation and the duration of the perfusion influenced the phage titer, as the titer in the patient’s blood. Personalized GMP bacteriophage therapy has the potential to be used as salvage therapy of *P. aeruginosa* intravascular implant infections.