

## **Phase I/II clinical trial of personalised phage therapy for the treatment of patients with CF and non-CF bronchiectasis**

### ***Lay Summary***

The increasing number of antibiotic-resistant infections, coupled with the slow rate of discovery of new antibiotics, pose a serious threat to people's health around the globe. Patients with cystic fibrosis, or with bronchiectasis not related to cystic fibrosis, are most commonly affected and face significant complications due to repeated exacerbations and the chronic use of antibiotics.

Bacteriophages, or simply phages, are viruses that infect and kill bacteria to survive. The antibacterial action of phages was discovered in the early twentieth century. Although they were initially used for the treatment of a variety of infections, they were later replaced by antibiotics, which were easier to manufacture and stock. Even though phage therapy is still considered today an experimental treatment, significant and longstanding experience in Eastern Europe points towards a safe and well tolerated treatment. Today, phage therapy is regaining interest as an alternative option against infections resistant to antibiotics.

Phage therapy is an excellent example of personalised treatment as phages are selected based on their activity against the patient's specific infection. In contrast to antibiotics, phages can only infect specific bacteria and they don't disturb the "beneficial" bacteria in our bodies. As a result, phage therapy is better tolerated and has fewer side effects. Because phages infect bacteria in different ways compared to the mechanism of action of antibiotics, phage therapy can be used for the treatment of infections that are resistant to antibiotics. Moreover, research has shown that the combination of antibiotics and phages can be effective against infections that are difficult to treat or than do not respond to antibiotics alone.

Despite these advantages, the efficacy of phage therapy still needs to be demonstrated in clinical trials in humans. The Lausanne University Hospital (CHUV) is establishing a program of personalised phage therapy intended for patients with bacterial infections for whom all therapeutic options have failed. This program includes all stages of phage therapy, from the identification of eligible patients and the search for active phages, to the production and purification of phages and, finally, to their administration to patients. As part of this program, we are planning a clinical trial of personalised phage therapy for patients with cystic fibrosis and bronchiectasis not related to cystic fibrosis. Patients will be considered eligible if they suffer from a serious bacterial infection that is resistant or not responding to antibiotics. Active phages will be identified within the phage collection of the Laboratory of Bacteriophages and Phage Therapy at CHUV, or from external laboratories. Phages will be prepared for administration at the Centre of Cell Production at CHUV according to the quality standards required by Swissmedic.

Securing funding for the clinical coordination of the trial will allow us to collect valuable information on the safety and effectiveness of phage therapy. This is the first study of personalised phage therapy in Switzerland and represents a significant and necessary step towards the approval of phage therapy as an established treatment against antibiotic resistant and difficult-to-treat infections.