

## Supporting Information for

Review

### **Recent advances in bacteriophage-based therapeutics: insight into the post-antibiotic era**

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**Table S1** Summary of clinical trials of bacteriophage therapy in the last three years.

NCT Number	Title	Condition	Drug	Intervention	Study type	Phase
NCT04787250	Bacteriophage therapy in patients with prosthetic joint infections	•Prosthetic joint infection	•Bacteriophage based on patient's matching results	NA	Interventional	•Phase 1 •Phase 2
NCT04650607	Bacteriophage safety cohort study	•Prosthetic joint infection •Bone and joint infection •Implant infection	•Bacteriophage will be administered based on patient's matching results	NA	Observational	NA
NCT04323475	Bacteriophage therapy for the prevention and treatment of wound infections in burned patients	•Wound infection	•Bacteriophage cocktail-SPK	•Drug: xeroform	Interventional	•Phase 1
NCT04684641	Cystic fibrosis bacteriophage study at yale (CYPHY)	•Cystic fibrosis	•Bacteriophage YPT-01	•Other: placebo	Interventional	•Phase 1 •Phase 2
NCT04289948	Assessing the efficacy of <i>anti-staphylococcal</i> bacteriophages in the management of infected foot ulcers in diabetes	•Diabetes •Diabetic foot •Diabetic foot infection	•Bacteriophage cocktail of at least 2–3 <i>anti-staphylococcal</i> bacteriophages produced by Intralytix Inc.	NA	Interventional	•Phase 1 •Phase 2
NCT04287478	Bacteriophage therapy in patients with urinary tract infections	•Urinary tract infection bacterial	•Bacteriophage administered based on patient's matching results	NA	Interventional	•Phase 1 •Phase 2

NCT02664740	Standard treatment associated with bacteriophage therapy versus placebo for diabetic foot ulcers infected by <i>S. aureus</i>	<ul style="list-style-type: none"> <li>•Diabetic toot</li> <li>•<i>Staphylococcal</i> infections</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage administered based on patient’s matching results</li> </ul>	<ul style="list-style-type: none"> <li>•Drug: topical anti <i>staphylococcus</i> bacteriophage therapy</li> </ul>	<ul style="list-style-type: none"> <li>•Industry</li> </ul>	<ul style="list-style-type: none"> <li>•Phase 1</li> <li>•Phase 2</li> </ul>
NCT04682964	Bacteriophage therapy in tonsillitis	<ul style="list-style-type: none"> <li>•Acute tonsillitis</li> </ul>	<ul style="list-style-type: none"> <li>•Pyobacteriophage complex liquid—PCL</li> </ul>	<ul style="list-style-type: none"> <li>•Drug: nebulizer inhalation irrigation of the mucous membranes of the tonsils with a bacteriophage.</li> </ul>	<ul style="list-style-type: none"> <li>Interventional</li> </ul>	<ul style="list-style-type: none"> <li>•Phase 3</li> </ul>
NCT01617122	Evaluate bacteriophage as a useful immunogen in patients with primary immune deficiency diseases (PID)	<ul style="list-style-type: none"> <li>•Primary immune deficiency diseases</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage 0X174</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>	<ul style="list-style-type: none"> <li>Interventional</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>
NCT04511221	Bacteriophage for gastrointestinal health 2 Study	Mild gastrointestinal symptoms in healthy adults	<ul style="list-style-type: none"> <li>•The commercial bacteriophage preparation—PreforPro</li> </ul>	<ul style="list-style-type: none"> <li>•Dietary supplement: bifidobacterium animals <i>subsp. lactis</i> <i>BL04</i></li> <li>•Other: placebo</li> </ul>	<ul style="list-style-type: none"> <li>Interventional</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>
NCT00945087	Experimental bacteriophage therapy of bacterial infections	<ul style="list-style-type: none"> <li>•Bacterial infections</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage lysates or purified bacteriophage formulations</li> </ul>	<ul style="list-style-type: none"> <li>Bacteriophage lysates or purified bacteriophage formulations for 10 pathogens</li> </ul>	<ul style="list-style-type: none"> <li>Interventional</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>
NCT03296631	Bacteriophages dynamics and influences during human gut microbiome establishment	<ul style="list-style-type: none"> <li>•Human gut microbiome development</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophages during infant gut development</li> </ul>	<ul style="list-style-type: none"> <li>•Other: collection of diapers with fresh stools</li> </ul>	<ul style="list-style-type: none"> <li>Observational</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>

NCT01818206	Bacteriophage effects on <i>Pseudomonas aeruginosa</i>	•Cystic fibrosis	•A cocktail of 10 bacteriophages	•Other: collection of induced sputum in order to evaluate the efficacy of a cocktail of 10 bacteriophages.	Interventional	NA
NCT02116010	Evaluation of bacteriophage therapy for the treatment of escherichia coli and <i>Pseudomonas . aeruginosa</i> (PA) wound infections in	•Wound infection	• <i>E. coli</i> bacteriophages cocktail • <i>PA</i> bacteriophages cocktail	•Drug: <i>E. coli</i> bacteriophages cocktail •Drug: standard of care: silver sulfadiazine •Drug: <i>PA</i> ,	Interventional	•Phase 1 •Phase 2
NCT03140085	Bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate	•Intravesical bacteriophage treatment for urinary tract infections	•PYO bacteriophage	•Biological: PYO bacteriophage •Drug: antibiotics •Other: sterile bacteriology media	Interventional	•Phase 2 •Phase 3
NCT04815798	Bacteriophage therapy for the prevention and treatment of pressure ulcers.	•Pressure ulcer	•Bacteriophage therapy combination product—BACTELIDE	•Combination product: bacteriophage loaded microcapsule spray •Combination product: placebo •Procedure: standard of care	Interventional	•Phase 1 •Phase 2
NCT03269617	Bacteriophage study: bacteriophages as novel prebiotics	•Gastrointestinal disorder, functional	•PeforPro	•Dietary supplement: bacteriophage mixture •Other: placebo control	Interventional	NA

NCT04724603	Bacteriophage safety retrospective cohort study	<ul style="list-style-type: none"> <li>•Bone and joint infection</li> <li>•Prosthetic joint infection</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage administered based on patient's matching results</li> </ul>	<ul style="list-style-type: none"> <li>•Other: patients having had avderse event after phagotherapy for bone or joint or implant infection</li> </ul>	Observational	NA
NCT00937274	Antibacterial treatment against diarrhea in oral rehydration solution	<ul style="list-style-type: none"> <li>•Diarrhea</li> </ul>	<ul style="list-style-type: none"> <li>•T4 bacteriophage cocktail</li> </ul>	<ul style="list-style-type: none"> <li>•Other: commercial T4 bacteriophage cocktail</li> <li>•Other: standard oral rehydration solution (ORS)</li> </ul>	Interventional	NA
NCT04596319	Ph 1/2 study evaluating safety and tolerability of inhaled APPA02 in subjects with chronic <i>PA</i> lung infections and cystic fibrosis	<ul style="list-style-type: none"> <li>•Cystic fibrosis</li> <li>•<i>PA</i></li> <li>•<i>Pseudomonas</i></li> <li>•Lung infection</li> <li>•Lung infection <i>Pseudomonal</i></li> </ul>	<ul style="list-style-type: none"> <li>•AP-PA02</li> </ul>	<ul style="list-style-type: none"> <li>•Other: placebo</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 1</li> <li>•Phase 2</li> </ul>
NCT04803708	Bacteriophage therapy TP-102 in diabetic foot ulcers	<ul style="list-style-type: none"> <li>•Diabetic foot ulcer</li> <li>•<i>PA</i> infection</li> <li>•<i>Staphylococcus aureus</i> Infection</li> <li>•<i>Acinetobacter</i> Infection</li> </ul>	<ul style="list-style-type: none"> <li>•TP-102</li> </ul>	NA	Interventional	<ul style="list-style-type: none"> <li>•Phase 1</li> <li>•Phase 2</li> </ul>

NCT00663091	A prospective, randomized, double-blind controlled study of WPP-201 for the safety and efficacy of treatment of venous leg ulcers	•Venous leg ulcers	•WPP-201	NA	Interventional	•Phase 1 •Phase 2
NCT03808103	Safety and efficacy of ecoctive on intestinal adherent invasive <i>E. coli</i> in patients with inactive Crohn's disease	•Crohn's disease	•EcoActive	•Biological: placebo	Interventional	•Phase 1 •Phase 2
NCT03395769	Individual patient expanded access for AB-SA01, an investigational <i>anti-Staphylococcus aureus</i> bacteriophage therapeutic	• <i>Staphylococcus aureus</i> infections	•AB-SA01	NA	Expanded access •Individual patients	NA
NCT03395743	Individual patient expanded access for AB-PA01, an investigational <i>Anti-pseudomonas Aeruginosa</i> bacteriophage therapeutic	• <i>PA</i> infections	•AB-PA01	NA	Expanded access •Individual patients	NA

NCT04325685	The effect of supraglottic and oropharyngeal decontamination on the incidence of ventilator-associated pneumonia	<ul style="list-style-type: none"> <li>•Trauma injury</li> <li>•Brain injuries</li> <li>•Abdominal sepsis</li> <li>•Pancreatitis</li> <li>•Meningitis</li> <li>•Encephalitis</li> <li>•Seizures</li> <li>•Acute respiratory distress syndrome</li> </ul>	•Sexthaphag	<ul style="list-style-type: none"> <li>•Drug: control</li> <li>•Drug: antiseptic solution</li> </ul>	Interventional	NA
NCT03326947	Bacteriophage II trial of stathmin as predictive biomarker for TPF Induction chemotherapy in OSCC	<ul style="list-style-type: none"> <li>•Neoplasm neck</li> </ul>	•Stathmin	<ul style="list-style-type: none"> <li>•Drug: docetaxel, cisplatin and 5-fluorouracil</li> </ul>	Interventional	•Phase 2
NCT03972826	Use of provodine to protect HCW Hands (Aim II.1)	<ul style="list-style-type: none"> <li>•Infection</li> </ul>	•Provodine	NA	Interventional	NA
NCT04191148	Safety, tolerability, and PK of LBP-EC01 in patients with lower urinary tract colonization caused by <i>E. Coli</i>	<ul style="list-style-type: none"> <li>•Urinary tract infections</li> </ul>	•LBP-EC01	<ul style="list-style-type: none"> <li>•Drug: lactated ringers solution for injection</li> </ul>	Interventional	•Phase 1
NCT00306878	Phase I study of BMS-188667 (CTLA4Ig) in patients with <i>Psoriasis vulgaris</i>	<ul style="list-style-type: none"> <li>•Psoriasis vulgaris</li> </ul>	•Abatacept	NA	Interventional	•Phase 1
NCT04737876	A study to evaluate the safety, tolerability, and fecal pharmacokinetics of BX002-A in healthy adults	<ul style="list-style-type: none"> <li>•Healthy volunteers</li> </ul>	•BX002-A	<ul style="list-style-type: none"> <li>•Other: placebo</li> </ul>	Interventional	•Phase 1

NCT00916292	Safety study of topical human FGF-1 for wound healing	<ul style="list-style-type: none"> <li>•Diabetic foot ulcers</li> </ul>	<ul style="list-style-type: none"> <li>•FGF-1 141</li> </ul>	<ul style="list-style-type: none"> <li>•Drug: FGF-1 141</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 1</li> </ul>
NCT00089180	T4N5 liposomal lotion in preventing the recurrence of nonmelanoma skin cancer in patients who have undergone a kidney transplant	<ul style="list-style-type: none"> <li>•Actinic keratosis</li> <li>•Basal cell carcinoma of the skin</li> <li>•Recurrent skin cancer</li> <li>•Squamous cell carcinoma of the skin</li> </ul>	<ul style="list-style-type: none"> <li>•Liposomal T4N5 lotion</li> </ul>	<ul style="list-style-type: none"> <li>•Drug: liposomal T4N5 lotion</li> <li>•Other: placebo</li> <li>•Other: laboratory biomarker analysis</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 2</li> </ul>
NCT00001145	Study of immune responses and safety of recombinant human CD40 ligand in patients with X-linked hyper-IgM syndrome	<ul style="list-style-type: none"> <li>•Immunoproliferative disorder</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage Phi-X 174</li> </ul>	<ul style="list-style-type: none"> <li>•Drug: bacteriophage</li> <li>•Drug: rhuCD40L</li> <li>•Drug: KLH</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 2</li> </ul>
NCT02828774	Peptide-drug-conjugates for personalized, targeted therapy of chronic lymphocytic leukemia	<ul style="list-style-type: none"> <li>•CLL</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage specifically internalized by B-CLL cells</li> </ul>	<ul style="list-style-type: none"> <li>•Other: there will be no intervention.</li> </ul>	Observational	<ul style="list-style-type: none"> <li>NA</li> </ul>
NCT00785967	Immune responses in patients treated with raltegravir	<ul style="list-style-type: none"> <li>•HIV infections</li> </ul>	<ul style="list-style-type: none"> <li>•Bacteriophage phiX174</li> </ul>	<ul style="list-style-type: none"> <li>•Biological: various vaccines</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 3</li> </ul>
NCT02757755	Ascending dose study of the safety of AB-SA01 when topically applied to intact skin of healthy adults	<ul style="list-style-type: none"> <li>•Healthy volunteers</li> </ul>	<ul style="list-style-type: none"> <li>•ABSA01</li> <li>•Placebo</li> </ul>	<ul style="list-style-type: none"> <li>•Biological: placebo</li> </ul>	Interventional	<ul style="list-style-type: none"> <li>•Phase 1</li> </ul>
NCT01640886	Study of the performance of the KeyPath MRSA/MSSA blood culture test - BTA	<ul style="list-style-type: none"> <li>•Bacteremia</li> </ul>	<ul style="list-style-type: none"> <li>•Microbacteriophage</li> </ul>	<ul style="list-style-type: none"> <li>NA</li> </ul>	Observational	<ul style="list-style-type: none"> <li>NA</li> </ul>



NCT00814151	Microbacteriophage <i>S. aureus</i> / MSSA / MRSA blood culture beta trial	<ul style="list-style-type: none"> <li>•Bacteremia</li> <li>•Staphylococcal infection</li> <li>•Sepsis</li> <li>•Infection</li> </ul>	•Microbacteriophage	<ul style="list-style-type: none"> <li>•Other: Microbacteriophage <i>S. aureus</i> / MSSA / MRSA Blood Culture Test (prototype)</li> </ul>	Observational	NA
NCT01184339	Prospective study into the performance of the Microbacteriophage <i>S. Aureus</i> /MSSA/MRSA test direct from blood culture positives	•Bacteremia	•Microbacteriophage	<ul style="list-style-type: none"> <li>•Device: Microbacteriophage <i>S. aureus</i>/MSSA/MRSA blood culture test</li> </ul>	Observational	NA
NCT01693965	Clinical course and changes in the respiratory microbiota based on antibiotic treatment in patients with cystic fibrosis	•Bronchopulmonary infection	•Bacteriophage based on patient's matching results	•Other: sputum samples	Interventional	NA
NCT03967236	Impact of intestinal virome on pediatric inflammatory bowel disease	•Inflammatory bowel diseases	•Bacteriophage based on patient's matching results	•Other: collection of stool and blood samples	Observational	NA
NCT04791644	Faecal microbiota characterization in lynch syndrome (LS) patients with or without colorectal neoplasia	•Lynch syndrome	•Bacteriophage based on patient's matching results	•Other: evaluation of the true role of gut microbiota in CRC carcinogenesis	Observational	NA

NCT03418454	The oral microbiome as a prognostic tool in oral malignant and premalignant lesions and in medication related osteonecrosis of the jaw	<ul style="list-style-type: none"> <li>•Oral squamous cell carcinoma</li> <li>•Medication related osteonecrosis of the jaw</li> <li>•Oral epithelial dysplasia</li> </ul>	•Bacteriophage based on patient's matching results	•Diagnostic test: buccal mucosa samples for extraction of bacterial DNA	Observational	NA
NCT02925533	Ph 1B B-701 in combination with pembrolizumab in metastatic transitional cell carcinoma of the urothelial tract	•Bladder cancer	•B-701	•Drug: pembrolizumab	Interventional	•Phase 1
NCT02695784	Probiotics after discharge	<ul style="list-style-type: none"> <li>•Microbiota</li> <li>•Bacteriophages</li> <li>•Infantile colic</li> <li>•Growth</li> </ul>	•Dietary supplement: probiotic continuation	NA	Interventional	•Phase 4

**Table S2** Summary of bacteriophages combined with other antibiotic against MDR infections.

Bacteriophage	Combination	Target bacterial	Ref.
<i>Staphylococcus aureus</i> bacteriophage Sb-1	Daptomycin Vancomycin Cefazolin	<i>Methicillin resistant S. aureus</i>	1

Bacteriophage ECA2	Ampicillin Kamanycin Tetracycline Ciprofloxacin	<i>E. coli</i>	2
Bacteriophage ELY-1	Ciprofloxacin	<i>E. coli</i>	3
Bacteriophage cocktails	Ciprofloxacin	<i>P. aeruginosa</i>	4
Bacteriophages PN05 and PN09	Carvacrol	<i>Pseudomonas syringae pv. actinidiae</i>	5
Bacteriophage PEV20	Ciprofloxacin	<i>P. aeruginosa</i>	6
Bacteriophage P22	Ciprofloxacin	<i>S. typhimurium</i>	7
Bacteriophage vB_KpnM_P-KP2	Gentamicin	<i>K47 serotype Klebsiella pneumoniae</i>	8
Bacteriophage Endolysin SAL200	Standard-of-care (SOC) antibiotics	<i>Staphylococcus aureus</i>	9
Bacteriophage phiIPLA-RODI	Lytic protein CHAPSH3b	<i>Staphylococcus aureus</i>	10
5-Bacteriophage <i>P. aeruginosa</i> cocktail, PAM2H	Ceftazidime Ciprofloxacin Gentamicin Meropenem	<i>P. aeruginosa</i>	11
Bacteriophage P100	Nisin and sodium lactate	<i>Listeria monocytogenes</i>	12
Bacteriophage EcSw	Kanamycin and chloramphenicol	<i>antibiotic-resistant Escherichia coli</i>	13
<i>Anti-S.aureus</i> purified bacteriophage	Linezolid	<i>Staphylococcus aureus</i>	14
Bacteriophage	Cationic photosensitizer	<i>A. baumannii</i>	15
Bacteriophage preparation	Lauric arginate ethyl ester	<i>Listeria monocytogenes</i>	16
Bacteriophage endolysin	Polysaccharide depolymerase	<i>Staphylococcus aureus</i>	17

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