

Preclinical Evaluation of the Tolerance of an Injectable Bacteriophage Suspension Developed in an Academic Setting

C. Marchand¹, B. Lapras¹, M. Medina², M. Grimopont¹, C. Merienne¹, F. Laurent^{2,3}, F. Pirot^{1,4}

29th GERPAC Congress – 2026 –
Poster Communication – Ref. COM26-76793

1 FRIPHARM Platform, Hospital Pharmacy, GH Centre, HCL, France • 2 Institute of Infectious Agents, GH Nord, HCL, France •
3 Université Claude Bernard Lyon 1, INSERM U1111 - CNRS UMR5308 CIRI, Lyon • 4 Université Claude Bernard Lyon 1, Faculté de Pharmacie, LBTI UMR CNRS 5305, Lyon

Background & Objective

Hospital-compounded injectable preparations usually involve well-characterized chemical substances. This work addresses an injectable suspension of four bacteriophages targeting anti-*Staphylococcus aureus*, produced in an academic hospital setting, whose toxicity profile had not been characterized. Objective: to evaluate the local and systemic tolerance of this preparation administered intravenously.

Methods

GLP-compliant repeated-dose toxicity study (Charles River, New Zealand White rabbit – Study No. 31962766).

Grp	Test material	Dose (PFU/kg)	Volume (mL/kg/day)	N (M/F)
1	Control (NaCl 0.9%)	0	0.6	5/5 + 5/5*
2	Test item (4 phages)	0.6×10 ⁹ **	0.6	5/5 + 5/5*

* main study + recovery. ** 10× the target clinical dose.

Treatment Day 0-14
(1 IV/day)

Recovery Day 14-28

▼ Day 16: terminal necropsy (half of the animals) – ▼ Day 29: recovery necropsy (remaining animals)

- Clinical observations, local tolerance, injection site
- Body weight, food consumption, body temperature
- Ophthalmology; hematology, coagulation, clinical chemistry
- Serum qPCR (attempted) and immunology (anti-phage antibodies); organ weights, macroscopic and full microscopic examination

Results

In-life & clinical pathology parameters

- No mortality and no test item-related clinical signs
- No local reactions at the injection site attributable to the test item
- No effect on body temperature, body weight or food consumption
- No findings in ophthalmology, hematology, coagulation or clinical chemistry

Organ weights & macroscopic examination

No test item-related differences in organ weights versus controls, and no treatment-related macroscopic findings at either necropsy.

Microscopic examination – spleen

Findings limited to a minimal-to-moderate increase in cellularity of the white-pulp germinal centers (test item group only; controls: 0/5 at all time points).

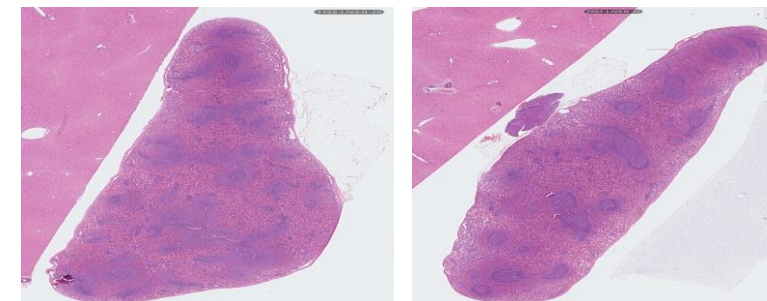
Test item group (n)	M J16	F J16	M J29	F J29
N examined	5	5	5	5
Increased cellularity	5	5	5	4
– Minimal	3	4	2	2
– Moderate	2	1	3	2

M/F Day 16 = terminal necropsy; M/F Day 29 = recovery necropsy (no recovery observed).

Pathologist's conclusion

Increased cellularity was observed at Days 16 and 29, similar incidence/severity (no recovery). Absent other lymphoid organ involvement, infectious/pro-inflammatory process, or clinical translation, this finding was considered non-adverse.

Histology



Control

Test material

Spleen sections (H&E), control vs. treated animal: increased germinal-center cellularity.

Discussion & Conclusion

This study confirms the favorable tolerance profile of a bacteriophage preparation formulated and produced using a hospital pharmaceutical approach, at a supra-therapeutic dose. This work illustrates the ability of a hospital-university platform to design, formulate and evaluate a phage therapy medicine meeting the requirements of pharmaceutical development for injectable forms, paving the way for the first clinical uses of GMP-manufactured bacteriophages produced in France by a public institution.

Keywords: Phage therapy, Toxicology, Preclinical safety