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IMPROVED BACTERIOPHAGE COCKTAIL SHOWS EARLY PROMISING RESULTS AGAINST URINARY TRACT INFECTIONS IN A PHASE 2 STUDY

Early results from a Phase 2 study showed promising outcomes for an improved **bacteriophage cocktail** enhanced with CRISPR, targeting urinary tract infections (UTIs) caused by *Escherichia coli*.

In the first part of the ELIMINATE Phase 2 trial, researchers aimed to define a dosing regimen for a cocktail of six bacteriophages designed with a CRISPR-Cas3 construct targeting *E. coli* genomes in patients with uncomplicated UTIs. A total of 39 patients were randomly assigned to receive three different combinations of **intra-urethral and intravenous doses**, along with daily oral doses of the antibiotic trimethoprim-sulfamethoxazole.

The primary measurable outcome was the level of bacteriophages in urine and blood during treatment, with an additional focus on safety for those who received at least one dose of the cocktail.

The results indicated that a regimen consisting of two days of intra-urethral bacteriophages (2×10^{12} **plaque-forming units** [PFU]) and three days of concurrent intravenous bacteriophages (1×10^{10}

PFU) combined with twice-daily oral **trimethoprim-sulfamethoxazole** was well tolerated, demonstrating high and consistent bioavailability in both urine and blood, along with promising pharmacodynamic effects.

A total of 44 adverse events were observed in 18 patients (46%) from the safety population, but no serious adverse events were reported.

The study also provided early indications of efficacy, with a rapid reduction of *E. coli* in the urine observed within four hours of treatment. This reduction was sustained in 16 patients at the day-10 cure assessment, with complete resolution of UTI symptoms by day 10.

The natural balance between bacteriophages and bacteria can be disrupted in favor of eradicating bacteria by selecting appropriate indications, dosing regimens, and delivery methods, which allow for high levels of direct exposure and the use of bacteriophage cocktails.

Adapted after Chris Dall, 12 August 2024

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