LABORATORY SPOTLIGHT: MAKING THE COMPLEX SEAMLESS FOR A CHALLENGING PHAGE STUDY

A multi-center surveillance study to investigate the microbiology of the urinary tract colonization/ infection in patients with an active infection or history of recurrent urinary tract infection.

OVERVIEW

The Sponsor was researching a novel approach to treat urinary tract infections (UTIs), including multi-drug resistant strains, using an enhanced bacteriophage therapy. Bacteriophages are bacteria specific viruses that infect and replicate within bacteria and target specific bacterial strains within a species. Therefore, the first step was to conduct a surveillance study to collect *E. coli* isolates from clinical samples in order to determine the appropriate phage cocktail to treat clinically relevant *E. coli* strains. Because this approach was a new modality of therapeutic that had not been used in a controlled clinical trial, mapping out a strategy for laboratory testing required a team of experts from various companies and functions working together to define the complex requirements, roles and responsibilities, and operational plan.

This was unchartered territory. To develop the comprehensive testing strategy, Medpace experts in infectious disease, phage technology, clinical operations, and laboratories worked in a collaborative and exploratory mode with the Sponsor and Medpace's specialty microbiology lab partner to devise and execute a plan that ultimately achieved all goals and beat timelines.

CHALLENGES

Complex Testing: There were a number of testing requirements throughout the study that needed to be defined and coordinated. A central lab, bioanalytical lab, and specialized central microbiology lab were all part of the equation. Bringing together experts to determine what testing was needed, how the testing would be developed, which lab would perform which testing, and coordinating how the data would be reported to the Sponsor required a highly proficient partner.

Evolving Requirements: Due to the pioneering nature of the study, there were ongoing adjustments and clarifications that required a great deal of flexibility and resourcefulness. Changing study details, multiple versions of the validation protocol, additional data requirements (*E. coli* isolates to be sent mid-way through the study, site reports to be provided for subjects with *E. coli* identified in their urine sample), and changing expectations of what organisms would be tested, quantified, and saved are examples of the fluidity of the study.

Feasibility and Patient Recruitment: Identifying the sites that could recruit patients at risk for developing a UTI by *E. coli* but were not yet presenting symptoms was a challenging start. Requiring those same sites to also participate in the follow-up Phase Ib study that required a seven-day hospitalization made it even more so. Site feasibility and selection required strong relationships and a creative approach.

Logistics and Process: Because samples would be shipped to both a central lab and a specialty microbiology lab within 24 hours of collection, anticipating potential issues and confusion was critical for mitigating costly errors. Exceptional communications and optimized requisition processes were necessary to avoid confusion and missteps.

SOLUTION

Multi-disciplined Team: Medpace pulled from a number of internal functional areas to build a team who brought a variety of approaches, perspectives, and experiences to the project. This included physicians specialized in infectious disease and gene therapies, lab scientists, and operational experts. This multi-disciplined approach proved to be extremely valuable and minimized any missteps as Medpace and the Sponsor worked collaboratively and transparently to design the surveillance study and upcoming Phase 1b study.

Lab Testing and Coordination: One of the advantages of working with Medpace is the integration of central and bioanalytical labs as well as an established partnership with IHMA, a specialty central microbiology lab. IHMA was instrumental in developing the required testing and performing culture, quantification, antibiotic susceptibility testing, and phage testing. Medpace orchestrated the logistics, communications, and overall strategy among the central labs. In preparation for the Phase Ib study, we worked with potential sites to obtain urine samples from enrolled subjects that would be cultured at the central microbiology lab. *E. coli* isolated from these cultures was then used to determine the appropriateness of the phage cocktail. In addition, the Sponsor was able to better understand the prevalence of *E. coli* colonization.

Feasibility and Site Selection: The appropriate patient population was identified first and then feasibility was done to determine if there were significant numbers of potential patients that met all the key criteria. This helped us select the optimal sites including VA hospitals that were important to the Sponsor.

Communication: Frequent communication and access to microbiological culture data from IHMA were critical to the success of the surveillance trial. Medpace had weekly calls with Medpace's CRO, the central lab, and IHMA. These calls were highly beneficial to keeping the teams on track and to have shared understanding of what samples were being shipped, what testing was being done, and later, how data was being transferred. Additionally, IHMA set up a portal that provided near real-time access to information on samples received and culture results. This allowed the team to identify issues such as missing samples early (versus waiting for a data transfer) while also providing insights into how the study was aligning with key milestones and metrics.

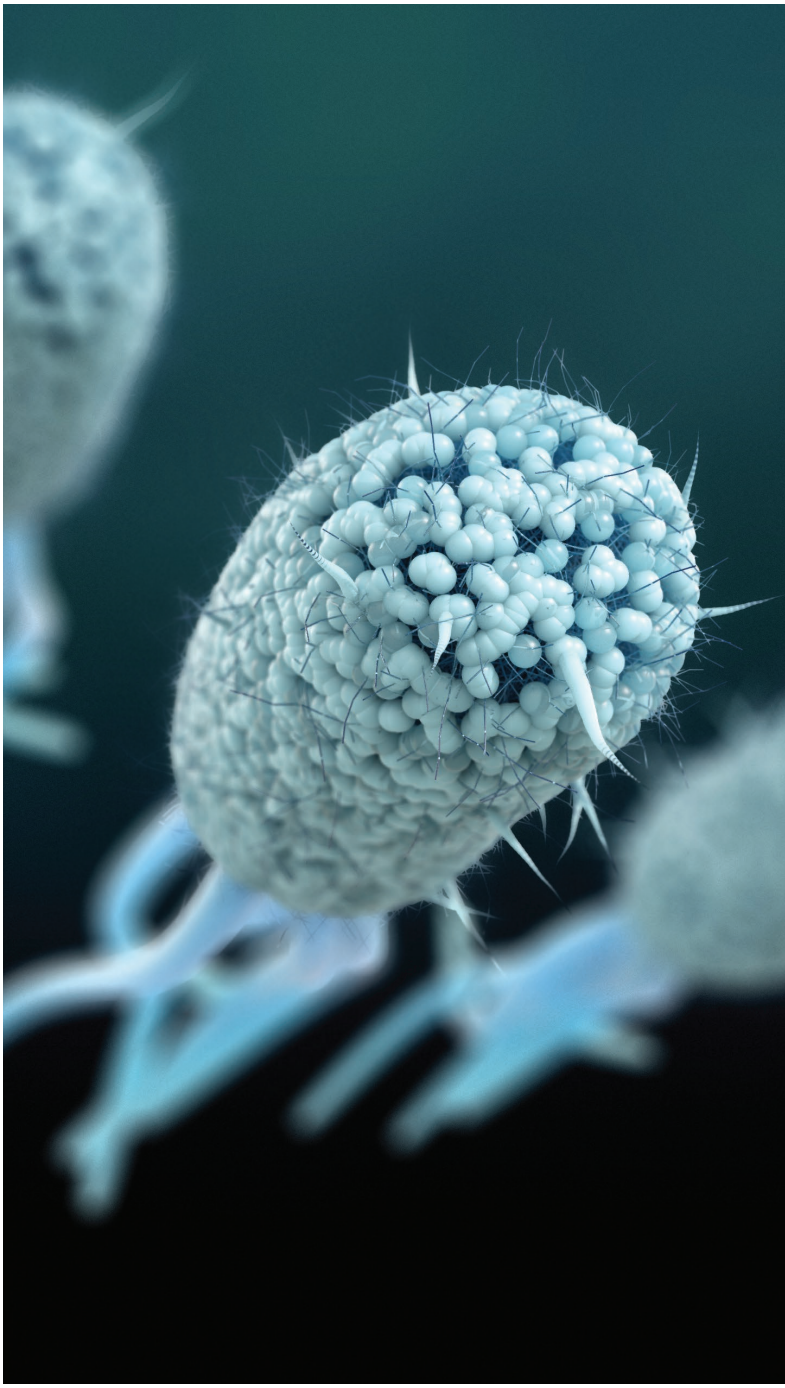
Site-Centricity and Logistics: The team approached the study with the site staff in mind, understanding that there was potential for confusion and errors. The goal was to "get it right the first time" which meant ensuring communication and documentation was clear and easily understood. With samples being shipped to multiple labs, requisition forms were revised with clear instructions to ensure there was no question as to which sample should be shipped to which lab. This enhancement will also increase efficiency in the upcoming Phase Ib where the number of samples will grow substantially. Additionally, lab manuals for Medpace and IHMA were combined so that sites didn't have to reference two documents and could easily follow the flow. This proactive planning was highly successful in minimizing shipping errors.

A Watchful Eye to Ensure Quality Data: We assigned a Strategic Operations Team in ID (SOLID) that worked closely with all of the labs and clinical sites to ensure quality and scientific integrity of the diagnostic data. As the laboratory results were a key component to the outcomes for this trial, this additional team support was integral in ensuring quality and reliable data.

The key to our success was experience. When challenges arose, we were able to resolve them quickly through the combined experience of Medpace and our lab partner. More importantly, we were able to foresee potential problems and mitigate them before they even happened.

RESULTS

- Completed enrollment six weeks ahead of target goal.
- Exceeded estimate for the collection of *E. coli* isolates from the collected urine cultures by nearly 10%. This provided the Sponsor with a larger library of clinical isolates to verify that the proposed drug product had good activities to the *E. coli* strains which colonized these patients and were accessible through the study's clinical sites.
- Well-positioned approach for the efficient execution of the Phase Ib study with sites, patients, testing, communications, and processes in place.
- Provided confidence for our Sponsor that Medpace was indeed the right partner for this complex and challenging phage program — Medpace made the complex seamless!



FULL-SERVICE CLINICAL DEVELOPMENT

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