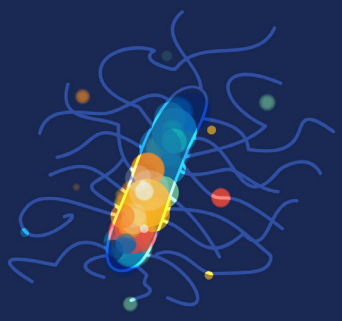
Case Study:

STRATEGIC APPROACHES TO ACHIEVING RAPID SITE START-UP AND FDA APPROVAL IN A PHASE III UTI STUDY



A PIVOTAL PHASE III REGISTRATIONAL TRIAL FOR A NEW CLASS OF ANTIBIOTIC FOR THE TREATMENT OF UNCOMPLICATED URINARY TRACT INFECTIONS (UTI).

>2,000	150	1
SUBJECTS	SITES	COUNTRY

CHALLENGES & SOLUTIONS

RAPID SITE ACTIVATION

Challenge: Original site activation goal was increased by 35 sites with a tight timeframe, requiring rapid site activation.

Solutions:

- Clear expectations regarding start-up timelines defined with site during feasibility and at the time of selection. Internal teams aware of all site-specific timelines.
- CTMs, RSM, and RSCs worked closely together to ensure sites adhered to timelines communicated during feasibility.
- Timing of each site activation tracked and monitored weekly to ensure targets were met.
- Escalations with Sponsor on portions of budget to expediate approval timelines.
- Engaged in selection and start-up with higher number of sites with plan to drop sites not meeting start-up timelines expectations.

RECRUITMENT

Challenge: Enrollment goal increased significantly following interim analysis with short enrollment timelines.

Solutions:

- Increased CTM outreach to sites on enrollment:
  - 2, 4, 8 weeks post-activation
  - No enrollment >30 days from last randomization (monthly)
  - Slow enrolling sites (monthly)
  - Poor enrolling sites (monthly)
- Prepared escalation emails for Sponsor to send after 8 weeks of no activity.
- Medpace and Sponsor collaboration on escalation calls for non-recruiting sites targeting discussion around patient recruitment pathways, next steps, and further escalation plans. Tracked sites adherence to specific plans communicated during escalation calls.
- Sites with high screen-failure rate, implemented pre-screening ICF.
- Increased study awareness by providing sites pins, retractable banners, yard signs, and pre-screener/digital ad campaign based on site preference.
- Site-specific recruitment plans generated to help troubleshoot any site-specific recruitment issues and increase enrollment pathways at the site.
- Supported Sponsor in-person visits to sites.
- Tracked realistic, worst-case, and best-case enrollment scenarios on a weekly basis for Medpace and Sponsor to understand potential outcomes and see how enrollment week-to-week was impacting potential LPFV.

MICRO-MITT POPULATION

Challenges:

- Mid-stream clean-catch urine samples had to be collected, processed, and sent timely and appropriately to the central microbiology lab for culture and confirmation of the baseline uropathogen.
- Subject baseline urine cultures not meeting criteria for the primary analysis population-microbiology modified intent to treat (micro-MITT). The micro-MITT included subjects with an entry urine culture positive for a uropathogen with colony count ≥ 10^5 CFU/mL.

Solutions:

- Monitoring:
    - Real time data review of urine culture data by microbiology specialist to monitor study conduct pertaining to subject meeting criteria for primary analysis population and to identify trends or issues with collection and processing of urine culture samples.
    - Weekly metrics containing total number randomized and percentage of subjects confirmed in the micro-MITT population.
    - Weekly meetings to review overall study and site-by-site trends and issues.
- Mitigation Strategies:
    - Updated protocol.
    - Robust site training on the optimum urine collection and processing techniques in order to decrease the risk of contamination and ensure quality urine culture samples for analysis.
    - Conduct calls with sites to discuss mitigation strategies to increase lower than anticipated mMITT rates and follow implementation of new/improved processes at the site to support micro-MITT rate improvement.

DATA REVIEW

Challenge: High volume of enrollment at the end of the study led to a higher number of data points to review, clean, and verify. Inconsistences noted around PI interpretations related to reporting of clinical outcome.

Solutions:

- CTM assigned subjects/sites to batches based on site last patient last visit (LPLV) and final routine monitoring visit (RMV) for batch cleaning.
- Close communication with Sponsor around query process including timeliness of responded queries allowing for a streamlined data cleaning process.
- Comprehensive data cleaning by entire study team and review including adding edit checks when needed.
- Reviews of PI-reported endpoints supported by retraining of PIs and CRCs on the Clinical Outcomes Assessment.
- Updated CRF Completion Guidelines to include additional guidance for sites.
- Highlighted updates of guidance to sites in eblasts and teleconferences.

SITE AND PATIENT BURDEN

Challenge: Due to the complexity of the study, strategies needed to be implemented to reduce the burden of the site and patient and to ensure compliance.

Solutions:

- Created training videos in-house for site personnel regarding how to train subjects, process samples, and ship samples correctly; and for subjects regarding how to correctly collect a midstream, clean-catch urine sample.
- Created guidance documents (i.e. visual laminate collection guide, shipping/processing checklist) for sites and subjects on how to collect mid-stream, clean-catch urine samples in manner that minimizes the risk contamination and process/shipped correctly to the central lab.

RESULTS

- SURPASSED THE SITE ACTIVATION GOAL BY 35 SITES
- RAPID SITE START-UP WITH STUDY AVERAGE SITE START-UP OF 2.5 MONTHS
- MAINTAINED A <10% SCREEN FAILURE RATE AND <5% DROP RATE
- COMPLETED ENROLLMENT 2 MONTHS AHEAD OF SCHEDULE
- DATABASE LOCK ACHIEVED 2 DAYS AHEAD OF SCHEDULE
- PRIMARY ENDPOINTS MET
- FDA APPROVAL RECEIVED

FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a scientifically-driven, global, full-service clinical contract research organization (CRO) providing Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries. Medpace's mission is to accelerate the global development of safe and effective medical therapeutics through its high-science and disciplined operating approach that leverages local regulatory and deep therapeutic expertise across all major areas including oncology, cardiology, metabolic disease, endocrinology, central nervous system and anti-viral and anti-infective.