CASE STUDY

EMERALD CLINICAL TRIALS

Emerald Clinical Provides Innovative Solutions to Mitigate Risks, Manage Fragile Biological Samples and Improve Patient Experience

Processes in multicenter study investigating safety and efficacy of combination drugs in patients with locally advanced or metastatic solid tumors amended successfully.

SITUATION

George Clinical was contracted by a small to mid-size biopharmaceutical company to conduct a Phase Ib open-label multicenter study investigating the safety and efficacy of combination drugs in patients with locally advanced or metastatic solid tumors. This trial was conducted over 15 activated sites, with a small patient population designed to be in ongoing expansion. In a trial of this type where peripheral blood mononuclear cells (PBMC) samples are collected from patients, the weight of the trial results depends on the accuracy, precision and reliability of data generated from these samples. The fragile nature of biological samples makes standardization of laboratory procedures an especially important focus, and there are many parameters that can affect data such as the time frame between sampling and processing, and storage/shipping temperature en route to the processing lab.

George Clinical provided a full-service approach to this trial which included the handling of patient samples but also a beginning-to-end support from feasibility and site identification and qualification, to patient concierge services including hotel arrangements, stipends and travel arrangements. This level of hands-on support was crucial in overcoming the many challenges faced.

CHALLENGES & SOLUTIONS

Challenge:
Investigational Product (IP) Management

Initially the control drugs were not provided by the sponsor and required patient insurance to cover their cost. Waiting for authorization from patient insurance delayed randomization and added to screen failure rates. In addition, one of the control drugs in the initial batch had a short expiration date which created the potential of sites using expired drugs or not having adequate usable supplies when needed.

Solution:

The team at George Clinical was quick to realize that IP management would be critical to this study, and having established trust and rapport with the sponsor, was able to recommend that they assume responsibility for providing the control/combination drug. The sponsor agreed with the recommendation, and protocol was amended to clarify the IP management cycle of the control/combination drugs.

Our hands-on service also included initiating a system for sending drugs to sites on an “as-needed” basis instead of in batches as originally planned. This operational change increased site efficiency and ensured that all sites had viable supplies at the appropriate time to make the patient experience as convenient and comfortable as possible.

George Clinical's comprehensive team indentified and proactively addressed issues affecting:

Investigative Product Management & Laboratory Procedures

Handling of Patients' Biological Samples

Protocol Design

Communication Processes Among All Stakeholders

Enrollment & Screen Failures

Patient Experience, Comfort & Safety

With these few incremental changes, patient financial and stress burdens were eased, sites were functioning in an optimum manner, and screen failures were reduced.

Challenge: Lab Management

CT scans were not getting uploaded by sites to a central reader portal in a timely manner and there were laboratory sample management challenges at the sites due to mislabeling and processing issues.

Solution:

In order to address CT scan upload delays, George Clinical's project team quickly implemented processes to enhance communication among all stakeholders. Tracking and reminder systems were created, and our team formed clear and structured Principal Investigator/Clinical Research Coordinator (PI/CRC) meetings to coordinate and motivate all stakeholders.

Since laboratory procedures were essential to the success of the trial and the comfort of the patients, George Clinical's CRAs retrained all site personnel in laboratory sample management and instituted sample management meetings with lab vendors to continuously and consistently review sample tracking, proactively mitigate risks and resolve any issues that arose during the trial.

Challenge: Slow Enrollment

Several issues were responsible for slow enrollment into the trial. Some eligible patients were prevented from enrolling due to key inclusion/exclusion criteria.

Also, standard-of-care changes during the enrollment timeframe necessitated the addition of a protocol amendment and the creation of an additional study arm using a new control/combo drug, which also resulted in a protocol amendment. In addition, as one of the control drugs was highly effective, investigators were hesitant to use the experimental drug in combination for their patients.

Solution:

George Clinical's team took the effort to analyze all issues affecting enrollment and presented support for protocol amendments that were initiated. Each site was thoroughly interviewed to identify specific procedures/issues and these findings led the sponsor to take our recommendation of adding additional sites to the trial.

The sponsor agreed on George's Clinical's adjustments to timelines and expectations as standard-of-care regimens changed that ultimately resulted in major protocol changes and new study arms added. Our team knows that internal engagement can have a direct effect on enrollment and our Project Manager took the opportunity in weekly PI/CRC meetings to include enrollment messages, provide information on enrollment progress, and offer feedback and motivational messages. This weekly open dialogue helped keep everyone invested in the success of the enrollment process.

Challenge: Protocol Design Changes

The trial required significant protocol design changes including addition of new arms and an increase in total number of patients.

Solution:

George Clinical teams always take a proactive approach to trial management and have the flexibility to adapt a trial to the most efficient processes for trial success. In this case, new sites were added and the feasibility questionnaire was revised. Our team also reassessed existing sites to determine their ability to enroll new patients and their continued commitment to the trial. After all sites were

reviewed, our team streamlined the process for maximum effectiveness by identifying sites for specific study arms instead of by their ability to enroll to all arms, since arms were different indications.

Challenge: PBMC Processing

PBMC processing was originally required at the site level rather than shipping whole blood samples to a central lab. This required each site to have special equipment and resources in their labs for the lengthy process.

Solution:

George Clinical knew that management of PBMC samples was critical to all aspects of this trial and implemented comprehensive solutions to meet this challenge. Most importantly, sites needed to understand and feel comfortable with the process. Lab manuals needed to be scientifically accurate and clearly communicate proper procedures, and our team provided a manual to sites during the feasibility phase. Each site was reviewed to identify local lab options for those sites without on-site capabilities.

Our concierge approach to trial management always includes the assurance of clear communication and open dialogue, so ad-hoc meetings were initiated with key site and sponsor personnel to troubleshoot issues and develop workaround options with all stakeholders involved.

Once all sites had been reviewed and processes had been clearly defined and communicated, the George Clinical team then developed workflows with sites and external labs to ensure that all samples were handled and processed to meet strict lab manual requirements. When all stakeholders clearly understood their roles, PBMC samples were better protected during the process, patients were ensured of a better trial experience and trial results were ensured to be the most accurate possible.

RESULTS

Enhanced patient experience and improved trial results.

- The sample management meetings initiated by George Clinical were successful in getting IP management on track and proactively addressing risks before they became issues.
- George Clinical established dosages for combination therapy.
- All 15 sites were initiated successfully.
- Issues with PBMC processing were solved with innovative and collaborative problem solving.
- Timely results from dose escalation supported the sponsor's needs for a larger ongoing global Phase II trial.
- Processes were amended to the most efficient and cost-effective solutions.
- Patient experience was enhanced and trial results improved.